

# The Thin Child

## PHYSIOLOGY

Leanness can only be the result of an imbalance of energy intake, absorption, metabolism and output such that:

$$\text{Absorbed intake} \leq (\text{Output} + \text{Utilization})$$

If intake were greater in childhood, the extra calories would be used first for growth and then for fat deposition.

The commonest cause of thinness is failure of intake either from protein/calorie malnutrition endemic in many nations, or for psychosocial reasons in areas where food excess is usually more of a problem.

Food may be malabsorbed for a variety of reasons, or lost through vomit, stool or urine. Excess utilization may occur from chronic illness in any system and there are a few specific syndromes in which the endocrinologist may play a role.

Leptin levels will be low in the thin individual and this, plus other central factors, usually provides a drive to increase intake if food is made available. For unknown reasons this may not occur in anorexia nervosa and in the child with persistent growth failure secondary to intrauterine growth retardation (IUGR). Leptin also acts as a signal to initiate and maintain puberty, so there will be central hypogonadism. Insulin levels will also be low (except in cases associated with lipodystrophy and insulin resistance) and this acts to increase growth hormone (GH) and insulin-like growth factor (IGF-1) binding as an adaptive response to lack of energy. Hence prolonged calorie deficit is usually accompanied by growth failure and failure to enter or maintain puberty. The basal metabolic rate falls and there is a decreased conversion of thyroxine ( $T_4$ ) to triiodothyronine ( $T_3$ ).

Children normally grow in bursts. Over-frequent weighing will produce periods of zero weight gain, or even brief weight loss, in *normal* children. Therefore, a reasonable time interval should elapse between each measurement, and parental size should always be taken into account. It should also be remembered that 'catch-down growth' may be a normal phenomenon in the first 2 years if there has been an abnormal *in utero* environment producing overgrowth, or in the

situation of a tall mother and a short father. Finally, because of the definition of full-term delivery, cross-sectional standards for weight/length on the charts are based on data obtained from a population of between 37 and 42 weeks' gestation and may account for early centile crossing in some individuals.

There is evidence from many studies that IUGR or poor growth in infancy followed by catch-up growth can lead to the later development of adverse cardiovascular risk factors and insulin resistance (the 'Barker hypothesis'). It is unclear how this statistical effect relates to the management of individuals with pathologies described in this chapter, whereas the short-term effects of malnutrition have an obvious impact on the individual.

## FAILURE OF INTAKE

### MALNUTRITION

Protein-energy malnutrition can be subdivided into marasmus, which is usually seen between 6 and 12 months of age and is characterized by wasting and growth failure (Figs 4.1 & 4.2). If dietary protein is the main deficiency (kwashiorkor), there may be edema, apathy, skin and hair changes, and a swollen abdomen secondary to hepatomegaly (Fig. 4.3). There is a tendency to immunodeficiency (Fig. 4.4); in many countries with a high rate of malnutrition, a large proportion of the childhood population is also HIV positive, worsening the situation.

There may be associated vitamin deficiency states such as rickets (Figs 4.5 & 4.6) and pellagra (Fig. 4.7).

### FAILURE TO THRIVE

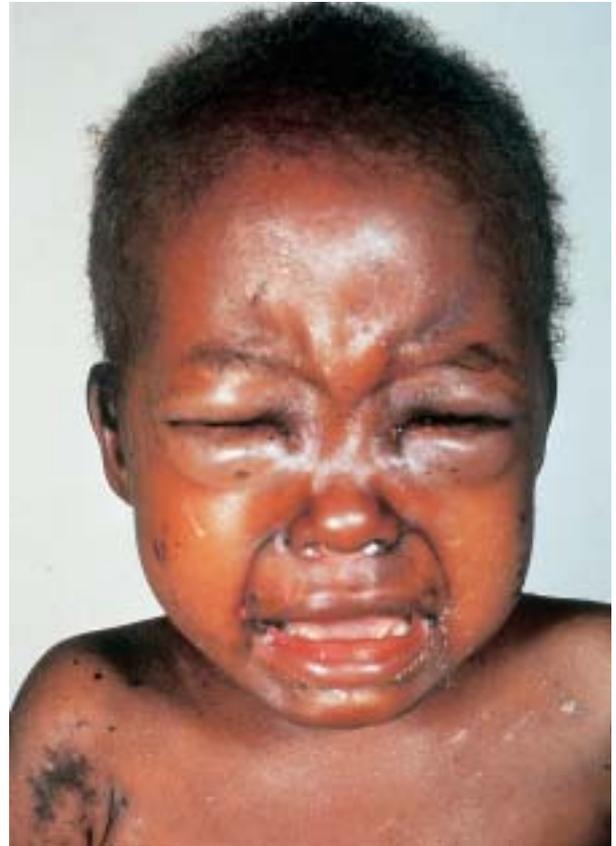
This is a label describing a young child who is not gaining weight at an adequate rate. Inadequacy may be defined by weight-centile channel crossing over a stated period, as long as the reference standard is specified. Charts that allow for normal regression to the mean and variations in weight gain have been produced as conditional standards for weight gain and may be used in population screening. Similarly formulae using regression equations to calculate expected weight gain over a specified period can be derived from population studies and applied locally.



**Fig. 4.1** Marasmus before nutritional rehabilitation.



**Fig. 4.2** Same patient as in Fig. 4.1 after nutritional rehabilitation.



**Fig. 4.3** Kwashiorkor.



**Fig. 4.4** Oral thrush and with angular stomatitis in B<sub>6</sub> riboflavin and niacin deficiency complicating severe malnutrition.

Each of these methods has different sensitivity and specificity at different ages and hence it is important to define the problem locally with appropriate referral guidelines. Parental (or medical) concern about poor weight gain may prompt referral. Intake is modified by psychosocial influences, and so maternal age and

parity, extended family support, income and education should be taken into account. A family history of previous children with failure to thrive, explained or unexplained, especially if associated with consanguinity is important, as are previous infant deaths. Most cases of failure to thrive will be non-organic in nature, and the



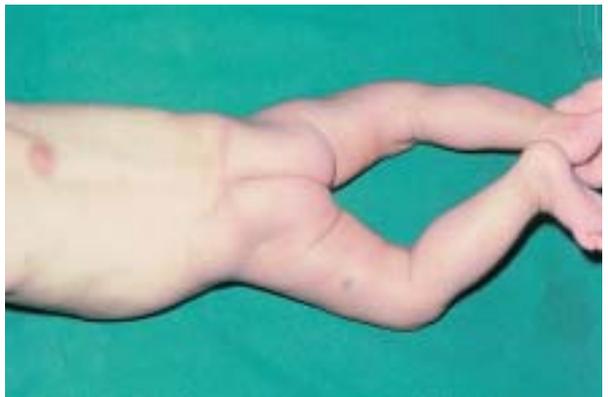
**Fig. 4.5** Nutritional rickets with expansion of the distal forearm epiphyses.



**Fig. 4.7** Pellagra with 'Casal's necklace'.



**Fig. 4.6** Radiograph of severe nutritional rickets.



**Fig. 4.8** Failure to thrive secondary to neglect, with bruise on upper back.

interaction between child and carer should be observed, as well as checking for neglect (**Fig. 4.8**). Cupping marks or scarification may be signs of use of traditional medicine and practices (**Fig. 4.9**). There is a recognized pattern of hyperphagic failure to thrive

with growth failure that may be difficult to distinguish from GH deficiency.

#### ANOREXIA NERVOSA

This condition is commonest in adolescent females and consists of weight loss, amenorrhoea and behavioral



**Fig. 4.9** Cupping marks. Reliance on traditional healing practices may delay referral for investigation and treatment.

changes related to food. Bulimia is a related disorder; sometimes occurring sequentially in the same individual where episodes of hyperphagia are interspersed with unusual means of weight reduction such as induced vomiting and laxative abuse. Luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels are low and estrogen is usually undetectable. Even after recovery there may be a prolonged interval before normal hormone secretion is restored (see Ch. 7). Adaptive hormonal changes, including reduced  $T_3$  levels, also occur. Osteoporosis and later fractures may be a consequence of the prolonged estrogen deficiency.

#### OTHER CAUSES OF FAILED INTAKE

Mechanical problems caused by cleft palate or neuromuscular abnormalities may prevent efficient feeding. If the 'critical window' for establishing enteral intake is missed in the first year, it may be difficult to teach to an older child who may require percutaneous gastrostomy PEG feeding. Breast-feeding failure is usually an early acute problem in some Western cultures, and can be overcome by support and education. Orange juice malnutrition is a specific recognized syndrome caused by the ingestion of large amounts of dilute orange squash; the child is thin with a distended abdomen and sloppy stools. Narcotic withdrawal and the fetal alcohol syndrome may produce early failure of weight gain.

#### FAILED ABSORPTION

Lactose intolerance usually is acquired following gastroenteritis with a loss of lactase in damaged microvilli in the small intestine. Severe congenital alactasia and other rare disaccharide deficiencies (amaltasia, asucrasia) are inherited as single-gene



**Fig. 4.10** Early-onset celiac disease.

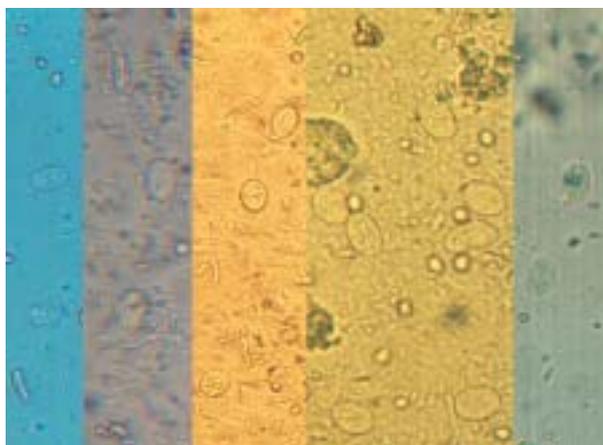
disorders. There are many non-caucasian populations with a high incidence of hypolactasia after infancy, and these individuals can tolerate only small amounts of dairy produce before suffering malabsorption and abdominal discomfort, but rarely fail to gain weight because of the aversive effects of lactose ingestion. However, lactose-containing feeds are inappropriate in famine-relief situations if the condition is common in the population.

Malabsorption may be secondary to the pancreatic exocrine failure seen in cystic fibrosis and the Schwachman–Diamond syndrome of growth failure, steatorrhea, metaphyseal dysplasia and neutropenia.

Celiac disease (Figs 4.10 & 2.38) and cow's milk protein intolerance (CMPI) may produce steatorrhea along with microcytic anemia and villus atrophy. Lymphangiectasia of the small intestine may also produce a protein-losing state.

Giardiasis (Fig. 4.11) and enteropathogenic *Escherichia coli* overgrowth may prevent nutrient absorption, as may the blind-loop syndrome and biliary problems.

Inflammatory bowel disease usually presents with abdominal pain and blood/mucus-containing stools,



**Fig. 4.11** Giardiasis showing birefringent 10- $\mu$ m cysts in stool.

although it may occasionally present with failure to thrive, especially in the infantile form of ulcerative colitis. Failure to grow is a prominent feature of Crohn's disease, especially encompassing the pubertal years (Fig. 2.33), and these individuals are usually very underweight unless cushingoid secondary to treatment.

### CALORIE LOSS

Vomiting from whatever cause will reduce calorie supply if it accounts for a significant portion of intake. It may be a component of abnormal bowel and seen in association with neurodevelopmental abnormalities. Rumination (regurgitation of feeds as a habit comforting behavior in severe developmental delay) can cause significant calorie loss and dental erosion. The aminoacidurias (see below) often have vomiting as a presenting component.

Diarrhea produces intestinal hurry and a degree of malabsorption. Both can be due to numerous pathologies and also be induced factitiously by carers.

### INCREASED UTILIZATION

Chronic infections, especially due to immunodeficiency and HIV, may produce severe wasting (Fig. 4.12). Congenital infections may produce IUGR with subsequent failure to thrive (Fig. 4.13). Overactivity may be secondary to attention deficit disorder or self-induced in athletes and gymnasts, sometimes coupled with anabolic steroid or laxative abuse. Malignancy, severe cardiac disease (especially in conjunction with chronic hypoxia) and liver disease can result in thinness or wasting. Chronic eczema, especially with nocturnal sleep disturbance from itching, can produce profound



**Fig. 4.12** Severe wasting in immunodeficiency.



**Fig. 4.13** Congenital cytomegalovirus infection, subsequent failure to thrive.



**Fig. 4.14** Niemann–Pick disease.

thinness. Renal failure with metabolic acidosis may cause weight loss and there are specific syndromes of renal tubular acidosis that are accompanied by vomiting,



**Fig. 4.15** Menke kinky hair disease.



**Fig. 4.16** Extreme hypotonia in biotinidase deficiency (completely reversed by subsequent biotin treatment).

rickets and growth failure. Bartter syndrome is caused by a failure of chloride reabsorption in the loop of Henle and a compensatory increase in plasma renin activity and hence hyperaldosteronism. It is characterized by hypochloremic alkalosis, hypokalemia, vomiting and failure to thrive. The de Toni–Fanconi syndrome of

aminoaciduria, organic aciduria, glycosuria and hypophosphatemia may be due to cystinosis and heavy metal poisoning. A large number of other metabolic disorders may produce failure to thrive (**Table 4.1**).

Williams syndrome and other causes of hypercalcemia (see Ch. 11) produce weight loss and failure to thrive.

Diagnosis	Biochemistry	Additional effects
Urea cycle disorders	Branched-chain amino acid and organic acidurias	Vomiting, acidotic breathing and apneas, CNS features. Odd smell
Storage disorders	Glycogenoses, Wolman disease, infantile Gaucher and Niemann–Pick disease	CNS features, hepato(spleno)megaly ( <b>Fig. 4.14</b> ). Calcified adrenals in Wolman disease
Galactosemia	Galactose-1-phosphate uridyl transferase deficiency. Positive reducing sugars in urine	Lethargy, vomiting, liver failure, infections. Late cataracts and CNS features.
Hypophosphatasia	Early (recessive) and late (dominant) forms. Abnormality on Ip34-36. Low alkaline phosphatase level	Skin dimpling (see <b>Fig. 1.152</b> ), CNS features, vomiting, fever. Poor bone mineralization
Menke disease	X-linked defect of copper transport	Lethargy, CNS features, abnormal temperature control. Abnormal hair ( <b>Fig. 4.15</b> )
Fructose intolerance	1-Phosphofruktaldolase deficiency	Vomiting, hypoglycemia, hepatomegaly
Biotin metabolic defects	Pyruvate carboxylase or biotinidase deficiency	Alopecia, floppiness ( <b>Fig. 4.16</b> ) rashes, lactic acidosis
Carnitine deficiencies	Fatty acid transport defect	Hypoglycemia, CNS features
Tyrosinemia type I	Fumarylacetoacetate hydrolase deficiency	CNS features, hepatomegaly and liver dysfunction, cabbage smell

**Table 4.1** Some metabolic causes of failure to thrive (list not exhaustive)

Diabetes mellitus (see Ch. 10) produces catabolism due to failure of glucose uptake, as well as increased loss from glycosuria. Rarely, chronic poor regulation of blood sugar in a diabetic child can lead to short stature, wasting and hepatomegaly (the Mauriac syndrome) (Figs 4.17 & 4.18).

### OTHER CAUSES OF EXTREME THINNESS

Russell–Silver syndrome (see Table 2.2) is characterized by IUGR, short stature, dysmorphic features and thinness. Leprechaunism (Donohue syndrome) (Figs 4.19 & 4.20) is characterized by IUGR, elfin facies, micrognathia with full lips, and hirsutism. The female may show clitoral hypertrophy, and both males and females may have sexual precocity. There is often hyperinsulinemia and acanthosis nigricans, and insulin receptor mutations have been described (see Ch. 10).

Partial lipodystrophies produce a muscular appearance and may again be associated with insulin resistance and cirrhosis in the autosomal recessive Berardinelli form (Fig. 4.21) or be acquired after infections when there is an associated abnormality of complement levels.

Progeria (Fig. 4.22), acrogeria and Werner syndromes are characterized by the appearance of early aging and cardiovascular disease with extreme thinness.

Diencephalic syndrome is a rare association of anterior hypothalamic tumors and extreme cachexia, usually presenting in early childhood (Figs 4.23–4.26). There is often hyperkinesia and later there may be associated endocrine abnormalities.

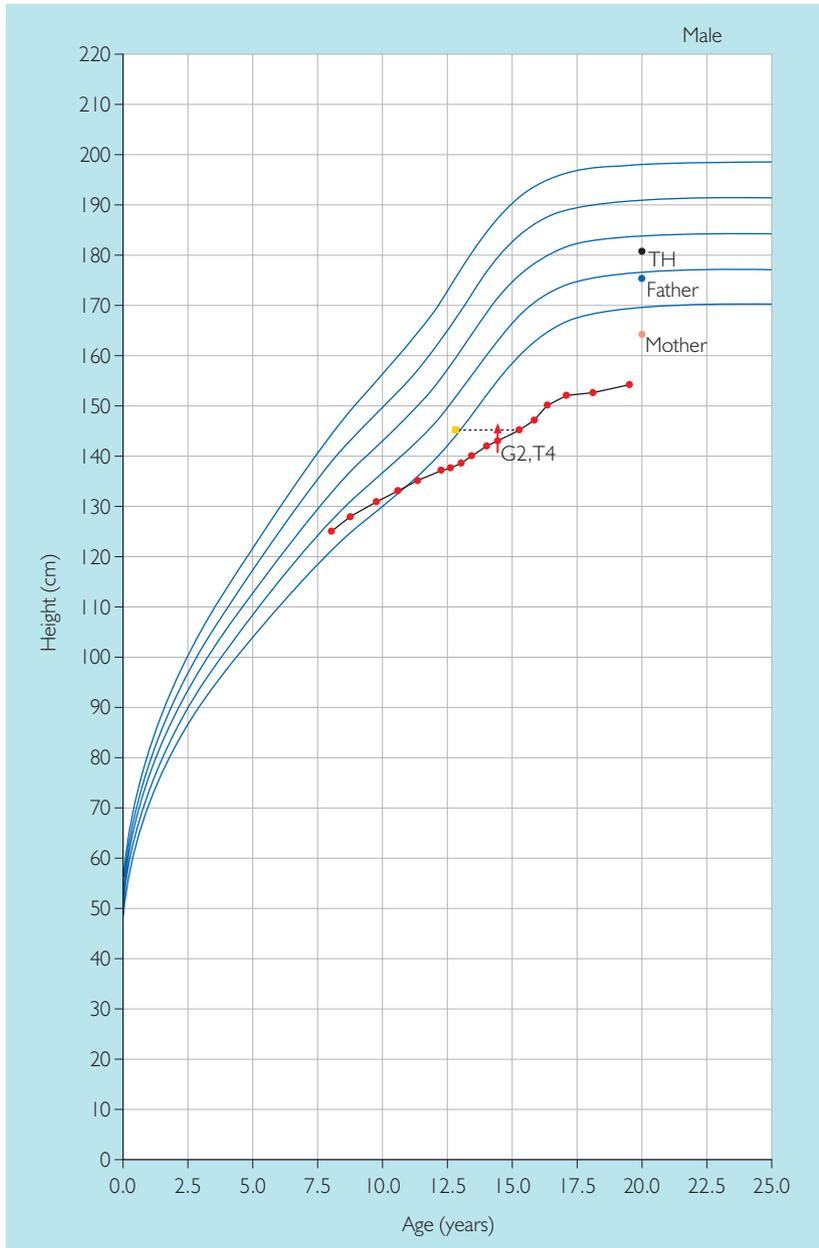
### WORK-UP OF THE THIN CHILD

#### HISTORY AND EXAMINATION

- Most children will have non-organic failure to thrive and be pale, miserable and possibly show signs of overt neglect.
- Abdominal distension is seen in celiac disease and excess orange juice ingestion.
- Pigmentary changes = kwashiorkor.
- Edema and hepatomegaly = kwashiorkor.
- Opportunistic infections = severe malnutrition, diabetes, immunodeficiency.
- Lanugo hair (see Fig. 1.147) = anorexia.
- Excoriated eczema = nocturnal itching, atopy.
- Scratches on roof of mouth = bulimia.
- Dental erosion = bulimia and rumination.
- Weakness, developmental delay = neuromuscular problems, metabolic abnormalities.
- Focal CNS signs, café-au-lait spots = diencephalic syndrome.
- Respiratory signs = cystic fibrosis.
- Anal signs (skin tags and fissures) = inflammatory bowel disease (see Fig. 1.95).
- Anemia = severe nutritional lack, celiac disease and CMPI.
- Smelly wind = malabsorption, giardiasis ('purple burps').
- Abnormal smell = amino and organic acidurias (maple syrup = maple syrup urine disease; mousy = phenylketonuria; dried malt = oast-house urine disease; rancid butter = isovaleric acidemia; cat urine =  $\beta$ -methylcrotonyl coenzyme A carboxylase deficiency; dead fish = trimethylaminuria).
- Extreme thinness = malnutrition in endemic areas or secondary to severe neglect; anorexia, the lipodystrophies and premature aging syndromes.

**Fig. 4.17** Mauriac syndrome showing limb wasting and distended abdomen secondary to hepatomegaly.





**Fig. 4.18** Mauriac syndrome: height SDS  $-4$  with delayed puberty and loss of final height secondary to long-standing poor diabetic control.



**Fig. 4.19** Leprechaunism with severe IUGR.



**Fig. 4.20** Leprechaunism with lack of facial fat and full lips.

**Fig. 4.22**  
Progeria with  
lipoatrophy and  
scloderma-like  
changes of skin.

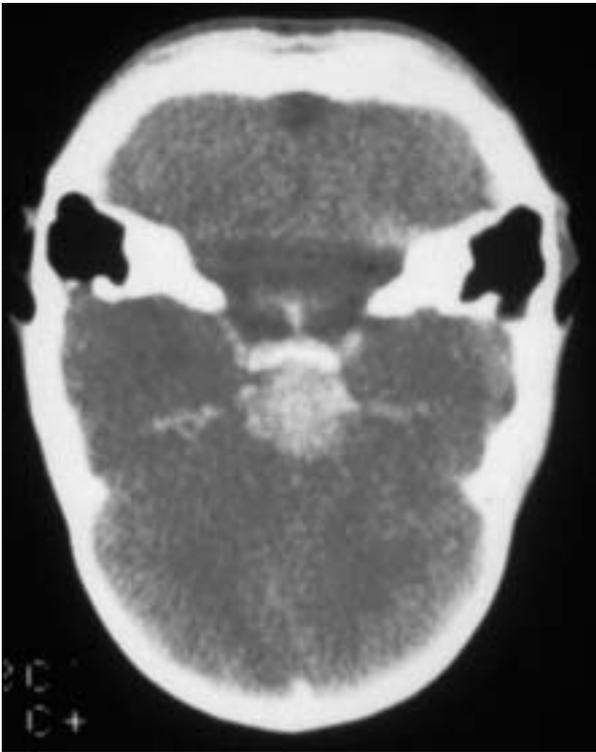


**Fig. 4.21**  
Berardinelli form  
of lipodystrophy.



**Fig. 4.23**  
Diencephalic  
syndrome with  
severe wasting.





**Fig. 4.24** Optic glioma in the patient shown in Fig. 4.23.

## INVESTIGATIONS

### Stool

- Macroscopic inspection for steatorrhea, blood, mucus.
- Microscopy for red blood cells (indicative of celiac disease, CMPI), *Giardia* cysts and fat globules – giardiasis; fat alone in cystic fibrosis and Schwachman syndrome.
- Culture for enteropathogenic *Escherichia coli*.
- Reducing substances are positive in lactose intolerance, alactasia and hypolactasia. Amaltasia and asucrasia also produce an acidic frothy stool positive for reducing substances; sugar chromatography will confirm the diagnosis in these rare cases.
- Stool pH is often reduced in presence of bacterial fermentation of undigested sugars.

### Urine

- Microscopy and culture because unrecognized urinary tract infections and even renal failure from, for instance, posterior urethral valves, can cause failure to thrive (**Fig. 4.27**).
- Reducing substances for diabetes and galactosemia – further biochemical testing is then indicated.

### Simple blood tests

- Full blood count for hemoglobin (Hb) and mean corpuscular volume (MCV) in particular. Microcytic anemia is a non-specific finding that may be secondary to inadequate iron intake or microscopic blood loss, and is present in renal failure and chronic ill health.
- Macrocytic anemia may be secondary to vitamin B<sub>12</sub> or folate malabsorption with steatorrhea.
- Urea, creatinine and electrolytes to exclude hidden renal failure and rare metabolic disorders causing failure to thrive (i.e. Bartter syndrome of hyperchloremic alkalosis).

After these simple screening tests, further investigations may be indicated depending on the results, for instance anti-gliadin or cow's milk antibodies and jejunal biopsy; sweat tests or immunoreactive trypsin and genetic tests for cystic fibrosis. Chromosome analysis is indicated if there are any dysmorphic features (ring chromosome abnormalities have a predisposition to cause failure to thrive, sometimes with relatively mild dysmorphic features). Organic and amino acids and other metabolic tests may be indicated.

Chest radiography and ultrasonography may be indicated to exclude rare non-cyanotic and murmurless cardiac lesions, such as aberrant coronary arteries (**Fig. 4.28**) or fibroelastosis.

Lymphangiectasia of the small intestine may be demonstrated by a small bowel enema. Early cystic fibrosis may be indicated by multifocal consolidation (**Fig. 4.29**). Toxicological examination of blood, vomit, urine and stool should be undertaken if factitious illness induced by the carer is suspected.

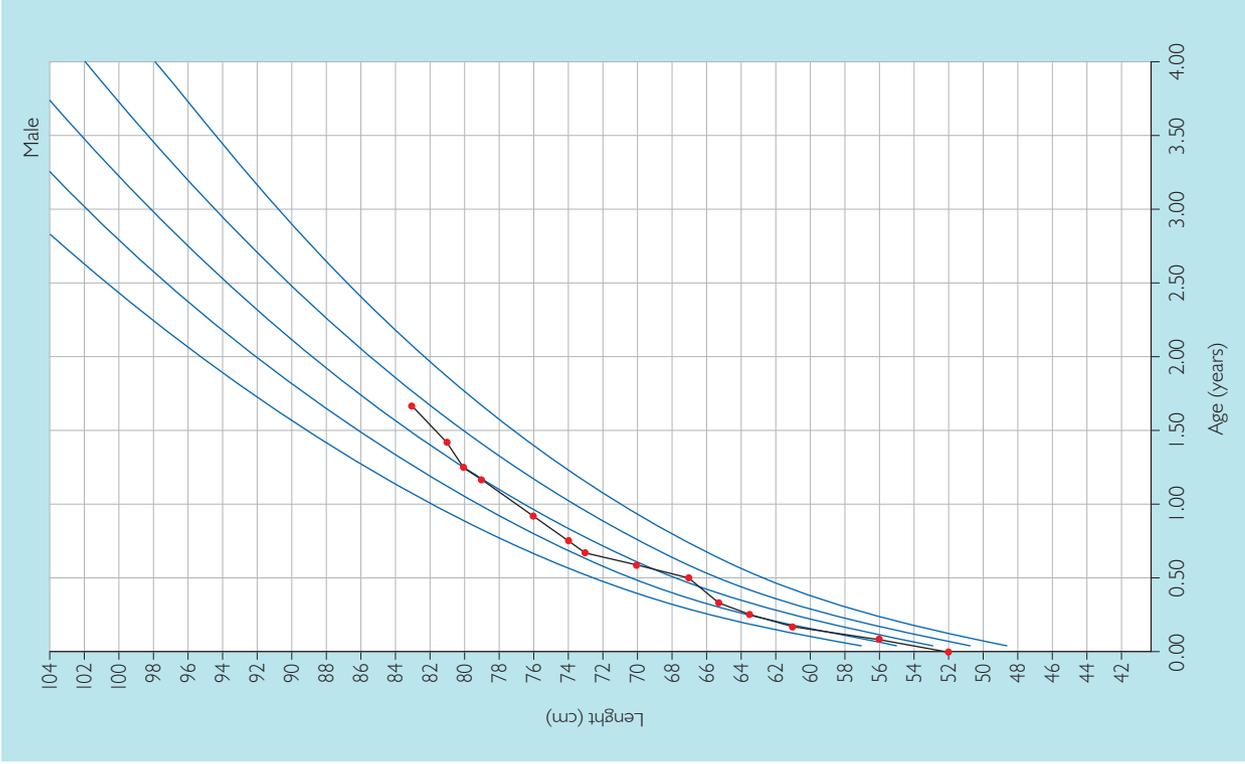
## TREATMENT

### Dietary

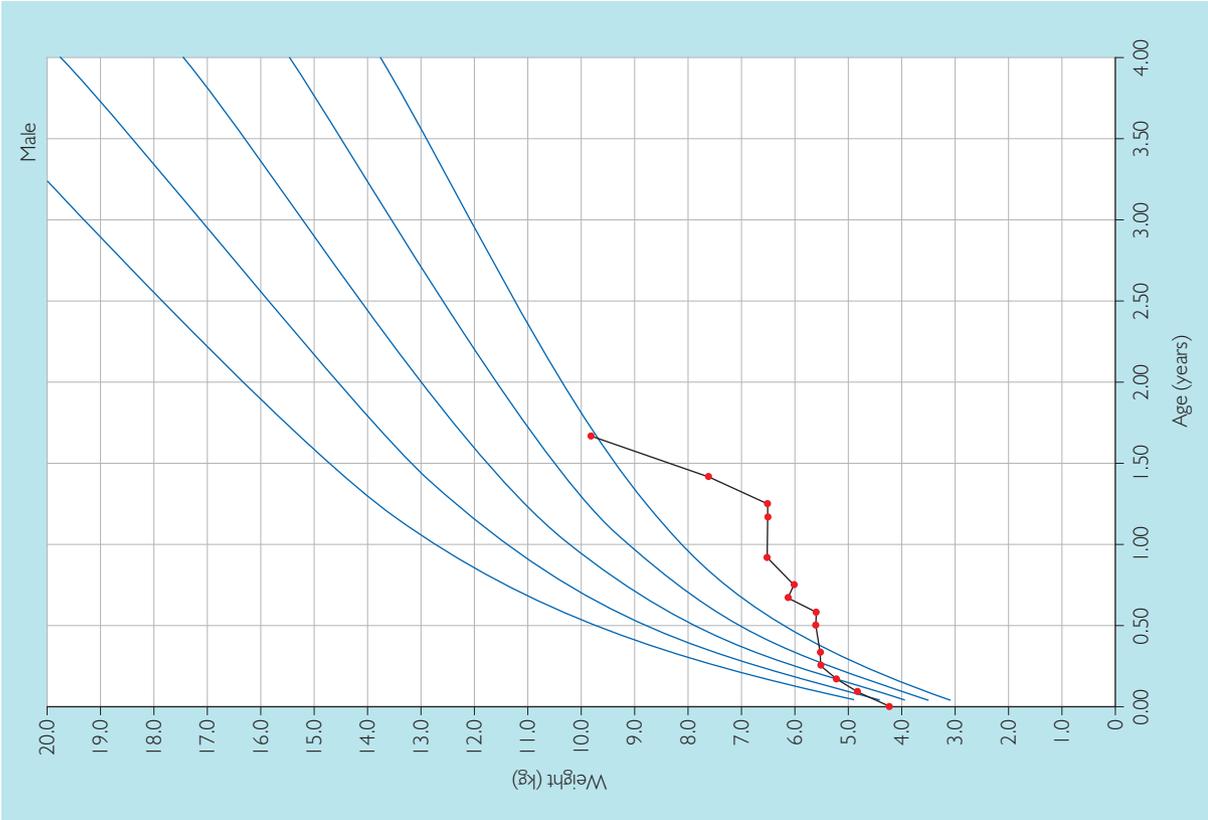
Monitored increased intake at a therapeutic feeding station, along with vitamin supplementation as necessary, is ideal in populations with endemic malnutrition.

To treat non-organic failure to thrive it may be necessary to plan a period of in-patient observation and increasing social worker or medical/health visitor surveillance and support in the community setting. A dietitian can advise on regularizing food intake and cutting back dilute drink consumption.

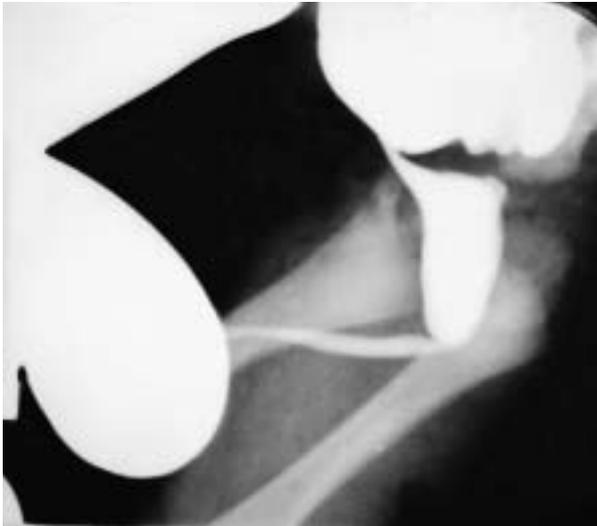
Anorexia requires input from a multidisciplinary team of psychiatrists, nurses and dietitians in a supervised setting, and may necessitate nasogastric or even parenteral nutrition to stabilize body weight.



**Fig. 4.26** Relatively mild height loss (-0.7 SDS) in the patient shown in Fig. 4.23. Dramatic weight gain at 1.5 years following 4 weeks of radiotherapy.



**Fig. 4.25** Growth chart of the patient in Fig. 4.23 with extreme cachexia (weight SDS -4.5).



**Fig. 4.27** Posterior urethral valves in 6-month-old male presenting with failure to thrive. Note distended posterior urethra and coexisting reflux.

### Other

Chronic vomiting may be a component of anatomical abnormalities of bowel anatomy and require surgical correction. It may also be seen in association with neurodevelopmental abnormalities. In these cases simple feed thickening and antireflux measures may suffice, but sometimes pro-kinetic agents are used. PEG feeds are often used for long-term management. Rumination may respond to phenothiazines.

Short-bowel syndrome may result from surgical resection or congenital abnormalities. If the absorptive surface is insufficient to allow normal growth even with dietary supplementation, then chronic intravenous nutrition may be required. There is some experimental evidence that GH may induce bowel lengthening.

Pancreatic exocrine failure can be treated with enzyme supplements with each meal, along with fat-soluble vitamins. Biliary abnormalities may respond to bile salt administration to emulsify feeds.

CMPI and celiac disease are treated by milk- and gluten-free diets respectively (initially there may be additional lactose intolerance in celiac disease until the villi have regrown, requiring a gluten- and milk-free diet), followed by re-biopsy to confirm response. Gluten enteropathy is life-long, but CMPI may remit after dietary intervention. Intestinal lymphangiectasia requires surgical resection as long as sufficient bowel length can be preserved for later successful feeding.

Temporary lactose intolerance requires 3–6 months of lactose-free diet to allow regeneration of the lactase-containing microvilli. Alactasia and the other autosomal



**Fig. 4.28** Aberrant left coronary artery causing silent ischemia and failure to thrive.



**Fig. 4.29** Early cystic fibrosis not detected on neonatal screening; multifocal changes.

recessive disaccharidase deficiencies require specific sugar-free diets life-long.

Poor weight gain secondary to immunodeficiency will improve with anti-retroviral or other immunotherapy, but relapses when infection recurs. There is some evidence that GH may have a useful anabolic role to play in these cases.

The insulin resistance in lipodystrophy is unresponsive to exogenous insulin but may be improved by recombinant leptin and IGF-1 administration.

Treatment of specific metabolic or organ disease may reverse the failure to thrive. In particular in young children with renal tract abnormalities, antibiotic prophylaxis and investigation of the renal tract with surgical intervention, if required, are mandatory.

Bartter syndrome may be treated with a combination of salt supplements, potassium-sparing diuretics and indometacin.