GUIDELINES FOR PEDIATRIC OBESITY

Pediatric Obesity—Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline

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Disclosures

Stocks in Bristol Meyer, Oragnovo, Teva

The Problem With Obesity

The Brookings Institution predicts that if all 12.7 million U.S. youths with obesity became obese adults, the individual average cost would be greater than \$92,000, and the societal costs over their lifetimes might exceed \$1.1 trillion

- Male Age 13 years
- BMI 35 kg/m² (>97th percentile)
- PMHX: Adenoidectomy age 6 yrs for snoring; Blount disease at 6 years old
- Social Hx: lives with parents, grandparents; 10 blocks from nearest playground; 8th grade
- ROS: sleep apnea requiring CPAP

Physical Exam:

- Height 85th percentile
- BP 98th percentile systolic/diastolic
- Generalized obesity but not Cushingoid
- Pink abdominal striae; acanthosis nigricans with skin tags present on axillae and neck
- Liver edge 1 cm below RCM
- Normal pulmonary and cardiac exams
- Genitalia stage 2, pubic hair stage 2

Case 1 Question

What evaluation will you perform?

- a. Fasting lipid panel
- b. Free T4 and TSH
- □ c. Urine free cortisol
- 🖸 d. Insulin
- e. All of the above

Case 1 Answer

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- Laboratory Assessment
- HbA1c 6.0%
 - Fasting blood glucose 105 mg/dL
 - ALT 56 (NL< 25)
 - Lipid profile
 - Total cholesterol
 - □ HDL-C
 - Triglycerides
 - □ LDL-C
 - Non-Hdl-C

228 mg/dL 28 mg/dL 289 mg/dL 138 mg/dL 150 mg/dl

Case 1 Question

Besides treating his hypertension and dyslipidemia, what would you do next? a. Enroll in intense lifestyle modification program b. Prescribe Orlistat 120mg TID c. Prescribe Atkins diet d. Refer for bariatric surgery e. Both a & b

Case 1 Answer

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- 6 y/o girl
- Weight gain started around age 3 years and now BMI: 34 kg/m² (>99th Percentile)
- Her mom says she eats a lot of pasta & bread and has food seeking behaviors

Past Medical History

- Floppy as infant, poor feeder due to weak suckle/low tone with FTT
- Extreme increased appetite at 2 years
- H/o developmental motor, cognitive and speech delay
- Family History Only child of a non consanguineous marriage

Physical exam

- Wt: 47.5 kg (> 95%), Ht: 117 cm (50%)
- BMI: 34 kg/m² (>99th Percentile)
- Bilateral epicanthal folds, almond shaped eyes, short philtrum, downturned corners of the mouth,

acanthosis nigricans at the neck and axillae, Brachydactyly



- Karyotype Normal female
- FISH study of SNRPN to R/O Prader Willi syndrome was negative
- Abnormal methylation of the PWS locus, confirming the diagnosis of Prader-Willi Syndrome

Case 2 Question

What should you order next to evaluate this patient?

- A. Exome sequencing for MC4 receptor
- B. Serum leptin for leptin deficiency
- C. FISH for SNRPN to R/O Prader Willi syndrome
- D. Methylation test for 15q11.2-q13
- E. PCR for CGG repeats for FMR
- F. None of the above

Case 2 Answer

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- 44 months old female
- BMI rose from 50th to 82nd percentile in 14 months
- Cared for by grandparents while parents work
- Drinks whole milk and 20 ounces juice daily

- Social Hx: Grandparents have health issues affecting mobility
- Child watches 4-5 hours TV/videos daily
- PMHx: BW 5 kg/gestational diabetes
- Family Hx
 - Hispanic ethnicity
 - Both parents with BMI > 30kg/m(squared)
 - Mother has "high blood pressure"
 - Paternal GF died at 55 of MI

Case 3 Question

What steps would you recommend to prevent the development of obesity?

- a. Alter the type of beverage intake
- b. Decease screen time to 2 hours per day
- c. Involve the family in lifestyle changes
- d. Encourage active play
- e. All of the above

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What steps would you recommend to prevent the development of obesity?

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Definition

 ■ 2.1 We recommend using BMI and the Centers for Disease Control and Prevention (CDC) normative BMI percentiles to diagnose pediatric overweight or obesity in children age 2 years or older.
 ■ (1 | ⊕⊕⊕O) CDC Definitions: BMI 85-95th percentile = Overweight BMI ≥95th percentile = Obesity BMI ≥ 120% of 95th centile = Extreme Obesity

Example:

- Boy, 13 years old
- Weight 154 lbs (70 kg)
- Height 5′0″ (152.4 cm)
- $\blacksquare BMI = 30 \text{ kg/m}^2$
- Extreme/Severe Obesity



Definition

■ 2.4 We suggest that a child younger than 2 years of age be diagnosed as obese if the sexspecific weight for recumbent length is greater than or equal to the 97.7th percentile on the World Health Organization (WHO) charts (2 | ⊕OOO)

Expert opinion

Prevalence Of High Adiposity Within BMI Categories Varies By Race



BMI-for-Age Percentile

Definition

- We suggest clinicians take into account that variations in BMI correlate to comorbidities in different ethnicities and that increased muscle mass increases BMI
 - Unrated
- Evidence: BMI cannot differentiate excess adipose tissue from increased lean muscle
- Ethnic differences in the percentage of fat at a specific BMI limits using BMI alone as a risk factor for comorbidities

- 2.5 We recommend against routine laboratory evaluations for endocrine etiologies of obesity in youths unless the child's stature and/or height velocity are attenuated. (1 | ⊕⊕⊕O)
- 2.6 We recommend that children with a BMI greater than or equal to the 85th percentile be evaluated for potential comorbidities. (1 | ⊕⊕⊕O)



Family History: Obesity, bariatric surgery, type 2 diabetes, GDM, hypertension, NAFLD, snoring/sleep apnea, C-Pap use, premature CVD events/deaths, infertility in women or PCOS.



Obesity Medical History: Polyuria/polydipsia, blurry vision/visual loss, acne/hirsutism,menses fungal vaginitis/discharge in girls, unexplained weight loss, frequent headaches, snoring, restless sleep, excessive Complications of Childhood Obesity Neurological Psychosocial Pseudotumor cerebri daytime sleepiness, GI Poor self esteem Risk for stroke Depression Cardiovascular Quality of life Dyslipidemia Pulmonary discomfort, musculoskeletal Hypertension Asthma Left ventricular hypertrophy Sleep apnea Chronic inflammation Exercise intolerance Endothelial dysfunction symptoms, psych disorders Renal Risk of coronary disease Glomerulosclerosis Endocrine Proteinuria Type 2 diabetes Gastrointestinal and medications, dietary, Precocious puberty Paniculitis Polycystic ovary syndrome (girls) Steatohepatitis Hypogonadism (boys) Liver fibrosis Hernia hyperphagia (food seeking Gallstones Risk for cirrhosis DVT/PE Risk for colon cancer behaviour), sedentary/activity Stress incontinence Musculoskeletal Risk of GYN malignancy Forearm fracture Blount's disease Slipped capital femoral epiphysis and developmental histories Flat feel Risk for degenerative joint disease

Physical Exam:



- Weight, Height and BMI calculation. - Blood Pressure: Height/age/sex normalized NHLBI BP Tables. - Skin: Acanthosis nigricans, skin tags, hirsutism, extreme acne (girls). - Funduscopic exam for pseudotumor - Thyroid exam for goiter - Abdomen/liver exam -Tenderness/range of motion of joints - Peripheral edema

Laboratory Evaluation/Screening Tests:

- Fasting Lipids
- HbA1c + random or fasting glucose
- OGTT if family and medical history +.
- Liver enzymes
- Free testosterone panel if: +Hx & PE for PCOS
- Thyroid function tests if: +Hx & PE for thyroid disorder
- Refer to pulmonology for PSG if: +Hx & FH for SDB
- Refer to psychiatry if: +Hx, FH and medications

- 2.7 We recommend against measuring insulin concentrations when evaluating children with obesity. (1 | ⊕⊕⊕O)
- Evidence: Despite severe deficiency in insulin secretion in youth with T2DM, fasting insulin concentrations are higher vs. non diabetic obese peers.
- Fasting insulin concentrations are similar between obese NGT and IGT

Why not Measure insulin?!

Insulin concentrations show considerable overlap between insulin resistant & Insulin sensitive youth



Why not Measure insulin?!

- There is no well-defined cut point differentiating normal from abnormal and no universally accepted, clinically useful, numeric expression that defines insulin resistance.
- Race ethnicity-related differences in insulin concentrations.
- □ Lack of standardized and reproducible insulin assays.

Why not Measure insulin?!

- Measuring plasma insulin concentrations remains a research tool with no clinical value for evaluation of obesity.
- Measuring fasting insulin concentrations to try to diagnose insulin resistance within general practice should be abandoned.

Table 2. Screening for Comorbidities of Pediatric Overweight or Obesity

Comorbidity	Tests and Interpretation
Prediabetes HbA1c IFG (verify fasting status)	5.7% to <6.5% (39 to <48 mmol/mol) (note the unpredictability of this test in pediatrics in the text) ^a Fasting plasma glucose of ≥100 but <126 mg/dL (≥5.6 but <7.0 mmol/L)
IGT (if OGTT is used)	Two-hour glucose of \geq 140 but <200 mg/dL (\geq 7.8 but <11.1 mmol/L)
Diabetes mellitus	HbA1c ≥ 6.5% (≥48 mmol/mol) ^{a,b} Fasting plasma glucose of ≥126 mg/dL (≥7.0 mmol/L) (fasting is defined as no caloric intake for 8 h) ^b Two-hour plasma glucose of ≥200 mg/dL (≥11.1 mmol/L) during an OGTT ^b In a patient with classic symptoms of hyperglycemia, a random plasma glucose of ≥200 mg/dL
Dyslipidemia	Fasting lipids Triglycerides (mg/dL) (multiply by 0.0113 to convert to mmol/L): $0-9 \text{ y} < 75$ (acceptable), 75–99 (borderline high), ≥ 100 (high); $10-19 \text{ y} < 90$ (acceptable), 90–129 (borderline high), ≥ 130 (high) LDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): <110 (acceptable), 110–129 (borderline high), ≥ 130 (high) Total cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): <170 (acceptable), 170–199 (borderline high), ≥ 200 (high) HDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L): <40 (low), 40–45 (borderline low), >45 (acceptable) Non–HDL cholesterol (mg/dL) (multiply by 0.0259 to convert to mmol/L) (can be nonfasting) <120 (acceptable), 120–144 (borderline high), ≥ 145 (high)
Table 2. Screening for Comorbidities of Pediatric Overweight or Obesity

Prehypertension and hypertension	3-11 y: (standardized according to sex, age, and height percentile) BP > 90th percentile to <95th percentile = prehypertension BP \ge 95th percentile to <99th percentile + 5 mm Hg = stage 1 HTN BP \ge 99th percentile + 5 mm Hg = stage 2 HTN 12-17 y: (standardized according to sex, age, and height percentile) BP of >90th percentile to <95th percentile or >120/80 = prehypertension BP \ge 95th percentile to <99th percentile + 5 mm Hg = stage 1 HTN BP \ge 99th percentile to <99th percentile + 5 mm Hg = stage 1 HTN BP \ge 99th percentile + 5 mm Hg = stage 2 HTN 18 to 21 y: BP \ge 120/80 to 139/89 mm Hg = prehypertension BP \ge 140/90 to 159/99 mm Hg = stage 1 HTN BP \ge 160/100 to 179/109 mm Hg = stage 2 HTN BP \ge 180/110 mm Hg = stage 3 HTN
NAFLD	ALT $>$ 25 U/L (boys) and $>$ 22 U/L (girls)
PCOS	Free and total testosterone and SHBG, per Endocrine Society PCOS guidelines ^c
Obstructive sleep apnea	If positive history, refer to pulmonary for nocturnal polysomnography and if not available overnight oximetry
Psychiatric	If positive history, refer to mental health specialist

Genetic evaluation

 ■ 3.1 We suggest genetic testing only in patients with extreme early onset obesity (<5 years of age), having clinical features of genetic obesity syndromes (extreme hyperphagia) and/or a family history of extreme obesity. (2 | ⊕⊕OO)

With Developmental Delay

Genetic Obesity Syndrome	Clinical Features
Obesity With Developmental Delay	
Dominant:	
Prader-Willi syndrome	Hypotonia, failure to thrive in infancy followed by weight gain, short stature (due to GH deficiency), hyperphagia, hypogonadotropic hypogonadism, sleep disturbance, obsessive behaviors
Albright's hereditary Osteodystrophy	Short stature in some but not all patients, skeletal defects, impaired olfaction and hormone resistance (e.g., parathyroid hormone) if a mutation is maternally inherited
SIM1 deficiency	Hyperphagia with autonomic dysfunction (characterized by low systolic blood pressure), speech and language delay and neurobehavioral abnormalities including autistic type behaviors
BDNF/TrkB deficiency	Hyperactivity, impaired concentration, limited attention span, impaired short-term memory and pain sensation
Recessive:	
Bardet-Biedl syndrome	Dysmorphic extremities (syndactyly/brachydactyly/polydactyly), retinal dystrophy or pigmentary retinopathy, hypogonadism and renal abnormalities/impairment
TUB deficiency	Retinal dystrophy, deafness

Without Developmental Delay

Obesity Without Developmental Delay		
Dominant:		
Alström syndrome	Retinal dystrophy, extreme insulin resistance, deafness, dilated cardiomyopathy and progressive pulmonary, hepatic, and renal dysfunction	
MC4R deficiency	Hyperphagia, accelerated linear growth, disproportionate hyperinsulinaemia, low/normal blood pressure	
SH2B1 deficiency	Hyperphagia, disproportionate hyperinsulinaemia, early speech and language delay which resolves, behavioral problems including aggression	
KSR2 deficiency	Mild hyperphagia and reduced basal metabolic rate, insulin resistance often with acanthosis nigricans, irregular menses and early development of type 2 diabetes	
Recessive:		
Leptin deficiency	Extreme hyperphagia, frequent infections, hypogonadotropic hypogonadism, mild hypothyroidism	
Leptin receptor deficiency	Extreme hyperphagia, frequent infections, hypogonadotropic hypogonadism, mild hypothyroidism	
POMC deficiency	Hyperphagia, cholestatic jaundice or adrenal crisis due to ACTH deficiency; pale skin and red hair in Caucasians	
PCSK1 deficiency	Small bowel enteropathy, hypoglycaemia, hypothyroidism, ACTH deficiency and diabetes insipidus	





- 4.1 We suggest that clinicians promote and participate in the ongoing healthy dietary and activity education of children, parents, and communities, and encourage schools to provide adequate education about healthy eating.
 - (2 | ⊕OOO)
 - Expert opinion

- 4.2 We recommend that clinicians prescribe and support healthy eating habits (1 | ⊕⊕OO)
- 5.2 We recommend($1 | \oplus \oplus OO$)
- Decreased consumption of fast foods
- Decreased consumption of added table sugar and elimination of sugar-sweetened beverages
- Decreased consumption of high-fructose corn syrup, with improved labeling of foods containing highfructose corn syrup

Treatment Guidelines

- Decreased consumption of high-fat, high-sodium, or processed foods
- Consumption of whole fruit rather than fruit juices
- Reduced saturated dietary fat intake for children older than 2 years
- U.S. Department of agriculture recommended intake of dietary fiber, fruits, and vegetables
- Timely, regular meals, avoiding constant "grazing" during the day
- Recognizing eating cues in the child or adolescent's environment, such as boredom, stress, loneliness, or screen time
- Encouraging single portion packaging and improved food labeling for easier use by consumers.

■ 4.3 & 5.3 We recommend that children engage in at least 20 minutes (optimally 60 minutes) of vigorous physical activity at least 5 days/ week to improve metabolic health, reduce the likelihood of developing obesity, and improve BMI. (1 | ⊕⊕OO)

■ 4.5 & 5.4 We recommend balancing unavoidable technology-related screen time in children with increased opportunities for physical activity.
 (1 | ⊕⊕OO)



■ 4.4 We suggest fostering healthy sleep patterns in all children to decrease the likelihood of developing obesity due to changes in caloric intake and metabolism related to disordered sleep.
 ■ (2 | ⊕⊕OO)

 4.8 We suggest using school-based programs and community engagement in childhood obesity prevention and treatment.

□ (2 | ⊕⊕OO)

- 4.9 We suggest using comprehensive behaviorchanging interventions to prevent and treat obesity.
- □ (2 | ⊕⊕OO)

- 4.6 We suggest that childhood obesity prevention efforts enlist the entire family.
 (2 | ⊕OOO)
- 5.1 We recommend clinicians prescribe, ageappropriate, culturally sensitive, familycentered lifestyle modifications (dietary, physical activity, behavioral) to promote a decrease in BMI. (1 | ⊕⊕⊕O)

- 4.10 We recommend breast-feeding infants for many health benefits, but can only suggest breast-feeding for prevention of obesity.
 (2 | ⊕OOO)

- 5.5 We suggest that the healthcare team identify maladaptive rearing patterns related to diet and activity, and educate families about healthy food and exercise habits. (2 | ⊕OOO)
- 5.7 We suggest that the healthcare team evaluate for psychosocial comorbidities and prescribe assessment and counseling if psychosocial problems are suspected.
 (2) ⊕OOO)

Psychosocial issues

■ 5.5 We suggest that the healthcare team identify maladaptive rearing patterns related to diet and activity, and educate families about healthy food and exercise habits. (2 | ⊕OOO)

Psychosocial Issues

■ 5.6 We suggest that the healthcare team probe for and diagnose unhealthy intrafamily communication patterns and support rearing patterns that seek to enhance the child's selfesteem. (2 | ⊕OOO)

Psych screening

- Parents and/or children should complete a mental health screening measure, such as the Pediatric Symptom Checklist (in the public domain):
- http://www.massgeneral.org/psychiatry/asse ts/PSC-35.pdf

Pharmacotherapy for Pediatric Obesity

■ 5.8 We suggest pharmacotherapy for children or adolescents with obesity only after a formal program of intensive lifestyle modification has failed to limit weight gain or to ameliorate comorbidities (2 | ⊕OOO).

Pharmacotherapy to Treat Pediatric Obesity

■ 5.8 We recommend against using obesity medications in children younger than 16 years who are overweight but not obese, except in the context of clinical trials. (1 | ⊕OOO)

Pharmacotherapy for Pediatric Obesity

■ 5.9 We suggest (FDA)-approved pharmacotherapy for obesity be administered only with a concomitant lifestyle modification program of the highest intensity available and only by clinicians who are experienced in the use of anti-obesity agents and are aware of the potential for adverse reactions.
 (2|⊕OOO)

Pharmacotherapy for Pediatric Obesity

- We suggest (FDA)-approved pharmacotherapy for obesity be administered:
 - Only by clinicians who are experienced in the use of antiobesity agents and are aware of potential adverse reactions.
 - Only with a concomitant lifestyle modification program of the highest intensity available (2 | ⊕OOO)

Pharmacotherapy for Pediatric Obesity
 5.10 We suggest clinicians discontinue medication and re-evaluate if the patient does not have a greater than 4% BMI/BMI z reduction after taking anti-obesity medication for 12 weeks at full dosage. (2 | ⊕OOO)

Metformin

Metformin is:

- Only modestly effective for weight reduction in obese children with hyperinsulinemia
- Is associated with reasonably well-tolerated adverse events
- Metformin cannot be recommended for routine use in obese children for weight reduction

Candidates for Bariatric Surgery

We suggest bariatric surgery only under the following conditions:

- Tanner 4 5 development and final/near-final adult height
 - BMI >35 kg/m² with major comorbidities of obesity (eg. type 2 diabetes, moderate to extreme sleep apnea) OR
 - BMI >40 kg/m² with mild comorbidities (eg. HTN, dyslipidemia extreme psychological distress secondary to their obesity)
 - Extreme obesity
 - Comorbidities persist despite attempting a formal program of lifestyle modification, with or without pharmacotherapy



- 5.11 We suggest bariatric surgery only under the following conditions: (2 | ⊕OOO)
 - Psychological evaluation confirms the stability and competence of the family unit, impaired QOL from obesity may be present, but the patient does not have an underlying untreated psychiatric illness
 - The patient demonstrates the ability to adhere to the principles of healthy dietary and activity habits

- □ 5.11 We suggest bariatric surgery only under the following conditions: (2 | ⊕OOO)
 - Access to an experienced surgeon in a pediatric bariatric surgery center of excellence employing a team capable of long-term follow-up of the metabolic and psychosocial needs of the patient and family and an institution that provides the necessary infrastructure.

Evidence for efficacy of surgery:

- Reversal of type 2 diabetes
- Improved glucose homeostasis in nondiabetics
- Improved insulin sensitivity and secretion
- Resolution of sleep apnea
- Improvement in NASH, severe arthropathy, CVD risk factors (dyslipidemia, HTN, inflammation) with cardiac workload.

□ 5.12 We suggest against bariatric surgery in preadolescent children; pregnant or breastfeeding adolescents (and those planning to become pregnant within 2 years of surgery); and in any patient who has not mastered the principles of healthy dietary and activity habits and/or has an unresolved substance abuse, eating disorder, or untreated psychiatric disorder. (2 | ⊕OOO)

Bariatric surgery is associated with Late Complications

- Adherence to recommended guidelines is essential as there is:
- Restricted nutritional intake
 - Protein calorie malnutrition
 - Vitamin deficiencies
 - Mineral deficiencies
- Decreased production intrinsic factor
- Decreased gastric acid production
- Food intolerance, esp with "dumping syndrome" assocd with RYGB and transient post-op nausea, esp with VSG

Conclusion

Childhood obesity remains an ongoing serious international health concern with a basis in genetic susceptibilities influenced by a permissive environment starting in utero and extending through childhood. ... screening for comorbidities of obesity should be applied in a hierarchal, logical manner with genetic screening for rare syndromes only in the presence of specific features.

Conclusion

The prevention of childhood obesity by promoting healthful diet, activity, and environment should be a primary goal, as achieving effective, long-lasting results with lifestyle modification once obesity occurs is difficult.
Conclusion

- The use of weight loss medications during childhood should be restricted to clinical trials.
- Bariatric surgery in the most seriously affected mature teenagers ..requires experienced teams with resources for long-term follow-up.
- Transition programs for obesity are an uncharted area requiring further research for efficacy.

Recommended Future Research Aims

- Effective methods of preventing and treating obesity
- Changes in environment and economy for global cultural changes in diet and activity
- Systemic changes in food environments and total daily mobility
- Methods to sustain healthy BMI changes
- Transition programs for adolescents with obesity entering adulthood.

Recommended Future Research Aims

Understand genetic and biological factors that predisposed to comorbiltities, increase risk of weight gain and influence response to therapeutic interventions