CRACK EVERY CASE.

A Pediatrician's Guide to Common Endocrinology Conditions

Many children/adolescents struggle with one or more of these four common endocrinology issues: abnormal menstrual patterns, abnormal thyroid, short stature and/or pediatric obesity .
To assist with patient diagnosis and referral, the Children's Mercy Endocrinology team created these recommendations.

Winter 2021

Evaluating Abnormal Menstrual Patterns

According to the American College of Obstetricians and Gynecologists, a number of medical conditions can cause abnormal uterine bleeding, characterized by unpredictable timing and a variable amount of flow. Although a long interval between cycles is common in adolescence for the first 2 years after menarche, it is uncommon for girls and adolescents to remain amenorrheic for more than 3 months or 90 days (the 95th percentile for cycle length). Girls and adolescents with more than 3 months between periods or those that remain otherwise irregular 2 years after menarche, should be evaluated for underlying causes.

1. Perform History and Clinical Evaluation

Family History:

- Ask about irregular menstrual patterns
- Thyroid conditions
- PCOS
- Diabetes

Personal History:

- Changes in weight
- Change in eating/exercise patterns
- Change in medications
- Pregnancy risk
- History of polyuria/polydipsia
- Changes in vison
- Headaches

Physical Exam:

- Look for or make note of male pattern hair growth (upper lip, chin, chest, lower abdomen and upper back) (see sidebars on PCOS and hirsutism)
- Prominent acne
- Signs of autoimmune disease (vitiligo)
- Signs of insulin resistance (acanthosis)
- Violaceous stretch marks

2. Initial Laboratory Evaluation:

- Rule out pregnancy
- TSH
- Total and free testosterone
- Prolactin
- LH, FSH

Further Potential Laboratory Evaluation (can be done in Endocrine Clinic):

- Hba1c
- DHEAS, androstenedione, 17-hydroxyprogesterone

3. When should patients be referred to Children's Mercy Endocrinology?

- If menstrual cycles are abnormal and there is physician or NP/PA concern for an endocrine condition. No prior labs required.
- If any of the above hormonal labs are out of range, a referral for that specific concern can be made (unless the patient tests positive for pregnancy).
- If there is concern for PCOS, refer directly to the Multispecialty Adolescent PCOS Program (MAPP).

PCOS

What is PCOS?

PCOS is a hormonal condition that affects 6-15% of women of reproductive age. PCOS develops in genetically predisposed females where the severity of clinical expression is compounded by environmental, nutritional and lifestyle factors. The genetic predisposition mainly affects ovarian function manifesting in a tendency toward ovulation dysregulation and hormonal imbalance which favors androgen production. Short- and long-term consequences of menstrual dysfunction and hormonal imbalance may include hirsutism and severe acne, depression and anxiety, insulin resistance, weight gain and diabetes, non-alcoholic fatty liver disease, heart disease, endometrial cancer, infertility and miscarriages.

When should patients with possible PCOS be referred?

Strongly consider a diagnosis of PCOS if there is menstrual irregularity coupled with biochemical or clinical hyperandrogenism (hirsutism/severe acne).

- Screening total testosterone > 40 ng/dL
- Hirsutism (hair on upper lip, chin, chest, lower abdomen, or upper back)
  - ◊ May use modified Ferriman-Gallwey Score (see chart)
- Menstrual irregularity as defined here

The MAPP clinic offers same-day diagnostic services for those with presumed PCOS such as ultrasound and oral glucose tolerance test. The clinic also offers professional nutritional counseling. Should the adolescent also have questions and concerns regarding psychological or reproductive health issues, Adolescent Medicine specialists are present for confidential discussion.

Referral Instructions

Refer concerns regarding abnormal menstrual cycles, suspicion of PCOS or hirsutism, to pediatric endocrinology for further evaluation.
At Children's Mercy, patients have access to an established, experienced team of more than 20 pediatric endocrinologists and nearly 100 staff members who specialize in endocrine disorders. Our Multispecialty Adolescent PCOS Program helps girls and teens manage the symptoms of PCOS, including irregular menstrual cycles and elevated levels of androgens in the female body.

To make a referral:

- Visit childrensmercy.org.
- Select "Health Care Providers" in the top navigation bar.
- Select "Refer a Patient."
- Select "Endocrine" from the list of specialties and "PCOS" under "Reasons for Consultation."
- Complete the remaining fields on the referral form and submit.

All new referral requests are processed within 48 hours. Two phone attempts to contact the family and a final notification to the family to schedule will be made. For assistance, call the Contact Center at (816) 234-3700 or toll-free at (800) 800-7300. The Contact Center can provide additional information regarding any supporting documentation needed for the referral.

For urgent requests to speak to a specialist, please call and ask to speak with the on-call pediatric subspecialist at 1 (800) GO-MERCY / (800) 466-3729.

Additional Resources

1. Witchel SF, Oberfield S, Rosenfield RL, et al. The Diagnosis of Polycystic Ovary Syndrome during Adolescence [published online ahead of print, 2015 Apr 1]. Horm Res Paediatr. 2015;doi:10.1159/000375530.
2. Teede HJ, Misso ML, Costello MF, et al. Recommendations from the International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. Fertil Steril. 2018;110(3):364-379. doi:10.1016/j.fertnstert.2018.05.004.
3. Escobar-Morreale HF, Carmina E, Dewailly D, et al. Epidemiology, Diagnosis and Management of Hirsutism: A Consensus Statement by the Androgen Excess and Polycystic Ovary Syndrome Society [published correction appears in Hum Reprod Update. 2013 Mar-Apr;19(2):207]. Hum Reprod Update. 2012;18(2):146-170. doi:10.1093/humupd/dmr042.

Excess Body Hair

What is on the differential for excess body hair?

- Hypertrichosis
  - ◊ Medication-induced side effect
  - ◊ Idiopathic/genetic
- Hirsutism related to hyperandrogenemia
  - ◊ PCOS
  - ◊ CAH
  - ◊ Androgen-secreting tumors
- Idiopathic hirsutism

What is hypertrichosis?

Hypertrichosis is excessive hair growth above normal for age, sex and race and can be seen on all areas of the body, not only androgen-dependent regions. Contrary to hirsutism, the hair in hypertrichosis is less coarse.

What is hirsutism?

Hirsutism is excessive terminal hair (longer, pigmented, coarse) in androgen-dependent areas of the female body. This includes areas such as the upper lip, chin, chest, lower abdomen and upper back. A detailed method for determining degrees of hirsutism is the modified Ferriman-Gallwey score (mFGS). A score of 4-6 suggests hirsutism.

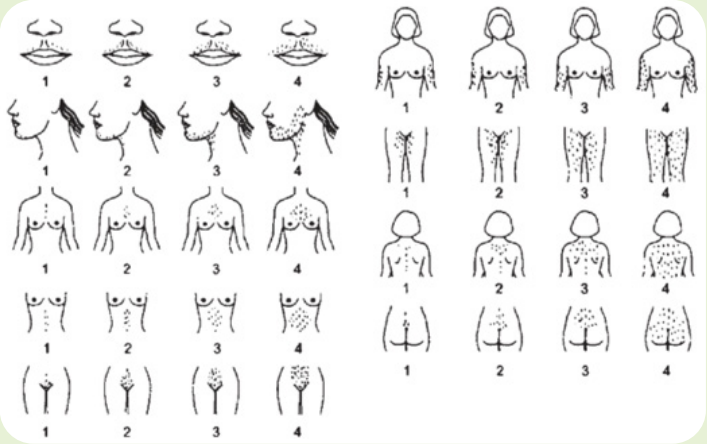


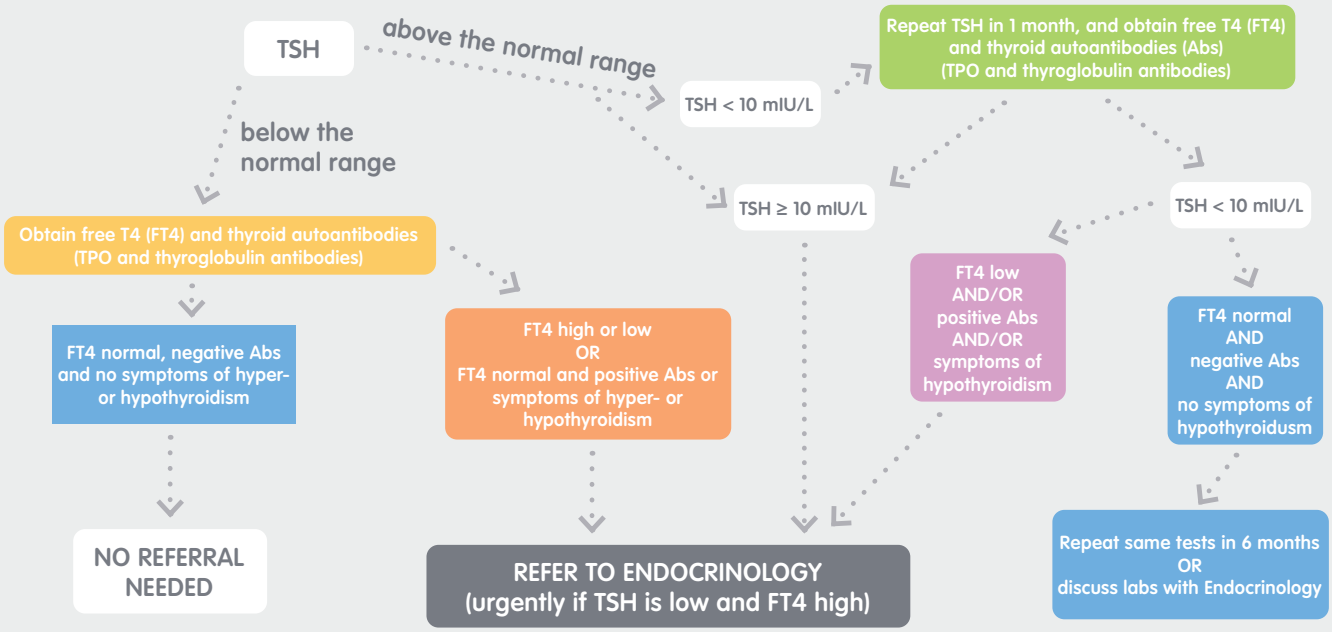
Figure 1: Schematic representation of the mFG score. Nine body areas (upper lip, chin, chest, arm, upper abdomen, lower abdomen, upper back, lower back and thighs) are scored from 1 (minimal terminal hairs present) to 4 (equivalent to a hairy man). If no terminal hairs are observed in the body area being examined the score is zero (left blank). Clinically, terminal hairs can be distinguished from vellus hairs primarily by their length (i.e. >0.5 cm) and the fact that they are usually pigmented. Reproduced with permission from R. Azziz (Yildiz *et al.*, 2010). Copyright Oxford University Press, 2010.

When should patients with hirsutism be referred?

Refer to pediatric endocrinology if there is a physical exam concerning for hirsutism (hair on upper lip, chin, chest, lower abdomen or upper back). Modified FGS score is not needed for referral.

Evaluating Abnormal Thyroid

When to Refer a Child with an Abnormal TSH



When should thyroid function tests be ordered?

Between 25-50% of the referrals to a pediatric endocrinology clinic are related to abnormal thyroid function tests (TFTs). The majority of these abnormal TFTs are not associated with a true thyroid problem, especially when these tests are ordered in the absence of any signs or symptoms suggestive of a thyroid disease.

We recommend TFTs be ordered in any of these situations:

- Any child with an enlarged thyroid (goiter) on physical examination
- Signs or symptoms of hypothyroidism:
  - ◊ New onset or worsened fatigue
  - ◊ Declining statural growth rate
  - ◊ Constipation, dry skin, cold intolerance
  - ◊ Declining school performance
  - ◊ Menstrual abnormalities
- Signs or symptoms of hyperthyroidism:
  - ◊ Unexplained weight loss
  - ◊ Hyperactivity, emotionality, depression-like behavior
  - ◊ Palpitations, tachycardia
  - ◊ Heat intolerance
  - ◊ Declining school performance
  - ◊ Menstrual abnormalities

Many of the symptoms of hypothyroidism are non-specific. However, the likelihood to be secondary to a thyroid disease increases in the presence of the following risk factors:

- Down or Turner syndrome
- Previous diagnosis of an autoimmune disorder, such as type 1 diabetes or celiac disease
- History of a thyroid disease in first-degree relatives
- Drugs, like lithium and amiodarone
- Head and neck radiation

Which TFTs should be ordered?

TSH is the single most sensitive test used to diagnose primary hypothyroidism (high TSH) or hyperthyroidism (low TSH). In these situations, free T4 (FT4) is low or high respectively; when this occurs, the diagnosis of an overt thyroid illness is very likely, and the child will need to be referred to a pediatric endocrinologist.

- It is important to evaluate TSH levels in the context of age, since TSH normal ranges are higher in infancy when compared to older children.
- A TSH measurement alone is not accurate in diagnosing central hypothyroidism, since TSH may be normal or low-normal while FT4 is typically below the normal range.
- Measuring FT4 without TSH may lead to an incorrect diagnosis of a thyroid disease. For example, a non-thyroidal illness, the use of drugs like valproate, carbamazepine and phenobarbital, or the inaccuracy of some free T4 immunoassays, can result in an under-estimation of FT4.

Thus, in case there is a suspicion of a thyroid disease, obtain both TSH and FT4.

What should be done if the TSH is abnormal?

High TSH

A high serum level of TSH is not an uncommon finding. Studies in large pediatric populations have identified ~4% of children with high TSH.

TSH levels above 10 mIU/L are typically associated with positive thyroid autoantibodies and/or low FT4. Thus, they need to be referred to a pediatric endocrinologist.

However, TSH values are often only slightly above the age-appropriate range (<10 mIU/L) and are typically found in asymptomatic children with normal FT4 ("subclinical hypothyroidism"). Evidence indicates that children with subclinical hypothyroidism experience none of the typical features of overt hypothyroidism. In addition, treating children with subclinical hypothyroidism has shown no benefit.

- Once a slightly high TSH is repeated, more than 70% of the time it is found to be normal.
- If repeat TFTs confirm a slightly high TSH, normal FT4, and negative thyroid autoantibodies, it is appropriate to repeat them one more time in ~6 months, or review them with a pediatric endocrinologist.
- An exception to this guideline is a slightly elevated TSH in an infant younger than 1 year of age. Given the child's higher risk to progress to overt hypothyroidism, we recommend referral to a pediatric endocrinologist before repeating the TFTs.

An isolated mild increase of TSH (associated with normal FT4), is a relatively common finding in overweight or obese children (7% to 23% in two studies). However, it seems to represent an adaptive response to obesity rather than a cause of it. Indeed, TSH usually normalizes after weight loss. The recently published Endocrine Society Clinical Practice Guidelines discourage from obtaining screening TFTs in children with obesity, unless excessive weight gain is associated with declining statural growth.

Low TSH

A low TSH is more rarely detected than a high TSH. It is typically found in children with overt hyperthyroidism when it is usually very low (< 0.01 mIU/L) and associated with high FT4 and/or total T3.

A slightly low TSH, along with a normal FT4 ("subclinical hyperthyroidism") is much less common in children than in adults. Prospective studies have shown that only ~1% of patients with subclinical hyperthyroidism progress to overt hyperthyroidism in a 5-year period, with the rest of them having a normalized or persistently slightly low TSH on repeat testing.

Thus, in an asymptomatic child with a slightly low TSH, normal FT4 and negative thyroid autoantibodies, there is no indication for a referral to a pediatric endocrinologist.

Biotin supplementation is known to cause falsely low TSH by interfering with biotin-based TSH immunoassays. Less often, it can cause falsely high free T4. Biotin is often used to promote healthy hair and nails, and in a number of metabolic disorders. If a child is taking high doses of biotin (>100 mg/day), this supplement should be discontinued at least 2 days before obtaining TSH and free T4.

Referral Instructions

Refer concerns regarding abnormal TSH or thyroid disease to pediatric endocrinology for further evaluation.

At Children's Mercy, patients have access to an established, experienced team of more than 20 pediatric endocrinologists and nearly 100 staff members who specialize in endocrine disorders.

To make a referral:

- Visit childrensmercy.org.
- Select "Health Care Providers" in the top navigation bar.
- Select "Refer a Patient."
- Select "Endocrine" from the list of specialties and "Hyperthyroidism" or "Hypothyroidism" under "Reasons for Consultation."
- Complete the remaining fields on the referral form and submit.

All new referral requests are processed within 48 hours. Two phone attempts to contact the family and a final notification to the family to schedule will be made. For assistance, call the Contact Center at (816) 234-3700 or toll-free at (800) 800-7300. The Contact Center can provide additional information regarding any supporting documentation needed for the referral.

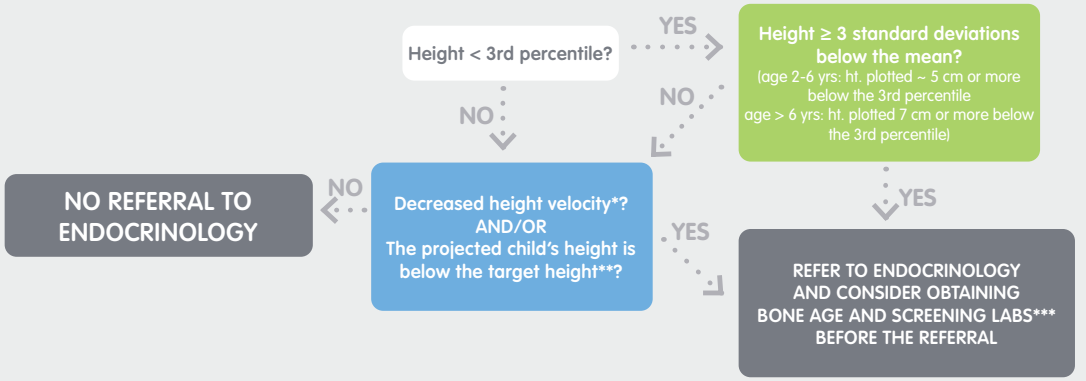
For urgent requests to speak to a specialist, please call and ask to speak with the on-call pediatric subspecialist at 1 (800) GO-MERCY / (800) 466-3729.

Additional Resources

1. Lazar L, Ben-David Frumkin R, Battat E, et al. Natural History of Thyroid Function Tests Over 5 Years in a Large Pediatric Cohort. J Clin Endocrinol Metabol. 2009; 94: 1678-1682.
2. Schushan I, Lazar L, Amitai N, Meyerovitch J. Thyroid Function in Healthy Infants During the First Year of Life. J Pediatr. 2016; 170: 120-125.
3. Gammons S, Presley BK, White PC. Referrals for Elevated Thyroid Stimulating Hormone to Pediatric Endocrinologists. J Endocr Soc. 2019; 3: 2032-2040.
4. Wasniewska M, Aversa T, Salerno M, et al. Five-year Prospective Evaluation of Thyroid Function in Girls with Subclinical Mild Hypothyroidism of Different Etiology. Eur J Endocrinol. 2015; 173: 801-808.
5. Vigone MC, Capalbo D, Weber G, et al. Mild Hypothyroidism in Childhood: Who, When, and How Should be Treated? J Endocr Soc. 2017; 2: 1024-1039.
6. Vadiveloo T, Donnan P, Cochrane L, et al. The Thyroid Epidemiology, Audit, and Research Study (TEARS): The Natural History of Endogenous Subclinical Hyperthyroidism. J Clin Endocrinol Metabol. 2011; 96 (5):1344-51.

Evaluating Growth Failure

When to Refer a Child for Suspected Growth Failure (≥ 2yr old)



* Decreased height velocity (HV):
- Age 2-4 yrs - HV less than 5.5 cm/year
- Age 4-6 yrs - HV less than 5 cm/year
- Age 6 yrs to puberty:
  - ◊ HV less than 4 cm/year for boys
  - ◊ HV less than 4.5 cm/year for girls

** Projected child's height: it is determined by extrapolating the child's current height percentile up to the 18-20 yr mark on the growth chart.

Target height: the range included within 8.5 cm above and below the mid-parental height.

*** Screening labs:
- CBC, Basic Metabolic Panel, ESR or CRP
- Urinalysis
- Celiac panel
- FT4, TSH, IGF-1, IGFBP3

Who should be referred to the endocrinologist for further evaluation of suspected growth failure?

The decision to refer a child with short stature usually depends on the answers given to these three questions:

- How short is the child?
- Is the child's height velocity (HV) impaired?
- Is the child's height/growth within the range for the family?

How short is the child?

1. If the child's height is above – 2 SD (above the 3rd percentile), he has a normal stature. Thus, he generally does not require further evaluation, unless his statural growth curve crosses height percentiles downward, the child has dysmorphic features, or evidence of underlying systemic disease, or if the child's height percentile is well below the target height.
2. If the child's height is below -2SD (below the 3rd percentile), he has short stature. If his height is above -3SD (within 5 to 7 cm below the 3rd percentile), an initial evaluation of the child's height velocity (see below) should be performed in the primary care setting. **A referral to the endocrinologist is appropriate if the height velocity is slow for age and gender.**
3. If the child's height is below – 3SD (it is plotted ~5 cm or more below the 3rd percentile between age 2 to 6 years, and ~7 cm or more below the 3rd percentile beyond age 6), the child has severe short stature. **Since there is a high likelihood of a pathologic cause of short stature, the child should be referred to the endocrinologist.**

Is the child's height velocity impaired?

Determination of the child's height velocity requires repeated measurements of the height, which should be measured with an interval of at least 6 months between measurements.

For children 2 years and older, growth failure is likely if the child is growing more slowly than the following rates:

- Age 2-4 years – HV less than 5.5 cm/year (<2.2 inches/year)
- Age 4-6 years – HV less than 5 cm/year (<2 inches/year)
- Age 6 years to puberty:
  - ◊ HV less than 4 cm/year for boys (<1.6 inches/year)
  - ◊ HV less than 4.5 cm/year for girls (<1.8 inches/year)

Is the child's height/growth within the range for the family?

The next step is to determine the height range expected for that child, based on the biologic family's height (child's genetic height potential) and compare it with the child's current growth trajectory.

An estimate of a child's genetic height potential can be obtained by calculation of the mid-parental height, which is based upon the heights of both parents and adjusted for the sex of the child (see formula). For both girls and boys, the range included within 8.5 cm above and below the mid-parental height represents what is called target height (3rd to 97th percentiles for anticipated adult height).

The projected height for a child is determined by extrapolating the child's current height curve/channel up to the 18- to 20-year mark on the growth chart. If the child's projected height is within the target height, then the child's height is within the expected range for the family. This child probably has familial short stature, which is considered a variant of normal growth, and thus he does not need to be referred to a specialist (unless his mid-parental height is significantly below the normal range).

If the child's projected height is below the target height, then the child can be considered abnormally short for his or her family, and thus may need to be referred for further evaluation.

Is an initial diagnostic evaluation in the primary care setting needed?

Once the primary care physician has decided to refer the child to an endocrinologist for suspected growth failure, the primary care physician may want to consider obtaining an initial diagnostic work-up.

Bone Age Determination

Bone age is typically determined from a radiograph of the left hand. The method most commonly used to determine the bone age is based on using the Greulich and Pyle Atlas. The bone age determination informs estimates of the child's growth potential and likely adult height.

A delayed bone age does not necessarily imply growth failure: it can be consistent with constitutional delay of growth and puberty (CDGP), which is considered a normal variant of growth. However, significantly delayed bone age is also seen in many types of growth failure, including nutritional deficiency, underlying systemic disease (such as inflammatory bowel disease), growth hormone deficiency and hypothyroidism.

A normal bone age is consistent with several diagnostic possibilities. In a child with short parents, a normal bone age supports the diagnosis of familial short stature. However, a normal bone age may also be seen in girls with Turner syndrome.

Laboratory Studies

Screening laboratory tests may be considered by the primary care physician in case of impaired growth velocity (see above) and if the history or physical examination raise suspicion for an underlying pathology.

Useful Screening Tests:

- Complete blood count (CBC) and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
- Electrolytes, creatinine, bicarbonate, calcium, phosphate, alkaline phosphatase, albumin
- Celiac serologies (e.g., tissue transglutaminase [tTG] immunoglobulin A [IgA] and total IgA)
- Free T4, TSH, IGF-1, IGFBP3

Suspicious Findings in the History:

- Systemic symptoms such as sluggishness, lethargy, cold intolerance, constipation
- Gastrointestinal symptoms, including decreased appetite, abdominal pain, diarrhea, and rectal bleeding
- Pulmonary symptoms, including severe asthma, recurrent infections
- Recurrent infections
- Arthralgia or arthritis
- Medications – Prolonged or frequent use of glucocorticoids (including inhaled glucocorticoids) or use of stimulants for attention deficit hyperactivity disorder.

Suspicious Findings of the Physical Examination:

- Weight loss, poor weight gain, underweight for height, and delayed puberty
- Developmental delay/learning disabilities
- Facial dysmorphisms
  - ◊ Hypertelorism, downward eye slant, low-set ears
  - ◊ Prominent forehead, Midface hypoplasia, frontal bossing, triangular face, downturned corners of the mouth
- Midline defects
- Webbed neck

The Difference Between Short Stature and Growth Failure

By definition, ~2% of the pediatric population is short; however, the majority of these children do not have growth failure. Short stature is defined as a length or height below the 2.3rd percentile for age and gender (for approximation, we often used the 3rd percentile, since the 2.3rd percentile is not included in the most-used growth charts). Often, but not always, short stature and growth failure coexist in the same child. An exception may be a child who may have a normal variant of growth, such as familial short stature and/or constitutional growth delay.

On the other hand, a child may have growth failure without short stature (for example, height percentile for age falling from 90th percentile to 50th percentile after age 3). Evidence indicates that a child with short stature without suspicious signs and/or symptoms of an underlying pathology (abnormal findings on history, review of systems, or physical exam), and with a normal growth velocity very rarely has growth failure (only ~2 % of the times). The likelihood of experiencing growth failure is higher in children with more severe short stature (e.g., whose height is significantly below the 3rd percentile) and/or reduced growth velocity.

Referral Instructions

Refer concerns regarding abnormal growth failure or short stature to pediatric endocrinology for further evaluation.

At Children's Mercy, patients have access to an established, experienced team of more than 20 pediatric endocrinologists and nearly 100 staff members who specialize in endocrine disorders.

To make a referral:

- Visit childrensmercy.org.
- Select "Health Care Providers" in the top navigation bar.
- Select "Refer a Patient."
- Select "Endocrine" from the list of specialties and "FTT/Short stature/ Growth Failure" under "Reasons for Consultation."
- Complete the remaining fields on the referral form and submit.

All new referral requests are processed within 48 hours. Two phone attempts to contact the family and a final notification to the family to schedule will be made. For assistance, call the Contact Center at (816) 234-3700 or toll-free at (800) 800-7300. The Contact Center can provide additional information regarding any supporting documentation needed for the referral.

For urgent requests to speak to a specialist, please call and ask to speak with the on-call pediatric subspecialist at 1 (800) GO-MERCY / (800) 466-3729.

Calculating Mid-parental Height

Children usually reach an adult height that is within 2 standard deviations (~8.5 cm) above and below their mid-parental height. This estimated range is known as the "target height."

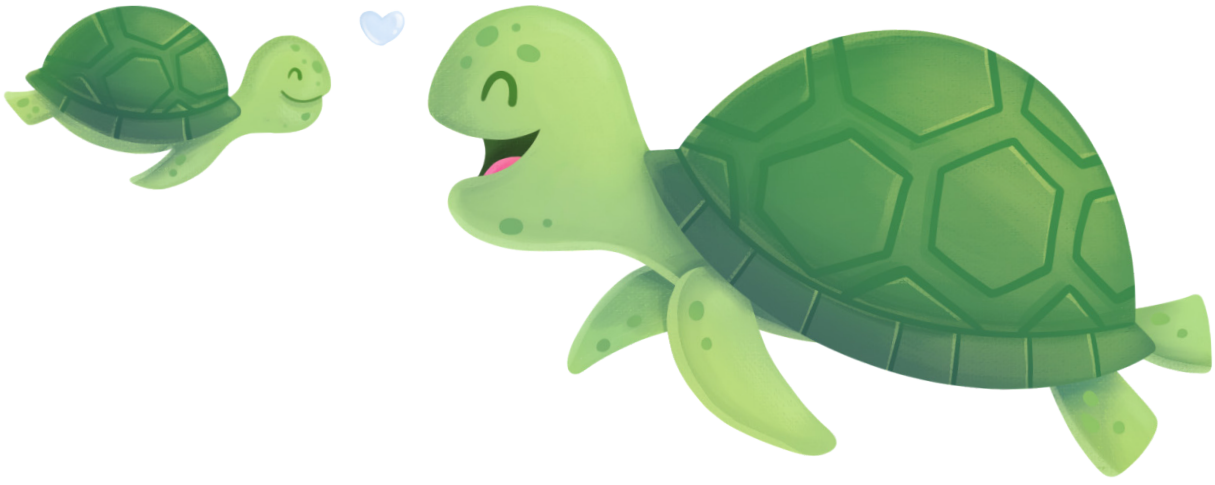
The mid-parental height is based on the heights of both parents and adjusted for the sex of the child:

- Girls: 13 cm (or 5 inches) is subtracted from the father's height and averaged with the mother's height.
- Boys: 13 cm (or 5 inches) is added to the mother's height and averaged with the father's height.

Nutritional deficits, organic diseases, or endocrine disorders may prevent a child from attaining the expected adult height.

Additional Resources

1. Sisley S, Vargas Trujillo M, Khoury J, Backelijauw P. Low Incidence of Pathology Detection and High Cost of Screening in the Evaluation of Asymptomatic Short Children. J Pediatr. 2013; 163: 1045-1051.
2. Pinhas-Amiel O, De Luca F, Allen DB. Chapter 2: Normal Growth and Growth Disorders. In Pediatric Endocrinology: Essentials for Practice, McGraw-Hill, 3rd edition, in press.
3. Rogol AD, Hayden G. Etiologies and Early Diagnosis of Short Stature and Growth Failure in Children and Adolescents. J Pediatr. 2014; 164: S1-14.
4. Savage MO, Backeljauw P, Calzada R, et al. Early Detection, Referral, Investigation, and Diagnosis of Children with Growth Disorders. Horm res Paediatr. 2016; 85: 325-332.
5. Oostdijk W, Grote FK, de Muinck Keizer-Schrama S. Diagnostic Approach in Children with Short Stature. Horm Res. 2009; 72: 206-217.
6. Richmond EJ, Rogol AD. Diagnostic Approach to Children and Adolescents with Short Stature. UpToDate, last updated in Jan 2020.
7. 2007 WHO Growth Charts; 2000 CDC Growth Charts.



Endocrine Assessment of Pediatric Obesity

Currently 1 out of every 5 children (18.5%) meets the body mass index criteria for obesity (BMI ≥ 95th percentile). Among adolescents 9.5% are affected by severe obesity, in which their BMI is at the 120% of the 95th percentile or higher.

Diagnosing and Classifying Obesity

For children 2 years of age and older, obesity is diagnosed by a body mass index of the 95th percentile or higher using the 2000 CDC BMI charts based on age and sex. Extrapolated growth charts are available that allow assessment of obesity at higher percentiles. As a result, additional classifications of obesity are more recently being used as described below:

Obesity Class	Body Mass Index Percentile	Body Mass Index (kg/m2)
I	95th to < 120% of the 95th percentile*	
II	120% to < 140% of the 95th percentile*	35 to < 40 kg/m2
III	≥ 140% of the 95th percentile or higher*	≥ 40 kg/m2

*(Child's BMI in kg/m2) divided by (BMI in kg/m2 at 95th percentile for age-sex) * 100

For children less than 2 years of age, weight-for-length rather than BMI is used for classifying overweight and obesity. While skinfold thickness and waist circumference are frequently used in the obesity research setting, currently the American Academy of Pediatrics (AAP) does not recommend use of these in routine practice due to sparse reference data for U.S. children, measurement errors, and lack of specific guidelines as basis for intervention.

Importance of Growth Charts

Growth charts are vital tool in the evaluation of obesity, not only for BMI classification, but to determine the age of onset of obesity. Having multiple measurements over time assists with determining the rate of weight gain, as well as linear growth velocity. Recognizing whether there is growth failure in height is critical for the evaluation of obesity.

Assessing for Etiology

Key questions to ask when determining an etiology of obesity include:

- When did the weight gain start?
- Were there any other changes in health at the time of weight gain onset?
- Has the child been growing normally in height while gaining weight?

The timing and context of weight gain, age of onset, and presence or absence of normal linear growth can provide guidance in the next steps of evaluation.

Several specific etiologies of obesity are detailed below:

Obesity Etiology	Diagnostic Clues
Endocrine	Attenuated height velocity (down-trending height percentiles)
Neurologic (Hypothalamic)	CNS insult just as injury, tumor, trauma, radiation
Iatrogenic	Corresponding with obesogenic medication start (antipsychotic, glucocorticoid, medroxyprogesterone, valproic acid, etc.)
Genetic/syndromic	Early onset, developmental delays, hyperphagia

Most children will not have a clearly identifiable etiology of their obesity. In these cases, they are diagnosed with "common obesity."

Identifying Comorbidities

History and Physical Examination

History and physical examination should be performed to assess for etiologies of and potential comorbidities related to obesity, which can impact nearly every body system. While not a comprehensive list, below are some considerations for screening of obese children presenting for routine care.

Obesity Comorbidities by Body System	
Endocrine	Prediabetes, type 2 diabetes, precocious puberty, PCOS (females), hypogonadism (males)
Psychosocial	Depression, low self-esteem, anxiety, bullying, disordered eating
Neurological	Benign intracranial hypertension (pseudotumor cerebrii)
Cardiovascular	Hypertension, dyslipidemia
Pulmonary/Sleep	Asthma, sleep apnea, exercise intolerance
Gastrointestinal	Nonalcoholic fatty liver disease, gallstones, GERD, constipation
Musculoskeletal	Blount's disease, degenerative joint disease, slipped capital femoral epiphyses (SCFE)
Dermatologic	Acanthosis nigricans, hirsutism (females), hidradenitis suppurativa

Laboratory Evaluation

There is significant practice variability among laboratory evaluation for obesity comorbidities across the country, likely due to lack of guidelines consensus.

Children's Mercy generally recommends that hemoglobin A1c, AST/ALT, serum glucose and lipid profile (preferably fasting) be assessed every 1-2 years for obese children in the primary care setting. Lab assessments in obese children can be performed as early as 2 years of age, though most guidelines agree they be performed by age 10. Additional considerations for commonly performed laboratory assessments in obese children are discussed below.

- **Hemoglobin A1c**
  In clinical practice, most experts agree a HbA1c of 6.0% or higher in children requires additional evaluation.
- **Oral Glucose Tolerance Testing (OGTT)**
  OGTT is a useful assessment of impaired glucose tolerance/type 2 diabetes in children, but because of its invasiveness and cost we recommend it be performed in the primary care setting only for children who lack clearly abnormal hemoglobin A1c and fasting glucose, and who are at high risk of type 2 diabetes (e.g., family history, race, age, acanthosis).
- **Insulin Levels**
  Fasting insulin levels are NOT recommended for routine use in obesity screening.
- **Thyroid Studies**
  Thyroid function testing should be performed in any obese child with growth failure. However, routine screening of thyroid function in obese children who have no signs or symptoms of thyroid dysfunction other than weight gain should be avoided. If mild TSH elevation is found, but free T4 is normal, repeat assessment in 6-8 weeks is useful.
- **Vitamin D Assessment**
  If vitamin D assessment is performed in obese children, it should be done using a 25-hydroxyvitamin D level.

When should patients be referred for endocrine evaluation of obesity?

- **Growth Failure**
  Any child with rapid weight gain or obesity that demonstrates growth failure (crossing height percentiles curves downward) should be referred for evaluation of potential endocrinopathy.
- **Abnormal Puberty**
  Any child with obesity and abnormal puberty should be referred for endocrinology evaluation.
- **Early Onset Obesity**
  Any child less than 5 years old, particularly if there are developmental delays or severe hyperphagia, should be referred to an endocrinologist (or geneticist).
- **Abnormal Comorbidity Screening**
  Children with the following lab abnormalities should be referred for pediatric endocrinology evaluation:
  - ◊ Fasting glucose 100mg/dL or higher
  - ◊ HbA1c of 6.0% or higher
  - ◊ 120 minute glucose following OGTT of 140mg/dL or higher
  - ◊ For those children with an HbA1c 8.5% or higher, or serum blood sugar of 250mg/dL or higher the on-call Endocrinology physician should be contacted for possible urgent insulin initiation.

If HbA1c and glucose are normal, but there are other comorbidity abnormalities (AST/ALT, lipids), intervention and referral to appropriate subspecialist depends on the severity of the abnormality.

Because modification of environmental factors (diet, activity, etc.) is the cornerstone of management for nearly all cases of childhood obesity, any patient with abnormal obesity comorbidity screening should also be directed to a registered dietitian, or if feasible, a comprehensive weight management program.

Referral Instructions

Refer concerns regarding pediatric obesity to pediatric endocrinology for further evaluation.

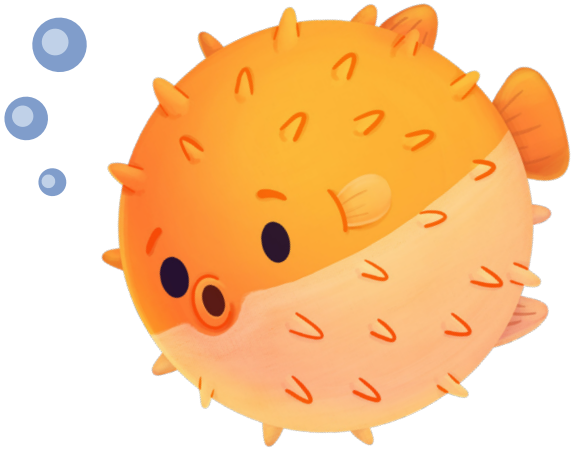
At Children's Mercy, patients have access to an established, experienced team of more than 20 pediatric endocrinologists and nearly 100 staff members who specialize in endocrine disorders. Obesity and obesity-comorbidity clinical resources in the division include:

- Type 2 Diabetes Prevention Clinic
- Polycystic Ovarian Syndrome Clinic
- Diabetes Center

Children's Mercy also offers a comprehensive weight management program including:

- Weight Management Clinic
- Special Needs Weight Management Clinic
- Metabolic/Bariatric Surgery Program

Consultative services are also available with the hospital's other service lines including the Ward Family Heart Center's Preventive Cardiology Clinic; the Division of Nephrology's Hypertension Clinic; the Division of Gastroenterology's Liver Care Center; and the Department of Nutrition's Outpatient Nutrition Clinic.



To make a referral:

- Visit childrensmercy.org.
- Select "Health Care Providers" in the top navigation bar.
- Select "Refer a Patient."
- Select "Endocrine" from the list of specialties and "Overweight (abnormal weight gain)" under "Reasons for Consultation."
- Complete the remaining fields on the referral form and submit.

All new referral requests are processed within 48 hours. Two phone attempts to contact the family and a final notification to the family to schedule will be made. For assistance, call the Contact Center at (816) 234-3700 or toll-free at (800) 800-7300. The Contact Center can provide additional information regarding any supporting documentation needed for the referral.

For urgent requests to speak to a specialist, please call and ask to speak with the on-call pediatric subspecialist at 1 (800) GO-MERCY / (800) 466-3729.

Additional Resources

1. Skinner AC, Ravanbakht SN, Skelton JA, Perrin EM, Armstrong SC. Prevalence of Obesity and Severe Obesity in U.S. Children, 1999–2016. Pediatrics. 2018;141(3):e20173459. (2018). Pediatrics, 142(3). doi:10.1542/peds.2018-1916.
2. Barlow, S. E. (2007). Expert Committee Recommendations Regarding the Prevention, Assessment, and Treatment of Child and Adolescent Overweight and Obesity: Summary Report. Pediatrics, 120(Supplement 4). doi:10.1542/peds.2007-2329c.
3. Pediatric Obesity—Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline. (2017). The Journal of Clinical Endocrinology & Metabolism. doi:10.1210/jc.2016-2573.
4. Estrada, E., Eneli, I., Hampl, S., Mietus-Snyder, M., Mirza, N., Rhodes, E., . . . Pont, S. J. (2014). Children's Hospital Association Consensus Statements for Comorbidities of Childhood Obesity. Childhood Obesity, 10(4), 304-317. doi:10.1089/chi.2013.0120.

21-END-0024

Children's Mercy