Pediatric Endocrine Society (PES) Board Review Course in Pediatric Endocrinology – 2025
"Disorders of Growth"
Susie Cabrera MD
Medical College of Wisconsin
Children's Wisconsin (Milwaukee, WI)
scabrera@mcw.edu

***Below is a copy of the ABP content specifications outline. If the information was reviewed in the presentation, then the slide number from the talk is listed after that specification. Specifications that were not covered in the talk are expanded on below if necessary and are in **bold.**

Pediatric Endocrinology ABP Content Domains (effective 2023)

Domain 1: Normal Physiology and Structural Development of Endocrine Systems

G. Growth

1. The GH/IGF-1 axis **Slide 6**
2. Regulation of growth in the fetus, neonate, child, and adolescent **Slide 4-5**

Domain 4: Disorders of Growth

A. Short Stature **Slide 19 and throughout presentation**
B. Congenital and acquired GH deficiency **Slides 22-24**
C. Disorders of GH action and GH sensitivity (primary IGF-1 deficiency) **Slides 25-26**
D. Idiopathic short stature **Slide 41**
E. Syndromes associated with short stature **Slides 35-40**
F. Growth disorders not related to the GH-IGF axis **throughout the presentation**
G. Skeletal dysplasia **Slide 36**
H. Effects of chronic illness on growth including cancer therapy **Slides 30-32**
I. Tall stature **Slides 47-48**
J. Overgrowth syndromes **Slides 48-52, 54**

Previous Content Specifications (before 2023)

A. Auxology

1.Standards
a. Know the origin of commonly used World Health Organization growth charts and their limitations and differences. **Slide 12**
b. Know the relationship of age to upper/lower segment ratio and to arm span. **Slide 13**

2.Measurements
a. Know proper technique and variances of linear measurements **Slide 11**
b. Know the techniques of assessing body composition and the differences and limitations
i. **Weight-to-height – measure of adiposity for those aged < 2 years. Does not correlate well with adiposity in those > 2 years.**
ii. **Body Mass Index (BMI) – kg/m2, standard measure of adiposity for those aged ≥ 2 years; varies by sex and age so percentiles are used. Extended growth charts are available for severe obesity.**

a. **Imprecise measure of adiposity because does not distinguish between fat and fat-free mass. Over-estimates obesity in children who are short or have high muscle mass; under-estimates obesity in those who are tall or have low muscle mass.**

iii. **Waist circumference – NHANES III data used to estimate percentiles for U.S. children and adolescents. When combined with BMI, waist circumference may be helpful in estimating obesity-related comorbidities.**

iv. **Waist-to-height ratio – measure of abdominal adiposity and is associated with cardiovascular risk, with better accuracy of risk in adolescents ≥ 12 years.**

v. **Anthropometrics like skinfold thickness or mid-upper arm circumference – easy to perform, inexpensive, noninvasive. However, low precision and reproducibility, especially in overweight/obesity. Perhaps more value in long-term monitoring of underweight/malnourished children**

vi. **Dual-energy X-ray absorptiometry (DXA) – more expensive but provides measures of fat-free mass, body fat, and bone mineral density. Quantitative magnetic resonance and air displacement plethysmography are also used as reliable noninvasive measures of fat mass.**

c. Know how regional distribution of body fat varies with age and sex

i. **During puberty: boys gain more lean body mass and girls gain more fat mass**

ii. **During puberty and adulthood: boys gain fat in an "android" (abdominal) distribution and girls in a "gynoid" (gluteofemoral) distribution**

3. Normal patterns of growth

a. Know the endocrine basis for the adolescent growth spurt. **Slide 4**

b. Know how to distinguish physiological from pathologic tall stature in childhood. **Slide 18**

c. Know the normal growth rates during fetal life, infancy, childhood, and adolescence. **Slide 4**

d. Know how factors such as twinning and maternal/paternal size influence fetal growth

i. **Maternal weight is an important variable for fetal growth and birthweight**

ii. **Twins tend to have lower birthweights than singletons**

e. Know the average and range of normal ages of growth cessation. **Slide 4**

f. Know how to utilize longitudinal growth data to distinguish between physiological and pathological patterns of growth **Slides 16-18**

g. Know the criteria used to distinguish normal variants of short stature from pathologic short stature in childhood **Slide 18**

h. Know how to calculate target adult height **Slide 14**

i. Know the effects of maternal illness and smoking on fetal growth **Slide 42**

4. Skeletal age

a. Understand the concept of skeletal age and the nutritional, hormonal and genetic factors that influence it **Slide 14**

b. Know the procedures and limitations of adult height prediction **Slide 14**

c. Know the effect of under- and over-nutrition on skeletal age **Slide 21**

d. Know the different methods utilized to determine skeletal age **Slide 14**

5. Dental development

a. Know the factors that influence the timing of dental eruption

i. **Females develop teeth earlier than males**

ii. **Delays in dental eruption can be genetic or d/t mutations in *PTH1R* or be related to syndromes such as Down Syndrome, achondroplastia, or chondroectodermal dysplasia or**

related to endocrinopathies: hypothyroidism, hypopituitarism, osteopetrosis, or rickets

iii. **Complete late of eruption may be due to lack of space in mouth (most common), but also associated with AHO, William syndrome, ectodermal dysplasias**

b. Know the normal sequence and ages of dental eruption and loss

i. **Primary teeth eruption (bilaterally symmetric):**
   a. **6-10 months of age: mandibular central incisors first. Then, maxillary central incisors, lateral incisors, first molars, canines, and second molars**
   b. **Completion of primary teeth eruption around 30 months of age**

ii. **Primary tooth exfoliation (loss):**
   a. **Usually begins ~ 6 years**
   b. **Early exfoliation (< 4 yrs old) – should be investigated as may signal a systemic condition/illness such as hypophosphatasia (loss can occur @ 1 yoa), cyclic neutropenia, Langerhans cell histiocytosis (ulcerative gingivitis, starts with posterior teeth)**
   c. **Delayed exfoliation d/t inadequate resorption of primary tooth root with permanent tooth emerging out of normal position**

iii. **Permanent teeth eruption**
   a. **Usually around 6 years of age with central incisors, then lateral incisors, canines, 1st premolar, then 2nd premolar. 2nd molars arrive ~12 years of age**

B. Determinants and regulation of normal growth

1.Genetic influences

a. Describe familial influences on prenatal and postnatal growth patterns

i. **Maternal weight affects birthweight; maternal and paternal weight and height influence postnatal weight gain and linear growth**

ii. **Height has a polygenic inheritance pattern (unless there is a monogenic syndrome as an etiology for overgrowth or short stature). GWAS studies have found < 12,000 independent SNPs associated with height, likely accounting for 40-50% phenotypic variation in height.**

2. Nutritional influences

a. Know how undernutrition and overnutrition affect growth **Slides 21, 51**

3. Classic hormones

a. GH (see V.C.1.a(3))

b. Thyroid hormones

1. Know linear and weight growth patterns that are suggestive of hypothyroidism or hyperthyroidism **Slides 27, 48**

c. Sex steroids

1. Know the hormonal factors controlling pubertal growth and the relationship between peak growth velocity and the stages of pubertal development **Slide 29**
   a. **1/5 of adult height accrues during puberty, taking about 2 years in total.**
   b. **Girls: pubertal growth spurt is in Tanner III (i.e. ~12 yo)**
   c. **Boys: pubertal growth spurt is in Tanner IV-V (i.e. ~14 yo)**
   d. **Boys have their pubertal growth spurt ~ 2 years later than girls, so have 2 additional years of prepubertal growth before the pubertal growth spurt begins. Boys also have a greater peak GV than girls.**

2. Know the effects of sex steroids on linear growth, body composition, and bone

maturation **Slide 4, 29**

d. Insulin

1. Know the effects of excessive serum insulin concentrations on fetal growth **Slide 48**

4. Growth factors

a. Insulin-like growth factors and binding proteins **Slides 6-9**

1. Structure, regulation, and function

a. Be familiar with the principal growth factor superfamilies and their members

b. Know that the production of IGF-I is under the control of GH as well as other factors such as nutrition, sex steroids, chronic disease

c. Know that IGF-I possesses insulin-like properties and that it stimulates sulfate uptake, DNA synthesis, RNA synthesis and protein synthesis

i. **IGF-1 binds IGF-1R (a tyrosine kinase receptor) and activates PI3K-AKT/PKB and the RAS-MAPK pathways, resulting in DNA and RNA synthesis. This affects cell growth, cell proliferation, protein synthesis, and apoptosis.**

d. Know that IGF-I is produced in multiple tissues and stimulates tissue growth by endocrine, paracrine, and autocrine modes of action **Slide 8**

e. Understand the role of growth factors IGF-I and IGF-II in normal prenatal and postnatal growth **Slide 8**

f. Know the structure of receptors for IGF-I and IGF-II

i. **IGF-1R is a transmembrane "heterotetrameric" tyrosine kinase receptor (2 alpha and 2 beta subunits). The alpha subunits are responsible for binding IGF-1, IGF-2, and insulin ligands. The beta subunits span the cell membrane and contain the tyrosine kinase domain, activated upon binding of the ligand. Homologous to insulin receptor. Binding of IGF-1R mediates growth and metabolic effects.**

ii. **IGF-2R is transmembrane protein with a very large extracellular domain. IGF-2 binds to IGF-2R and internalizes IGF-2, resulting in its degradation or recycling. There is no signaling.**

g. Know that IGF-I exerts anti-apoptotic effects **Slide 8**

h. Know that there is positive correlation between serum IGF-I levels and certain malignancies

i. **IGF-1 promotes oncogenesis by inhibiting apoptosis and stimulating cell proliferation. In epidemiologic studies, IGF-1 levels are positively associated with increased risk of several cancers, including breast, prostate, colorectal cancer.**

2. Factors affecting serum concentrations and their measurement

a. Understand the clinical usefulness and limitations of total serum IGF-I determinations **Slides 43-44**

b. Know the age-dependent changes in the serum concentrations of IGF-I and IGF-II **Slide 8**

c. Know that girls have a higher and earlier mid-pubertal peak in plasma IGF-I concentrations than boys (see 4.A.2.f.)

d. Recognize that hypothyroidism will lower plasma IGF-I concentrations

i. **Thyroid hormones stimulate GH synthesis and, in turn, IGF-1 synthesis. Thyroid hormone also increases IGF-1 expression by various tissues. Individuals with hypothyroidism have significantly decreased IGF-1 levels.**

L-T4 replacement results in increased IGF-1 levels.

e. Recognize the dose and route dependency of estrogen administration on IGF-I concentrations

i. **Oral exogenous estrogen reduces IGF-1 concentrations, likely by decreasing hepatic IGF-1 production. Oral estrogen also increases IGF-BP1, which reduces IGF-1 bioavailability.**

f. Understand the relationship between levels of IGF-I and peak height velocity

i. **Girls: pubertal growth spurt is in Tanner III (i.e. ~12 yo)**
ii. **Boys: pubertal growth spurt is in Tanner IV-V (i.e. ~14 yo)**
iii. **IGF-I peak is higher in girls than boys, but girls have lower peak velocity.**

g. Know the effects of obesity on GH and insulin-like growth factors **Slide 51**

3. Binding proteins

a. Recognize that serum IGF-I and IGF-II are associated with carrier proteins **Slide 9**

b. Know that the large molecular weight circulating complex of IGF-I is GH dependent **Slide 6**

c. Know that IGF-I concentrations are relatively stable throughout a 24-hour period **Slide 44**

d. Know that the major normal circulating form of IGF-I and IGF-II is a three subunit 150 kD complex of IGF peptide, IGFBP-3, and an acid labile subunit **Slide 6**

e. Understand the functional characteristics of the IGFBPs **Slide 9**

f. Know the factors that regulate IGFBP -1, -2, -3, -4, -5, and -6, physiologically

i. **IGFBP-1 is inhibited by insulin and stimulated by counter-regulatory hormones (glucagon, cortisol) and proinflammatory cytokines. Prolonged fasting stimulates IGFBP-1 production.**
ii. **IGFBP-2 stimulated by fasting and inhibited by insulin. Decreased in obesity. Rapidly regulates how much IGF-1 is available to enter the extravascular space and bind peripheral tissue receptors**
iii. **IGFBP-5 inhibited by prolactin in mammary glands, stimulated by PTH in osteoblasts**

g. Know that IGFBPs have IGF-independent effects

b. Other growth factors

1. Epidermal growth factor

a. Know that epidermal growth factor is a potent mitogen for ectodermal and mesodermal cells and tissues

i. **EGF binds to EGFR to stimulate intracellular signaling, resulting in cell division and proliferation.**

2. Fibroblast growth factor **Slide 5, 36**

a. Know the disorders due to fibroblast growth factor receptor mutations

b. Know the effects of inflammation on IL-1, IL-6, and TNF-alpha **Slide 5, 30**

3. Erythropoietin

a. Recognize that erythropoietin production is stimulated by hypoxia, androgens, GH

i. **EPO is required for production of red blood cells in the bone marrow**
ii. **Primary driver of EPO production is hypoxia.**
iii. **Secondary factors that stimulate EPO are IGF-1 and androgens (testosterone) – this is why males have higher hemoglobin levels than females and why H&H should be monitored in those on long-term testosterone replacement**

4. Oncogenes
    a. Know the relationship of oncogenes to growth factors and growth factor receptors
        i. **Oncogenes are mutated versions of genes that regulate cell growth and division, resulting in uncontrolled cell growth**
        ii. **Oncogenic mutations of several growth factor receptors have been described, including EGFR, IGF-1R, and FGFR, resulting in a mitogenic response to maintain cancer growth. Aberrant activation of GFRs in malignancy can occur by autocrine/paracrine activation, chromosomal rearrangements, gain-of-function mutations, or genomic amplification.**
    b. Understand the basic mechanisms that underlie neoplastic transformation
        i. **Neoplastic transformation is a multistep process by which normal cells become cancerous. This is usually driven by accumulation of genetic (somatic mutations in oncogenes or tumor suppressor genes, DNA damage, or chromosomal rearrangements like translocations that create fusion genes) and epigenetic alterations (changes in DNA methylation, histone modifications), that disrupt normal cell growth/regulation.**
    c. Know that oncogenes have roles in both normal and pathologic states
        i. **Proto-oncogenes (i.e., RAS, MYC, HER2(neu), EGFR, Wnt, etc) are normal genes that can become cancer-causing oncogenes. Proto-oncogenes are needed for normal cell growth and division. Proto-oncogenes are involved in cell cycle regulation, growth and differentiation, and regulation of apoptosis. Further mutation or over-expression of proto-oncogenes to oncogenes is when pathology occurs.**

C. Disorders of growth

1. Fetal
    a. Intrauterine growth restriction (IUGR) **Slide 42**
        1. Know the causes and clinical features of intrauterine growth restriction
        2. Know the proportion of small for gestational age children that remain short
        3. Know the relationship between first year growth rate and subsequent stature in patients with intrauterine growth restriction
        4. Know the risks associated with intrauterine growth restriction, such as type 2 diabetes in later life
        5. Know the effect of deficiencies of IGF secretion or action on fetal growth
        6. Understand the role of IGF-II action in disorders of fetal growth
            i. **IGF-2 overexpression: fetal overgrowth**
            ii. **IGF-2 deficiency: fetal undergrowth/SGA**
        7. Differentiate the fetal alcohol syndrome from other causes of IUGR
            i. **Fetal alcohol syndrome characterized by pre- and post-natal growth failure, facial dysmorphology (microcephaly, thin upper lip), CNS dysfunction (learning/attention difficulties, social/emotional problems, and motor coordination problems) with history of maternal alcohol consumption**
        8. Know the association of intrauterine growth restriction and premature pubarche
        9. Know the association of intrauterine growth restriction and metabolic syndrome (insulin resistance syndrome)
        10. Know the genes responsible for pancreatic ontogenesis
            i. **Activating mutations in: KRAS2 (present in 90-95% pancreatic cancers), AKT2, AIB1 and C-MYC, GATA6, ERBB2**

ii. **Inactivating mutations in: BRCA1, BRCA2, TP53, CDKN2A (most common; present in 50-75% pancreatic cancers), SMAD4**

b. Russell-Silver syndrome **Slide 34**

1. Know the clinical features of Russell-Silver syndrome
2. Know the causes of Russell-Silver syndrome

c. Perinatal insulin deficiency

1. Know the intrauterine and postnatal growth pattern of infants with congenital diabetes

i. **Fetal insulin is a key driver of growth, especially in third trimester**

a. **IUGR or SGA common due to in utero insulin deficiency**

b. **Lowest birth weight seen in those with 6q24 overexpression**

ii. **Postnatal growth depends on severity of insulin deficiency**

iii. **Catch-up growth possible with improved glycemia, with normalization to population levels by 9-12 months of age**

2. Postnatal

a. Growth failure

1. Intrinsic defects of growing tissues

a. Skeletal dysplasias and chondrodystrophies **Slide 36**

1. Know how to recognize and diagnose the skeletal dysplasias

b. Genetic syndromes (Turner syndrome, Prader-Willi syndrome)

1. Know the expected growth pattern of untreated Turner syndrome **Slides 37-38**
2. Know the genetic abnormalities and clinical features of Noonan syndrome **Slide 39**
3. Know the relationship of karyotype to clinical features in Turner syndrome

i. **There are general association between phenotype and karyotype and presence/location of mosaicism**

a. **Non-mosaic 45,X has most "classic" TS phenotype and highest frequency of primary amenorrhea**

ii. **Presence of Y chromosome material → ↑ risk gonadoblastoma**

iii. **Isochromosome Xq (46,X,i(Xq)) → ↑ risk autoimmune disorders**

iv. **Ring chromosome X (r(X)) → ↑ risk developmental delay, potential for atypical TS features (severe growth failure, syndactyly, atypical facial dysmorphism)**

4. Know the clinical features of Prader-Willi syndrome **Slide 40**
5. Know the inheritance of Prader-Willi syndrome and the appropriate tests that establish the diagnosis **Slide 40**
6. Know that short stature in Turner syndrome is due, at least in part, to SHOX haploinsufficiency **Slide 37**
7. Be able to recognize various forms of PTH resistance syndromes **Slide 35**
8. Recognize the physical findings characteristic of Turner syndrome **Slide 37**
9. Know the clinical features and causes of dyschondrosteosis (Leri-Weill syndrome) **Slide 36**
10. Know the effects and adverse events of GH therapy in Prader Willi syndrome **Slide 40**

2. Abnormalities in environment of growing tissues

a. General metabolic abnormalities

1. Know the effects of general metabolic abnormalities (eg, hypoxia, acidosis) on growth stunting **Slide 19, 30**
2. Know the effect of specific metabolic disorders (eg, cystinosis) on growth

a. **Cystinosis**

i. **Autosomal recessive amino acid storage disorder; 1:200,000**
ii. **Failure of transport of cystine out of lysosomes, resulting in development of cystine crystals (amino acid storage disorder)**
iii. **Marked growth retardation in 1st decade without intellectual impairment**
iv. **Severe and progressive decrease in renal function and Fanconi syndrome, resulting in ESRD and need for transplant by end of 1st decade**
v. **Photophobia**
vi. **Hypothyroidism commonly occurs**

3. Know the effect of chronic renal insufficiency on metabolism, including growth **Slide 30**

4. Know the effects of various medications on linear growth in children (eg, inhaled corticosteroids, stimulants, etc)

i. Inhaled corticosteroids and stimulant medications may minimally suppress growth but benefit of treatment of asthma and ADHD, respectively, must be considered in relation to height impact.
ii. Minimize potential growth attenuation by using the lowest effective dose and adjusting dose as needed

5. Know the effects of chronic systemic illness and their therapies on linear growth and body composition **Slide 30**

b. Nutrient insufficiency

1. Know the effects of protein/calorie malnutrition on the GH-IGF-IGFBP axis

2. Be able to recognize and diagnose the gastroenterologic/nutritional disorders that may present as growth failure **Slide 21**

3. Disease of endocrine system

a. GH deficiency

1. Know the clinical characteristics and growth patterns of children with isolated GH deficiency and multiple pituitary hormone deficiencies **Slides 22-24**

2. Recognize possible hormonal causes for a poor response to appropriate GH replacement therapy

i. Response to GH therapy can be impeded by hypothyroidism, hypercortisolism, and hypogonadism.

3. Know findings on physical examination that are suggestive of or associated with GH deficiency **Slides 23-24**

4. Know the laboratory tests used to diagnose GH deficiency and their limitations **Slides 43-44**

5. Know the conditions, diseases, and treatments that produce GH deficiency **Slides 23-24**

6. Understand the rationale for GH treatment for GH deficiency in infancy, childhood, adolescence, and early adulthood **Slide 45**

b. Hypercortisolism

1. Be able to recognize growth failure due to hypercortisolism **Slide 28**

2. Understand the mechanism of growth suppression by glucocorticoid excess **Slide 28**

c. GH-resistant syndromes (See also V.C.1.b.(3)(b))

1. Know the clinical characteristics, molecular basis, and inheritance patterns of GH

unresponsiveness syndromes **Slides 25-26**

2. Know that the lack of functional GH receptors in Laron syndrome (GH insensitivity syndrome) is often but not always reflected in a decrease in GH binding protein **Slide 25**

a. GHBP = cleaved extracellular domain of GH-R

b. Main source of GHBP = liver

3. Know that IGF-I can be used to treat children with GH insensitivity and GH gene defects **Slide 25-26**

b. Overgrowth

1. Syndromes/metabolic disease/hormonal

a. Klinefelter syndrome **Slide 52**

1. Know the genetic cause and clinical features of Klinefelter syndrome

b. Marfan syndrome **Slide 54**

1. Know the clinical features of Marfan syndrome
2. Know the prognosis of Marfan syndrome
3. Know that the fibrillin gene is defective in Marfan syndrome

c. Homocystinuria **Slide 54**

1. Recognize that homocystinuria can be distinguished from Marfan syndrome by the presence of homocystinuria due to cystathionine synthase deficiency, mental retardation (present in 50% of patients), fine sparse hair and thromboembolic phenomena
2. Know that tall stature, arachnodactyly, and ectopia lentis are features of Marfan syndrome and homocystinuria

d. Cerebral gigantism (Sotos syndrome) **Slide 49**

1. Know the clinical features of Sotos syndrome
2. Know that serum GH and IGF-I concentrations are normal in Sotos syndrome

e. Weaver syndrome **Slide 48**

1. Know that tall stature occurs in Weaver syndrome

f. Acromegaly/gigantism **Slide 53**

1. Know appropriate diagnostic and therapeutic approach to patients with suspected growth hormone excess
2. Recognize hypothalamic and pituitary causes of GH oversecretion
3. Know that IGF-I and IGFBP-3 are increased in acromegaly/gigantism
4. Differentiate GH excess from other overgrowth syndromes
5. Know that GH excess can be associated with McCune-Albright syndrome
6. Recognize the metabolic effects of GH excess
7. Know the side effects of the therapies for GH excess
8. Know the therapeutic modalities used to treat GH excess (surgery, irradiation, somatostatin analogs, GH antagonists)
9. Know the methods that are useful in assessing the response to therapy for GH excess

a. **IGF-1 levels monitored every 3 months after surgery, medication, or radiation therapy. Then space to every 6-12 months. Imaging (MRI) should be obtained 4 months after surgery, then yearly for several years. Monitor clinically and for resolution of GHC excess symptoms (i.e., QoL, sleep apnea, dysglycemia, headaches)**

3. Evaluation and diagnosis

a. Clinical evaluation

1. Know the criteria which identify the child with short stature due to intrinsic or genetic factors **Slide 19**

2. Know the criteria which identify the child with constitutional growth delay **Slide 17**

3. Know the criteria which distinguish the child with pathologic growth failure from physiological variants of growth **Slide 18**

4. Know the significance of previous growth measurements, and how to use growth velocity charts, mid-parental height, and target vs. predicted heights **Slides 11-14**

5. Know how to obtain and evaluate a dietary history for qualitative and/or quantitative nutritional deficiencies **Slide 21**

6. Understand the diagnostic utility and appropriateness of observation of growth rates without treatment

b. Laboratory evaluation

1. Know that a low plasma IGF-I level in a growth retarded child is consistent with but not diagnostic of GH deficiency **Slide 44**

2. Be able to select appropriate diagnostic studies to identify the cause of short stature **Slide 43**

3. Know the effects of GH deficiency on IGF-I, IGF-II, and specific binding proteins

a. **Classic GHD: low levels of IGF-I, IGFBP-3 and ALS; increase with rhGH Rx**

4. Understand the role of magnetic resonance imaging in the evaluation of possible pituitary hormone deficiencies **Slide 44**

D. Therapies to alter growth and stature

1. General

a. Understand the role for reassurance in the child with intrinsic short stature or constitutional delay in growth **Slides 16-17**

b. Understand therapeutic options for the short child with psychosocial stress **Slide 17**

2. GH

a. Understand the appropriate use of GH in the treatment of disorders including short stature, such as Turner syndrome, Prader-Willi syndrome, SGA, and renal failure **Slide 45**

b. Understand the issues surrounding use of GH in treatment in children with idiopathic short stature **Slide 41**

c. Know the adverse effects of GH therapy (early and late) **Slide 45**

3. Sex steroid manipulations

a. Androgens

1. Know the pros and cons of using hormonal therapy in a child with constitutional delay in growth **Slide 17**

i. Short course of androgens may be helpful for peer concordance if desired by a boy with CDGP; may help improve psychological health. Caution in not using doses that could accelerate skeletal maturation and truncate final adult height.

2. Know the forms and appropriate dosages of androgens for treatment of constitutional delay of growth

i. No consensus on best dose/course; testosterone esters most commonly used. Possible course of 50-125 mg SC monthly x 6 months, then reassess for spontaneous onset of puberty (evidenced by testicular enlargement and/or increased LH level), repeat as needed.

b. Low dose estrogens **Slide 7, 29**

1. Know the effects of low dose estrogen on growth, bone maturation, feminization, and lipid

carbohydrate metabolism in girls with CDGP and Turner syndrome

i. **Low dose estrogen therapy in girls with CDGP, TS, or hypogonadism will cause: accelerated skeletal maturation (with eventual epiphyseal fusion), feminization (secondary sexual characteristics), uterine growth, improved bone mineral density. There is inadequate/mixed data on the impact of E2 on cardiovascular health, lipid, and glucose metabolism.**

c. Delaying puberty

1. Know the effects of pubertal delay on growth, adult height, and skeletal maturation **Slide 29**

2. Understand the use of GnRH analogs and aromatase inhibitors to delay skeletal maturation

i. **GnRH analogs delay skeletal maturation by reducing sex hormone production, resulting in a longer period of potential growth. This works well in attaining a normal adult height in treatment of CPP but limited/mixed efficacy in those with typical pubertal timing or other conditions. Inadequate studies.**

ii. **Aromatase inhibitors given to boys with CDGP *may* increase adult height but potential safety concerns may exceed benefit.**

iii. **Strategies to combine rhGH with either a GnRH analog or letrozole have been done, with mixed results on adult height.**

d. Estrogen/androgen therapy for tall stature/unwanted growth

1. Know the appropriate therapy and indications for hormonal treatment for familial tall stature

i. **Treatment is reassurance and destigmatization of tall stature.**

ii. **Medical treatment discouraged but sex steroids were used historically and were started when the bone age was between 10-12 years.**

2. Understand the value versus limitations/risks regarding the use of estrogen therapy in girls with tall stature

a. Understand the rationale for and approaches to growth restriction therapy in specific situations

i. **Rationale was to fit within societal/cultural norms but there is much greater acceptance of tall girls and growth restriction therapy is now strongly discouraged**

a. **Side effects: infertility, depression, patient dissatisfaction**

ii. **Epiphysiodesis (surgical damage of the growth plates of tibia and femur) can be considered to restrict excessive growth in those with extreme tall stature.**