Pediatric Endocrinology Review MCQs

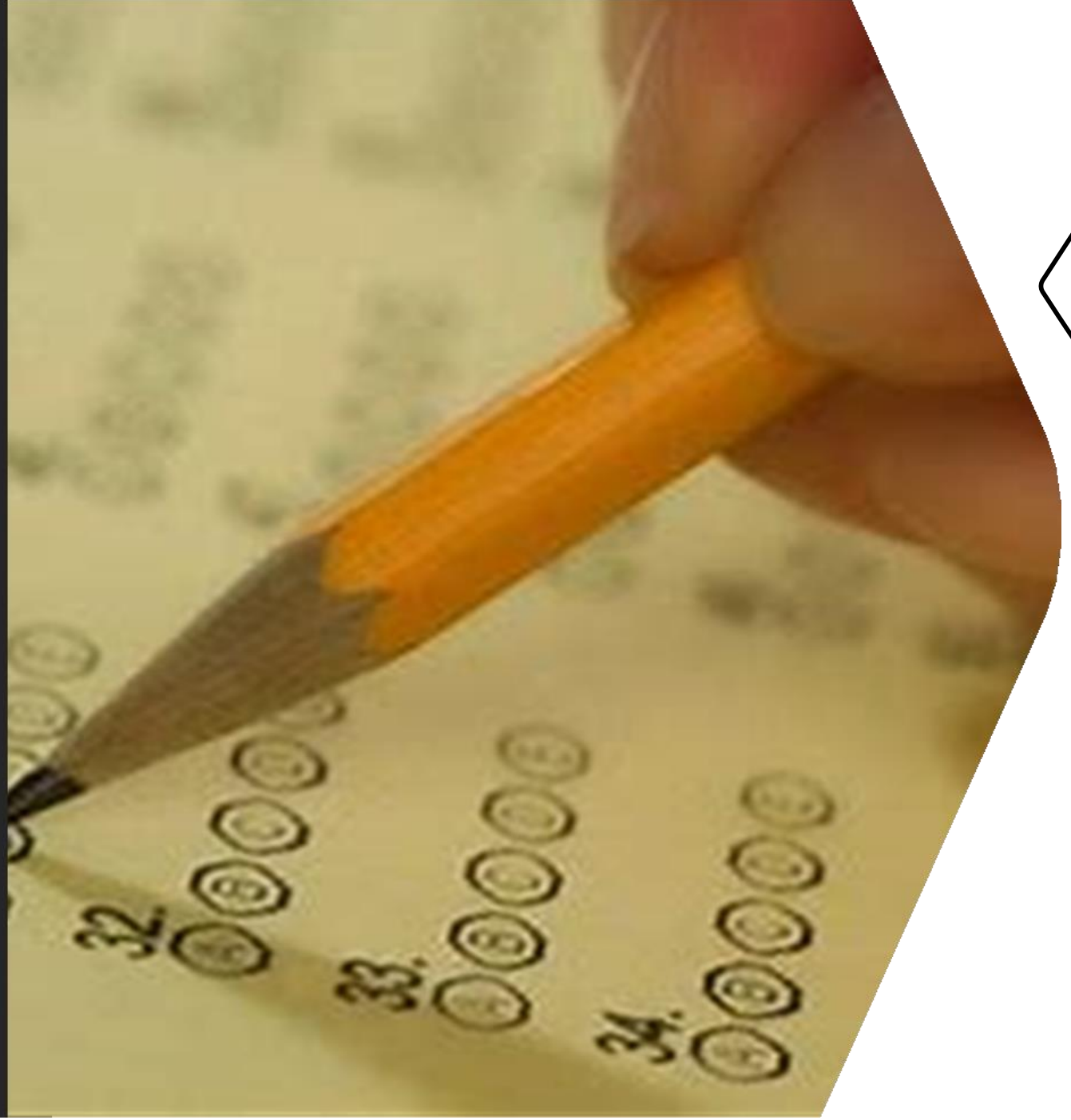
2024

Abdulmoein Eid Al-Agha, FRCPCH.

Professor & Head of Pediatric Endocrinology section.

King Abdulaziz University.

http://aagha.kau.edu.sa



During your PICU shift, you have a 12-year-old female with diabetes mellitus who is having diabetic ketoacidosis. Upon admission, her blood glucose level was 756 mg/dL, with a pH of 7.15 and 4+ ketones. Following an initial bolus of normal saline and 5 hours of intravenous fluid therapy with normal saline, along with an insulin infusion, her glucose level improved to 215 mg/dL. However, her pH remains suboptimal at 7.2, and her serum anion gap and ketone levels persist. Which intervention is most appropriate?

a) Continue normal saline infusion rate and transition from IV insulin infusion to a long-acting subcutaneous.
b) Substitute the IV fluid regimen with dextrose-containing solution and potassium, while continuing the IV insulin infusion.
c) Sustain the existing normal saline infusion rate and decrease the IV insulin infusion to half its current rate.
d) Scale down the IV fluid administration to a maintenance level and continue the IV insulin infusion.

The answer is B: change the intravenous (IV) fluid regimen to D5NS with potassium at the present rate, while simultaneously sustaining the IV insulin infusion.

Explanation: In managing diabetic ketoacidosis, it's crucial to uphold IV insulin infusions until serum ketones are eliminated. As blood glucose dips below 250–300 mg/dL, it's necessary to introduce dextrose into the IV infusion to uphold glucose levels while ketones are being cleared, preventing the risk of hypoglycaemia.

A female patient visits your clinic complaining of short stature. Her weight percentile is higher than her height, and she exhibits short fingers and toes. Notably, several family members share a similar physical appearance. Upon reviewing her laboratory results, you find her calcium level is low at 6.8 mg/dL, phosphorus is high at 7.0 mg/dL, and PTH is elevated at 100 pg/ml. Which of the following diagnoses is the most likely diagnosis?

a) Pseudohypoparathyroidism.
b) Vitamin D–deficient rickets.
c) Pseudopseudohypoparathyroidism.
d) Hypoparathyroidism.

Answer A suggests pseudohypoparathyroidism as the likely diagnosis.

- This diagnosis is supported by the patient's short stature, short fingers & toes, family history, and weight percentile greater than height.
- Pseudohypoparathyroidism involves resistance to parathyroid hormone .
- Hypoparathyroidism presents with normal physical appearance but low PTH levels, low calcium & high phosphorus.
- Pseudopseudohypoparathyroidism shares physical features with pseudohypoparathyroidism but has normal laboratory findings.
- Vitamin D–deficient rickets display low calcium & phosphorus levels.
- Hypophosphatemic rickets manifest with low phosphorus levels alongside a normal PTH.

A 9-year-old boy attends his regular check-up appointment. He maintains growth at the 5th percentile for both height and weight. Which diagnostic test can distinguish constitutional growth delay from familial short stature?

a) Thyroid-stimulating hormone (TSH)
b) Assessment of bone age
c) Insulin-like growth factor 1 (IGF-1) & (IGF-BP3)
d) Basal GH level

The correct answer is B: Bone age

- Patients with familial short stature and constitutional growth delay often have a normal growth velocity (3rd to 5th percentile).
- The crucial difference lies in bone age assessment.
- Familial short stature typically presents with a normal bone age, matching chronological age.
- Constitutional growth delay is characterized by a delayed bone age.
- Other laboratory tests mentioned (IGF-1, IGF-BP3, and TSH) are commonly used for screening in cases of abnormal growth velocities.
- Random growth hormone levels do not help diagnose growth hormone deficiency due to the pulsatile secretion of growth hormone. Growth hormone stimulation testing is preferred for this diagnosis.

A 16-year-old male with a history of color blindness presents with delayed puberty. He also underwent cleft lip/palate repair shortly after birth. Notably, his voice tone has not deepened, he lacks facial hair and shows minimal muscle development. Testicular volume is t 4 ml. Which of the following clinical findings is likely to be identified?

a) Small, deformed pinna associated with preauricular tags or pitting
b) anosmia or hyposmia
c) Coloboma
d) Multiple café au lait spots associated with axillary freckling

The answer is B: Abnormal results during testing of the first cranial nerve.

- Kallmann syndrome is characterized by: Anosmia or hyposmia, detected during testing of cranial nerve 1 (olfactory nerve) associated with red-green color blindness, midline facial abnormalities, urogenital tract issues, hearing loss, and mirror movements.
- Agenesis of the olfactory bulbs.
- Delayed puberty or incomplete sexual development is common.
- Additional findings may include prepubertal testes, micropenis, and cryptorchidism.
- Small, deformed pinna with preauricular tags or pitting is associated with Goldenhar syndrome.
- Colobomas are part of the CHARGE association or may occur in Treacher-Collins syndrome.
- Port-wine nevi are seen in Sturge-Weber syndrome or Klippel-Trénaunay syndrome.
- Multiple café au lait spots with axillary freckling are characteristic of neurofibromatosis.

A 9-year-old boy presents to the clinic with complaints of bone pain and difficulty walking. His parents report noticing that he seems to have bowed legs. Upon examination, you observe characteristic signs of rickets, including bowed legs, rachitic rosary, and delayed dentition. parathyroid hormone (PTH) levels are within the normal range. Which form of rickets is indicated by normal parathyroid hormone (PTH) levels?

a) Renal rickets (renal osteodystrophy)
b) Hypophosphatemic rickets
c) Vitamin D–dependent rickets
d) Rickets due to deficiency of 25-OH

- Familial hypophosphatemic rickets is a rare condition characterized by increased renal phosphate loss.
- Inheritance: Primarily X-linked, but can also be autosomal dominant or recessive.
- Clinical presentation: Skeletal deformities, such as the "rachitic rosary", are more pronounced in males.
- Calcitriol levels may appear normal but are disproportionately low given the degree of hypophosphatemia.
- Parathyroid hormone (PTH) levels typically remain normal due to inadequate phosphorus loss-triggered secretion.
- Laboratory findings: Normal calcium, low serum phosphorus, elevated alkaline phosphatase.
- Other answer choices would likely lead to increased PTH secretion due to hypocalcemia, the primary stimulus for PTH release.

A 6-year-old boy presents with a recent onset of increased urination frequency. His mother reports he urinates 2–3 times per hour and wakes multiple times at night to drink and urinate. Despite previously being dry at night, he now experiences nocturnal enuresis. Additionally, he exhibits constant thirst. Urinalysis revealed specific gravity below 1.005 (normal range: 1.001−1.035). Further assessment reveals a urine osmolality of 75 mOsm/kg (normal range: 50–1,200 mOsm/kg) and a serum osmolality of 305 mOsm/kg (normal range: 275–295 mOsm/kg). Which of the following statements regarding this child's condition is accurate?

a) Primary polydipsia.
b) Administering DDAVP will distinguish between central and renal diabetes insipidus.
c) Urine sodium concentration is expected to be elevated.
d) Serum sodium levels will likely be below 135 mEq/L.

The answer is B: Administration of DDAVP aids in distinguishing between central and renal etiology.

- Presentation consistent with acquired diabetes insipidus (DI), likely central in origin.
- In DI, inability to concentrate urine due to lack of ADH (central) or insensitivity to it (nephrogenic).
- Diagnosis relies on observing low urine osmolality despite high serum osmolality.
- Water deprivation test helps; if serum osmolality rises without a corresponding increase in urine osmolality, DDAVP distinguishes central from nephrogenic DI.
- In central DI, urine concentrates due to ADH deficiency; in nephrogenic DI, response is diminished due to renal defects.
- Primary polydipsia causes low serum and urine osmolality.
- Serum sodium is expected to be high in both central and nephrogenic DI due to water loss; urine sodium is low due to free water loss.
- Elevated ADH levels are seen only in nephrogenic DI; low in central DI, making DDAVP administration a more likely choice.
- Syndrome of inappropriate ADH secretion causes water retention, opposite to DI's water loss.

During a routine annual health check-up for a 3-year-old girl, you observe a single central incisor during your examination. This finding prompts consideration of her potential risk for certain conditions. Which of the following conditions is the most likely?

a) Neonatal diabetes
b) Primary hypothyroidism
c) Addison's disease
d) Growth hormone deficiency

The answer is growth hormone deficiency

- Solitary median maxillary central incisor (SMMCI) is a rare midline malformation (incidence 1:50,000 live births).
- Associated with increased risk of pituitary maldevelopment (empty sella) & panhypopituitarism.
- SMMCI is often associated with other midline defects like cleft lip/palate, midline brain structure abnormalities, and nasal passage obstructions.
- Syndromes linked to SMMCI include holoprosencephaly, Goldenhar syndrome, oromandibular limb hypogenesis syndrome Type 1, CHARGE syndrome, and VACTERL association.
- Ectopic neurohypophysis (EN) is found in up to 43% of short-statured children with GH deficiency, more common in panhypopituitarism.
- Pituitary maldevelopment implicated in EN, alongside anterior pituitary hypoplasia.
- Close growth monitoring is recommended for children with SMMCI, with evaluation for GH deficiency to enable early diagnosis and treatment.

At 35 weeks of gestation, a 3.95 kg boy is delivered via cesarean section after an otherwise uneventful pregnancy. Apart from his larger-than-average size for his gestational age, he presents with notable clinical features including a protruding tongue, easily palpable and enlarged kidneys, hepatosplenomegaly, and persistent hypoglycemia.
Which additional physical finding is expected to be found of this baby?

a) Myelomeningocele
b) Aniridia
c) Sensorineural hearing loss
d) Omphalocele

The Answer is Omphalocele

- Clinical features suggest Beckwith-Wiedemann syndrome (BWS), characterized by excessive somatic growth.
- BWS associated with chromosomal abnormalities on 11p15.5, impacting methylation of imprinted genes.
- Infants with BWS may have prematurity, macroglossia, hemihypertrophy, hepatosplenomegaly, and nephromegaly.
- Increased risk of abdominal wall defects like omphalocele, diastasis recti, and umbilical hernia.
- Hyperplasia of pancreatic β-cells leads to severe hypoglycemia.
- Require screening for embryonal tumors, including Wilms tumor or hepatoblastoma, via abdominal ultrasound and α-fetoprotein (AFP) measurements.
- Additional screening includes renal ultrasound and urinary calcium/creatinine ratio assessments.
- Not associated with coarctation of the aorta, myelomeningocele, aniridia (linked with WAGR syndrome), or sensorineural hearing loss.

At 5 days old, a full-term infant arrives at the emergency department following a Hypocalcaemic seizure. The baby was delivered at home, and no prenatal care or birth history records are available. This episode of seizure is reported to be the first by the mother. What is the most likely cause of the seizure?

a) An infant of a diabetic mother
b) Hypoparathyroidism
c) Sepsis
d) Birth asphyxia

Answer is Hypoparathyroidism

- Differential diagnosis for Hypocalcaemic seizures in newborns involves early onset (within 72 hours of life) and late-onset (after 72 hours of life) categories.
- Hypoparathyroidism is the sole late-onset cause among the answer options.
- Early-onset hypocalcemia causes include:
  - Infant of a diabetic mother: Maternal hyperglycemia leads to fetal hyperinsulinemia, which suppresses fetal parathyroid hormone secretion.
  - Intrauterine growth restriction: Decreased fetal calcium stores due to poor placental perfusion.
  - Sepsis: Systemic inflammatory response can disrupt calcium homeostasis.
  - Birth asphyxia: Reduced oxygen delivery affects calcium metabolism.
- Late-onset hypocalcemia is primarily associated with hypoparathyroidism.

A 10-year-old child is brought to the pediatric clinic by their concerned parent, who reports episodes of unexplained hypoglycemia. The child has experienced multiple hospital admissions and emergency room visits due to these episodes. The parent states that the child seems fine at home but suddenly becomes lethargic, shaky, and sweaty, prompting the parent to administer sugary snacks. Laboratory tests confirm hypoglycemia during these episodes. Which of the following findings is suggestive of factitious hypoglycemia rather than a genuine metabolic disorder?

a) Persistent hypoglycemia during fasting.
b) High insulin with undetectable C- peptide.
c) Low insulin-to-glucose ratio during hypoglycemia.
d) Elevated ketones in the urine.

- Factitious hypoglycemia is a condition where a patient intentionally induces episodes of low blood glucose levels, often for various psychological or secondary gains.
- Patients may present with recurrent episodes of hypoglycemia, which seem inconsistent with their usual medical history. Symptoms may include sweating, shakiness, and altered mental status during these episodes.
- Factitious hypoglycemia typically occurs when the individual is under observation, such as in a healthcare setting or in front of family members or caregivers.
- To differentiate factitious hypoglycemia from genuine metabolic disorders, consider the following:
    - Lack of symptoms during hypoglycemic episodes when unsupervised.
    - A rapid return to normal glucose levels after administration of glucose.
    - A high insulin-to-glucose ratio during episodes.
    - A discrepancy between the patient's reported symptoms and laboratory findings.
- To confirm the diagnosis, conduct laboratory tests during a suspected episode, including:
    - Measurement of plasma insulin and C-peptide levels.
    - Assessment of serum cortisol levels.
    - Assessment of ketone levels in the urine to rule out true hypoglycemia.
- Treatment should involve a multidisciplinary approach, including psychiatric evaluation and therapy to address the underlying psychological issues that drive the patient to induce hypoglycemic episodes.

Seven-year-old girl, presented to the endocrine clinic because of short stature, which was reported since birth. She continued to be shorter than her schoolmates. On examination (photo). Which one of the following is a diagnostic investigation?

a) Bone age assessment.
b) Skeletal survey.
c) Thyroid function test.
d) Chromosomal analysis.

Achondroplasia

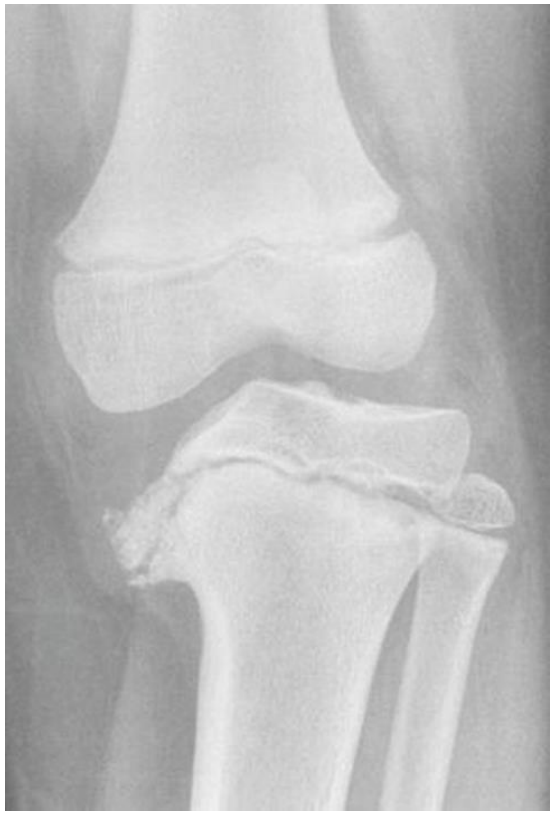
- Occurs due to sporadic mutations in the majority of cases but can be inherited as autosomal dominant condition.
- Achondroplasia is the most common form of disproportionate short stature.
- Generally recognizable intrauterine because of short limbs & macrocephaly.
- Limb shortening is predominantly in the proximal segment (rhizomelic).
- A **trident hand** is a description where the hands are short with stubby fingers, with a separation between the middle and ring fingers.
- Children with achondroplasia have normal intelligence.
- Specialized growth charts have been developed for head circumference, height.
- They have significant midface hypoplasia, which increases the risk of obstructive sleep apnea.
- The narrowing of the foramen magnum can cause brainstem compression with an increased incidence of sudden infant death.

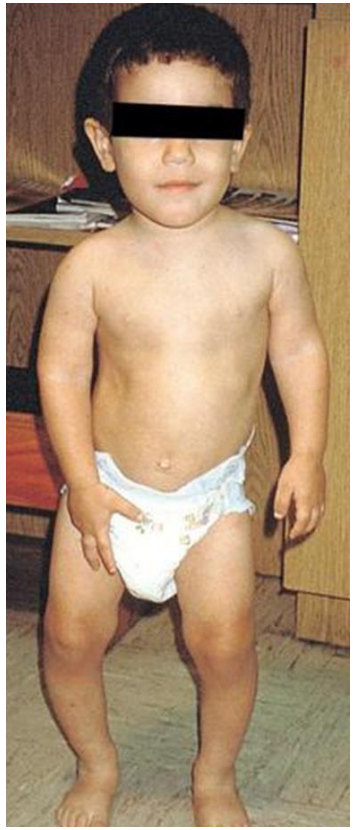
Vosoritide (New modality of therapy)

- Vosoritide is a C-type natriuretic peptide (CNP) analog.
- Vosoritide mimics CNP is a natural regulator of growth plate function, and vosoritide, as a synthetic CNP analog, seeks to harness the benefits of CNP's actions to address the underlying cause of achondroplasia, which is the disruption of bone growth due to the FGFR3 genetic mutation.
- Vosoritide holds the potential to stimulate longitudinal bone growth and improve the stature of individuals with achondroplasia.

Eighteen–month–old boy, brought by his parents because of increasing bowing of his legs (photo). Nutritional history was unremarkable. He has been on a vitamin D prophylactic daily dose (400 units) since birth. His limb x-ray (photo). His bone profile including calcium, phosphate, and alkaline phosphatase were normal. Which one of the following is the most likely diagnosis?

a) Osteodystrophy.
b) Vitamin D resistant rickets.
c) Blount's disease.
d) Hypophosphatasia.





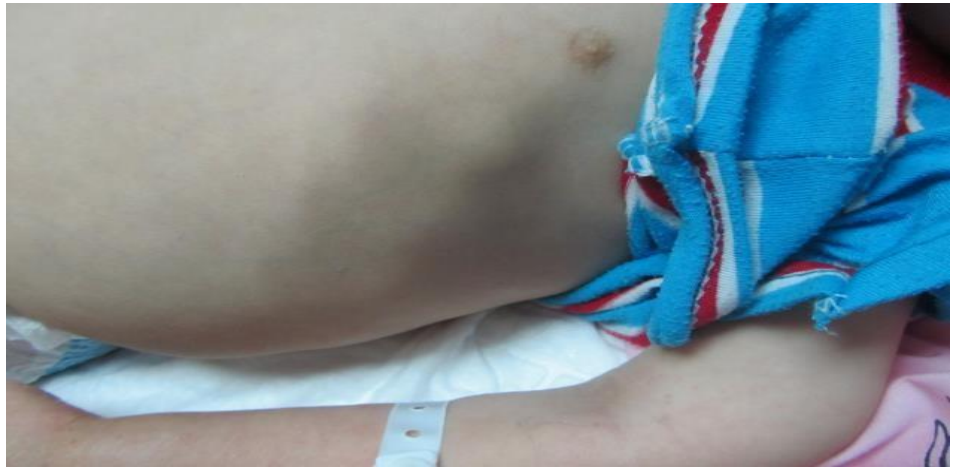
Tibia vara (Blount's disease)

- Described by Dr. Walter Blount (1900–1992) "American pediatric orthopedic surgeon".
- The cause in the majority of cases is unknown.
- Sometimes associated with obesity because of weight on the growth plate.
- Is progressive disease.
- Severe bowing of the legs "unilateral or bilateral".
- Blount disease involves a growth plate disturbance in the upper tibia, leading to excessive inward angulation (varus) of the bone.
- Blount disease is categorized into infantile (before age 4) and adolescent forms.
- Infantile Blount disease may involve bracing or surgery, while adolescent Blount disease often requires surgical correction, such as osteotomy.

Differential Diagnosis of Bowing of Legs in Children

- Physiologic Genu Varum: normal bowing of the legs in infants and toddlers, typically resolves as the child grows.
- Blount Disease (Tibia Vara): growth disorder causing abnormal leg bowing, especially in early childhood.
- Rickets: vitamin D deficiency or other metabolic bone disorders leading to bowed legs.
- Skeletal Dysplasia: genetic conditions like achondroplasia, can cause short stature and bowing.
- Metabolic Disorders: e.g., hypophosphatasia affecting bone development.
- Trauma or Fractures: Injuries can lead to bowed legs if improperly managed.
- Skeletal Infections: Osteomyelitis or other infections affecting the bones.
- Osteogenesis Imperfecta: genetic disorder causing brittle bones and bowing.

A two-year-old boy was referred for further assessment of his increasing bowlegs. His brother has rickets. On chest examination (photo). Investigations revealed obtained: serum calcium: 2.37mmol/l, phosphate: 0.13mmol/l, alkaline phosphatase: 805IU/l, PTH: 1.3pmol/l. Which one of the following is the most likely diagnosis?

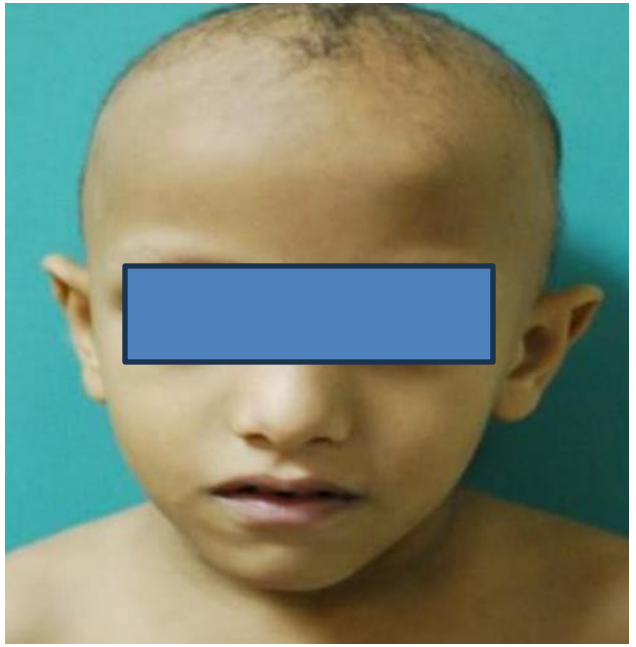


a) Nutritional rickets.
b) Vitamin D dependent type 1 rickets.
c) Vitamin D dependent type 2.
d) X- linked hypophosphatemic Rickets.

X-linked hypophosphatemic Rickets (XLH)

- Is a genetic disorder characterized by a phosphate-wasting renal tubular defect, leading to low phosphate levels in the blood, which results in impaired bone mineralization.
- Is an X-linked dominant disorder, primarily affecting females but can also manifest in males.
- Mutations in the PHEX gene cause XLH, leading to increased FGF23 levels and reduced phosphate reabsorption.
- XLH typically presents during childhood and includes symptoms like bowed legs, short stature, bone pain, dental abnormalities, and muscle weakness.
- Laboratory tests reveal low phosphate levels (hypophosphatemia) and high levels of fibroblast growth factor 23 (FGF23), which impairs phosphate reabsorption in the kidneys.
- The primary treatment for XLH is oral phosphate and active vitamin D supplementation to correct hypophosphatemia. This helps improve bone mineralization and growth.
- Burosumab (monoclonal antibody) was licensed in 2018 as the first drug for this condition.

An Eighteen-month-old boy was referred for further assessment of his increasingly bowing legs. His parents are first-degree cousins. He has been on vitamin D3 therapy for the last 6 months, a dose of 3000 units/day with good compliance. On examination, in addition to the manifestation of rickets, he has alopecia capitis. Serum calcium:1.37mmol/L, phosphate: 0.13mmol/L, alkaline phosphatase: 805IU/L, PTH: 100 (6-15) pmol/L. Which one of the following is a diagnostic investigation?



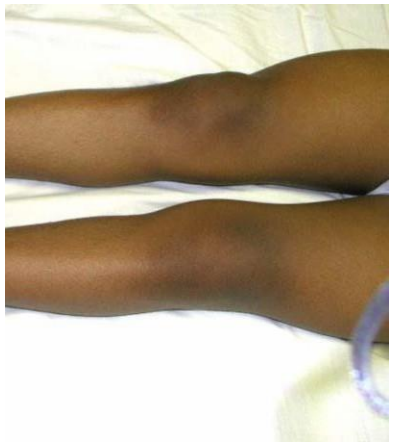
a) Wrist X-ray to confirm active rickets.
b) 25- hydroxy vitamin D metabolite.
c) 25 &1,25- di hydroxy vitamin D metabolites.
d) FGF23 level.

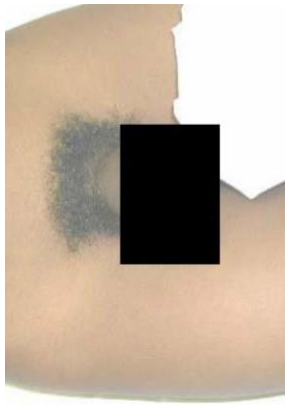
HRVD type 2

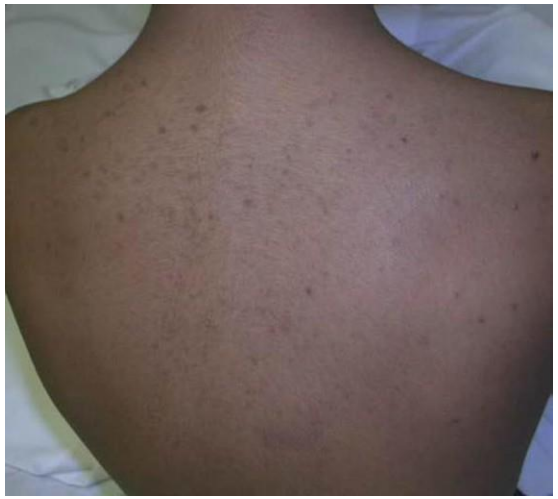
- Is a rare, autosomal recessive form of rickets.
- Reported so far worldwide in approximately 100 cases only.
- Is associated with end–organ resistance to 1,25-dihydroxyvitamin D.
- Caused by mutations in the gene encoding the vitamin D receptor.
- Affected children usually appear normal at birth, develop rickets within the first two years of life.
- Alopecia and ectodermal anomalies resulting from the lack of vitamin D receptor activity within keratinocytes develops in approximately two-thirds of cases and is a marker of disease severity (HRVD type 2A).
- Other patients without alopecia or other ectodermal anomalies (HRVD type 2B).

A five-year-old boy previously well, started to develop pubic hair, which has been increasing steadily, adult-type body odor, and acne on his back (photos). On examination, pubic hair and penis Tanner stage 2, testicular volumes of 3 ml bilaterally. Which one of the following is the most likely diagnosis?

a) Non – classical CAH
b) Premature Adrenarche.
c) Hypothalamic hamartoma.
d) Idiopathic precocious puberty.





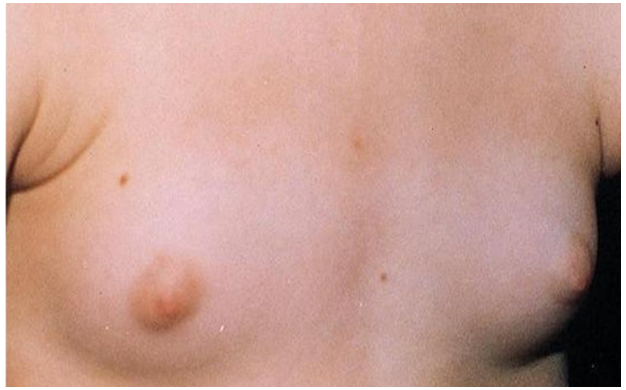


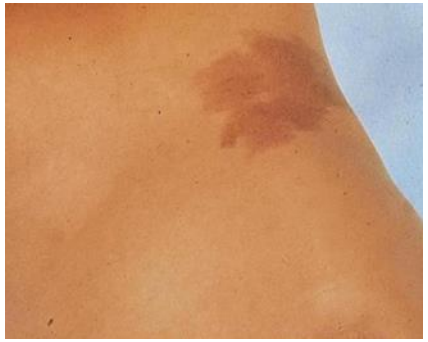
"Nonclassical" / late-onset CAH

- It does not manifest with neonatal genital ambiguity; rather, it presents later in life with signs of androgen excess.
- Clinical features in late childhood include premature pubarche, acne, and accelerated bone age.
- In adolescent girls and adult women, non-classic CYP21A2 deficiency is characterized by acne, hirsutism, and menstrual irregularity (oligoovulation) that are indistinguishable from polycystic ovary syndrome.
- Never presents with adrenal crisis.

A Three-year-old girl was brought by her mother because of bilateral breast enlargement and spotty vaginal discharge. On examination (see photo). Her basal pubertal investigations revealed low levels of LH and FSH with high Estradiol. Which one of the following, is the most important confirmatory investigation you will order?

a) GnRH stimulation test.
b) Gene mutation screening.
c) Thyroid function test.
d) Skeletal survey.





McCune-Albright syndrome (MAS) consists of at least 2 of the following 3 features:

- Polyostotic fibrous dysplasia.
- Café-au-lait skin pigmentation.
- Autonomous endocrine hyperfunction (e.g., gonadotropin-independent precocious puberty).
- Other endocrinopathies may be present, including:
  - hyperthyroidism, acromegaly, & Cushing syndrome.
- Activating mutation of the GNAS1 gene, which is involved in G-protein signaling.

A 16-year-old male presents to the pediatric endocrinology clinic with concerns about his delayed puberty. His parents are worried because they've noticed that he hasn't shown any growth of facial hair or a deepening voice. There was a past surgical repair of a cleft lip/palate. Upon examination. red-green color blindness and his Tanner staging were prepubertal with Testicular volume estimated at 4–5 ml. Which of the following cranial nerve examinations is important?

a) First cranial nerve
b) Third cranial nerve
c) Fifth cranial nerve.
d) Seventh cranial nerve.

Kallmann syndrome

- Patients with hypogonadotropic hypogonadism associated with one or more nongonadal congenital abnormalities often have Kallmann syndrome.
- Characterized by anosmia or hyposmia detected during testing of cranial nerve 1 (olfactory nerve),
- patients may also have:
  - red-green color blindness
  - midline facial abnormalities (cleft lip/palate)
  - urogenital tract abnormalities
  - neurosensory hearing loss and mirror movements.
- Hypogonadism is secondary to failure of gonadotropin-releasing hormone (GnRH)-producing neurons to migrate from the olfactory placode to the brain, and agenesis of the olfactory bulbs.
- Patients with Kallmann syndrome usually present with delayed puberty or incomplete sexual development. Anosmia or hyposmia is present in 80% of patients and confirms the diagnosis in individuals with isolated gonadotropin deficiency.
- Prepubertal testes, micropenis, and cryptorchidism are common additional findings.

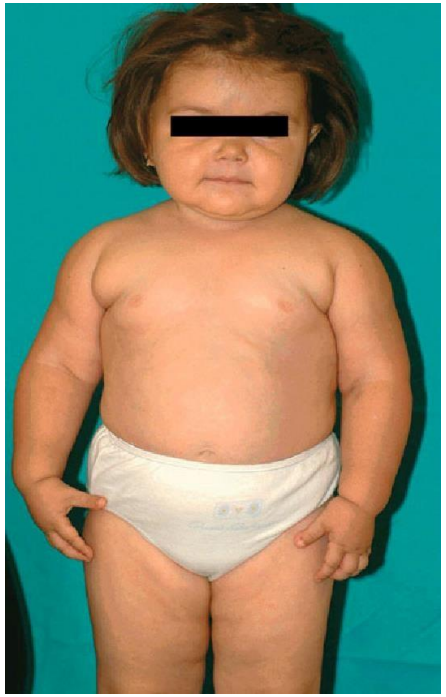
A 15-year-old male presents to your clinic with concerns about delayed puberty, bilateral gynecomastia, and sparse facial hair. He reports that he has not started shaving yet. Physical examination reveals gynecomastia and small testes. He has a history of learning difficulties in school. His initial laboratory investigations reveal Testosterone low, High LH, and high FSH for age and gender. What is the most likely diagnosis for this patient?

a) Kallmann syndrome.
b) Klinefelter syndrome.
c) Androgen Insensitivity Syndrome.
d) Fragile X Syndrome.

Klinefelter syndrome

- Klinefelter syndrome is a genetic condition characterized by the presence of an extra X chromosome (XXY) in males.
- Common clinical features include delayed puberty, gynecomastia, small testes, tall stature, and learning difficulties.
- It is one of the most common sex chromosome disorders, affecting approximately 1 in 500 to 1,000 male births.
- This patient's clinical presentation is highly suggestive of Klinefelter syndrome, and the karyotype analysis confirmed the diagnosis.

Five-year-old girl, presented with short stature since birth. Both parents were first cousins. On examination, she looked dysmorphic (photo). She had a growth hormone stimulation test with a good response, but her basal IGF-1 and IGFBP3 level was low. The bone age was 2 years. Which one of the following is the most likely diagnosis?



a) Achondroplasia.
b) Turners' syndrome.
c) Laron syndrome.
d) Noonan syndrome.

Growth hormone receptor mutations (Laron syndrome)

- Is the most commonly known cause of genetically mediated growth hormone receptor insensitivity.
- Is characterized by severe postnatal growth failure.
- Clinical features of Laron syndrome include:
  - Characteristic facies with saddle nose & prominent forehead.
  - Delayed skeletal maturation.
  - Small genitalia and testes.
  - Short limb length compared with trunk length.
  - abnormal body composition.
  - osteopenia and obesity.
- Characterized by normal or increased circulating levels of GH with low circulating levels of IGF-1 & IGFBP-3.

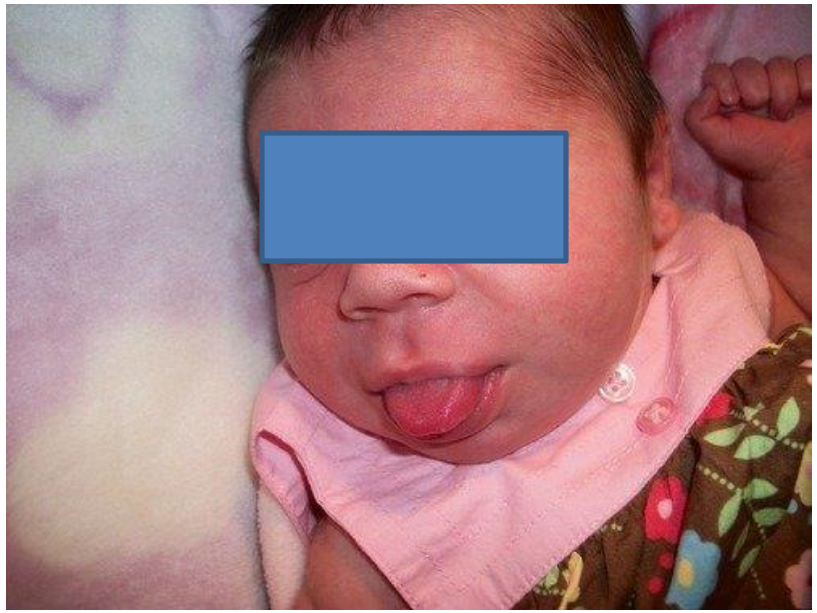
A thirteen-year-old boy was growing well until 2 years ago when his family noticed slow growth. He is an otherwise healthy child. On his examination, his height percentile dropped below 3rd. percentile in comparison to 25 %, 2 years ago. His Tanner's stage was prepubertal. Bone age was 9 years. Which one of the following, is the MOST likely cause of short stature?

a) Familial short stature.
b) Growth hormone deficiency.
c) Constitutional delay.
d) Hypogonadism.

Constitutional delay of growth and puberty (CDGP)

- Children with CDGP usually grow at a low-normal rate (e.g., about 4 to 5 cm/year in preadolescent girls, and 3.5 to 4.5 cm/year in preadolescent boys).
- In addition to a low preadolescent height velocity, they tend to have delayed pubertal development.
- This leads to a marked height discrepancy during the early teenage years compared with their peers but is followed by catch-up growth when they do enter puberty with normal final adult height.
- In many cases, there is a family history of delayed growth and puberty in one or both parents (sometimes described as being a "late bloomer").

Four–day–old boy, with a birth weight of 4.5 kg, with normal antenatal & and natal histories. He developed seizures because of repeated hypoglycemic attacks down to 32 mg/dl). His general look (photo). What is the most likely cause of hypoglycemia?



a) Large for gestation age.
b) Infant of diabetic mother.
c) Septicemia.
d) Beckwith-Wiedemann syndrome.

Beckwith-Wiedemann syndrome (BWS)

- BWS is an overgrowth syndrome.
- Is a genetically heterogeneous disorder that involves an imprinted region of chromosome 11p15.
- Characterized by:
  - Antenatal & postnatal overgrowth.
  - Macroglossia.
  - Hypoglycemia.
  - Hemihypertrophy.
  - Ear creases or pits
  - Abdominal wall defects (omphalocele).
  - Increased risk of embryonal tumors (Wilms 'tumor & hepatoblastoma).
  - Mental retardation is uncommon and usually related to early hypoglycemia.

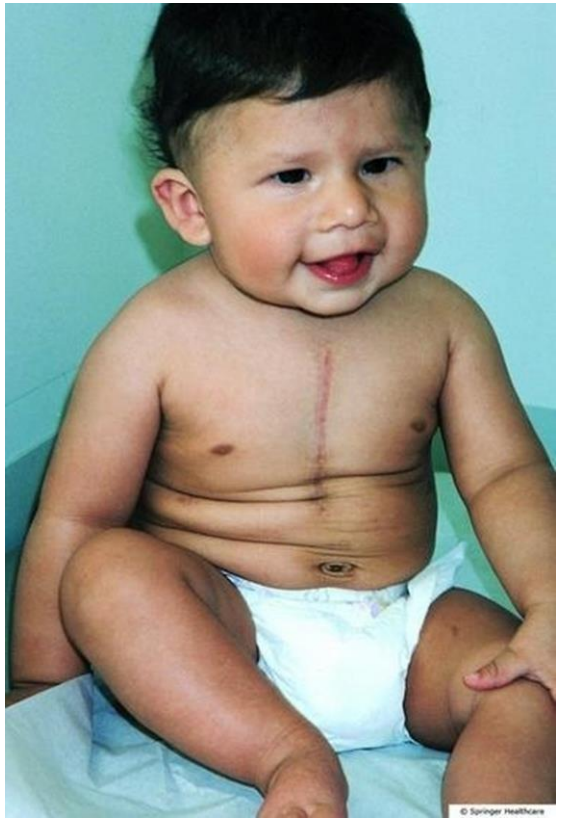
Eleven-year-old boy, presented with mental subnormality, facial dysmorphism (photo), and severe growth failure. Which diagnostic laboratory investigation, you are going to order?

a) Chromosomal analysis.
b) GH provocative test.
c) Bone age.
d) Serum calcium, phosphate & PTH.

- Sanjad Sakati syndrome (SSS) is an autosomal recessive disorder found exclusively in people of Arabian origin.
- It was first reported from the Kingdom of Saudi Arabia in 1988 as a newly described syndrome mainly from the Middle East and the Arabian Gulf countries.
- Children affected by this condition are:
  - Severe growth failure in both intrauterine & and extra uterine.
  - Mild to moderate mental retardation.
  - Present with hypocalcemic tetany or seizures due to hypoparathyroidism at an early stage in their lives.
  - Dysmorphic features include; a long narrow face, deep-set small eyes, beaked nose, large floppy ears, and micrognathia.

Nine-month-old boy was brought by his parents due to repeated attacks of hypocalcemia since birth, with a past history of open heart surgery during the neonatal period. His general examination (photo). Which one of the following investigations is essential to reach the diagnosis of hypocalcemia?

a) Serum ionized calcium.
b) Serum phosphate.
c) Serum 25- hydroxy vitamin D.
d) Serum Parathyroid hormone.

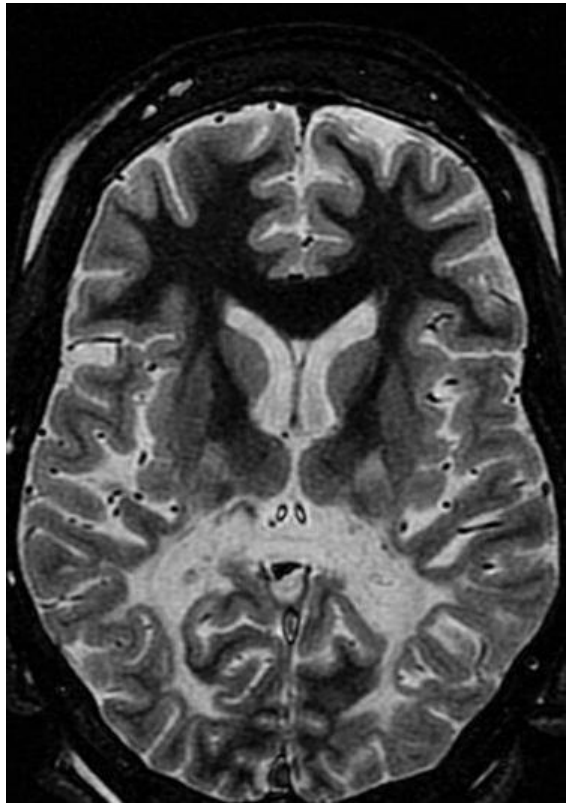


DiGeorge syndrome, “22q11.2 deletion syndrome”

- Is caused by deletion of a small segment of chromosome 22.
- The major features include congenital heart disease, hypocalcemia
  - due to hypoparathyroidism & defective T-cell immunity.
- Truncus arteriosus or interrupted aortic arch are common.
- Facial features include low-set ears, microstomia, & hypertelorism.
- Embryologic development defects of the third & and fourth brachial arches and their derivatives, which include the parathyroid glands, aortic arch, and thymus gland.
- Infants with low T-cell functions are at risk for common pathogens including candida and herpes simplex, and opportunistic infections, such as *Pneumocystis carinii*.
- The diagnosis can be confirmed by the absence of thymus as detected by chest radiography or by direct inspection during surgery to correct their congenital heart defect.

A four-year-old boy was diagnosed sine neonatal period with primary adrenal insufficiency. Since then, he has been on hydrocortisone replacement therapy with good compliance from his family. The mother has reported that, for the last 6 months, he started to have on/off seizures accompanied by regression of his motor milestone development. He was seen by a neurologist who ordered an MRI brain (photo). Which one of the following is an important diagnostic investigation you are going to order?

a) Do serum ACTH & cortisol level.
b) Do 17 hydroxyprogesterone level.
c) Do serum electrolytes.
d) Do Very long chain fatty acid (VLCFA).

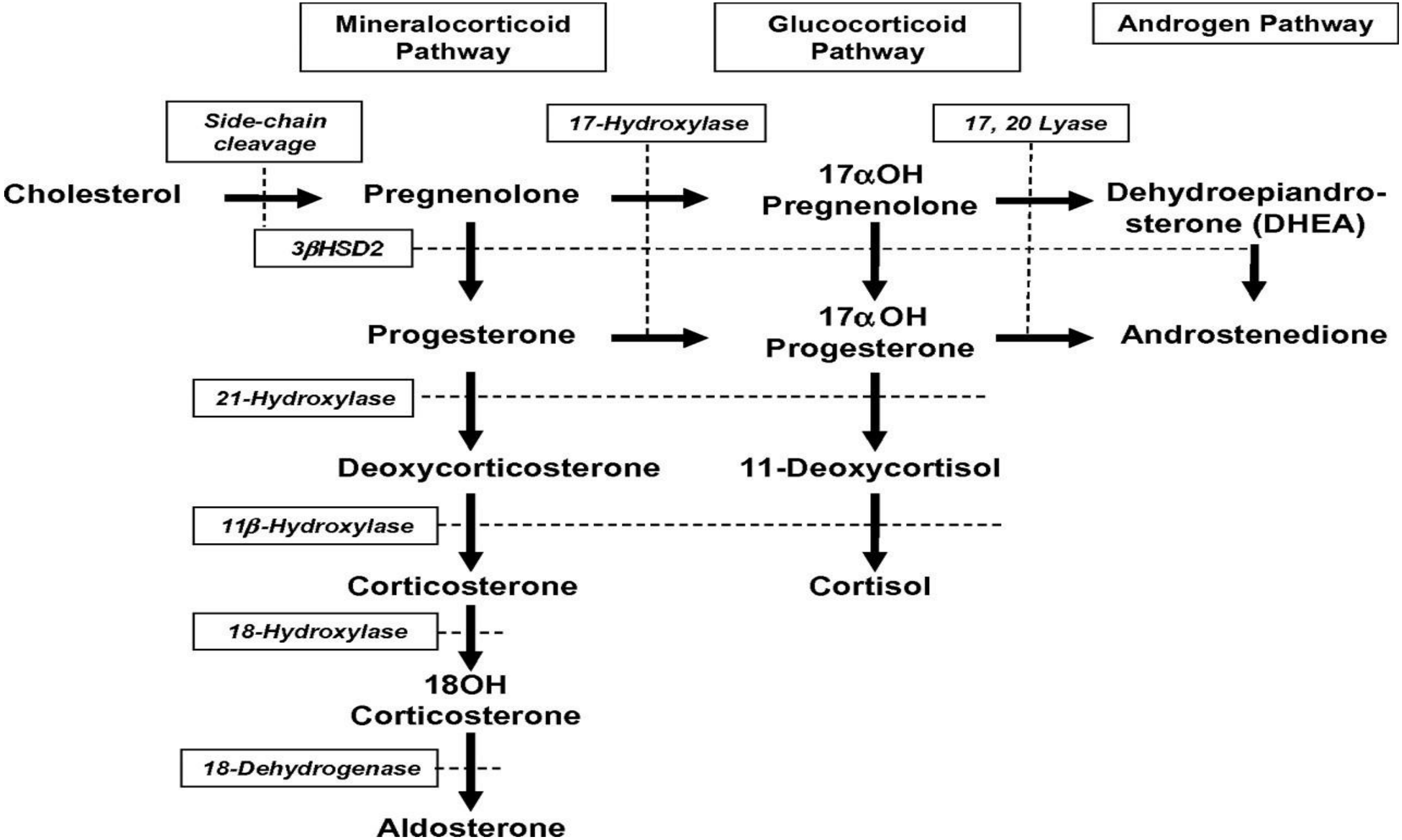


Adrenoleukodystrophy (ALD)

- ALD is one of a group of disorders caused by a defect of peroxisomes, which are essential for the breakdown of fatty acids in cells.
- ALD mostly affects boys because the disease-causing mutation is located on the X chromosome.
- The condition results in the accumulation of very long-chain fatty acids in the nervous system, adrenal gland, and testes.
- There are three major categories of disease:
  - Childhood cerebral form: appears in mid-childhood (ages 4 to 8 years)
  - Adrenomyelopathy: occurs in men in their 20s or later in life.
  - Impaired adrenal gland function (Addison-like phenotype) .

Ten-day-old boy, presented with hypertension & metabolic alkalosis. He was diagnosed with congenital adrenal hyperplasia. Which of the following enzyme deficiencies could be the cause?

a) Aldosterone synthase deficiency.
b) 21-hydroxylase deficiency.
c) 3-β-hydroxysteroid dehydrogenase deficiency.
d) 17- hydroxylase deficiency.


Mineralocorticoid Pathway
Glucocorticoid Pathway
Androgen Pathway
Side-chain cleavage
17-Hydroxylase
17, 20 Lyase
Cholesterol
Pregnenolone
17αOH Pregnenolone
Dehydroepiandro-sterone (DHEA)
3βHSD2
Progesterone
17αOH Progesterone
Androstenedione
21-Hydroxylase
Deoxycorticosterone
11-Deoxycortisol
11β-Hydroxylase
Corticosterone
Cortisol
18-Hydroxylase
18OH Corticosterone
18-Dehydrogenase
Aldosterone

- 17-Hydroxylase (17-OH) deficiency is a rare form of congenital adrenal hyperplasia.
- It causes decreased production of glucocorticoids and sex steroids, resulting in 46, XY DSD.
- Increased synthesis of mineralocorticoids precursors, resulting in hypertension and hypokalemia
- Exogenous glucocorticoid therapy is the treatment of choice that suppresses (ACTH) secretion, decreases 11-DOC and corticosterone levels, and normalizes serum potassium and blood pressure.

Elven-year-old boy, known case of congenital adrenal hyperplasia, on hydrocortisone replacement therapy with not good compliance. Three months ago, started to have right-sided testicular swelling. The mother was worried, and the patient was referred for further assessment. Ultrasound of the testes revealed a right-sided small hypoechoic mass. Which one of the following is the most likely diagnosis?

a) Testicular adrenal rest tumor (TART).
b) Leydig cell hyperplasia.
c) Testicular abscess.
d) Testicular tumor.

Testicular adrenal rest tumors (TART)

- One of the most important and frequently detected complications in male CAH patients is the development of testicular tumors.
- These tumors were first reported in 1940 by Wilkins et al.
- Because of the morphological and functional resemblance with adrenal tissue they are called “testicular adrenal rest tumors” (TART).
- These tumors can be found in childhood and puberty.
- Is an important complication leading to gonadal dysfunction & and infertility.
- Usually, only tumors of more than 2 cm are detectable by palpation because of their location within the rete testis.
- Therefore, the tumors can be easily missed when additional imaging techniques such as ultrasound or (MRI) are not performed.

Sixteen–year–old phenotypically female, presented with primary amenorrhea. Height 160 cm, weight 45 kg. Tanner stage of B3 PH 1-2. What is the most likely diagnosis?

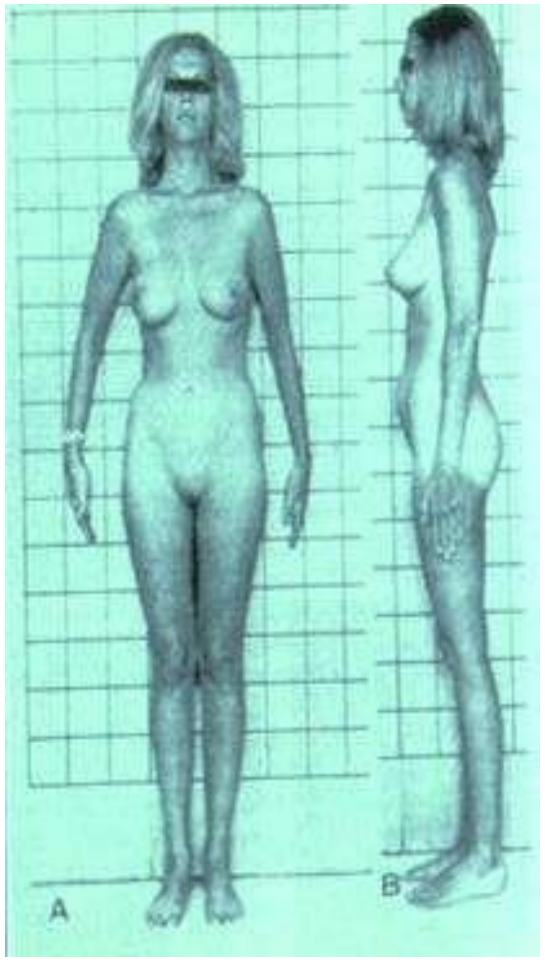
a) Mullerian dysgenesis.
b) Turner’s syndrome.
c) Complete androgen insensitivity syndrome.
d) Kalman's syndrome.

Complete androgen insensitivity syndrome (CAIS)

XY Genotype

Testosterone → ~~*Androgen Receptor*~~

Testosterone —Aromatase→ **Estradiol** → *Estrogen Receptor*



Complete androgen insensitivity syndrome(AIS)

- Formerly known as testicular feminization.
- X-linked recessive condition.
- Resulting in a failure of normal masculinization of the external genitalia in 46 XY.
- Males with complete androgen insensitivity syndrome have completely normal female external genitalia.
- Affected males have normal testes with normal production of testosterone and normal conversion to dihydrotestosterone (DHT).
- No fallopian tubes, uterus, or upper vagina.

A three-year-old boy, presented to the emergency room with severe bronchopneumonia. He was admitted to PICU and then ventilated. His chest x-ray revealed bilateral batch infiltrates. The next day, the in-charge nurse reported a decreased urine output of 0. 3 ml/kg/ hour. His serum electrolytes revealed serum sodium was 115 mmol/l, chloride 98 mmol/l with low serum BUN & and creatinine.
Which one of the following is the expected findings?

a) Low serum osmolality with high urinary osmolality.

b) Low serum and urine osmolality.

c) High serum and urine osmolality.

d) High serum osmolality and low urine osmolality.

The syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

- Is a disorder of impaired water excretion caused by the inability to suppress the secretion of antidiuretic hormone (ADH).
- It should be suspected in any child with hyponatremia, serum hypoosmolality, and urine osmolality above 100 mosmol/kg.
- ADH secretion results in concentrated urine and therefore a reduced urine volume.

Four-month-old infant, presented with failure to thrive. His mother was complaining of too many diaper changes and urine was leaking out of diapers most of the time. On examination, he was having, moderate to severe dehydration. His initial sodium was 175 mmol/l, urine osmolality was 105 mosmol/l, and serum osmolality was 315 mosmol/l. Which one of the following is the most common cause in the differential diagnosis of this infant?

a) Langerhans cell histiocytosis.
b) X-linked dominant nephrogenic DI.
c) DIDMOAD syndrome.
d) Psychological polydipsia.

Congenital nephrogenic diabetes insipidus

- Two genetic mutations have been identified causing nephrogenic diabetes insipidus present at birth.
  - Vasopressin receptor gene mutation (AVPR2) is responsible for 90% of all cases of congenital diabetes insipidus, sex-linked dominant (happens in boys).
  - The remaining 10% of cases, caused by AQP2 gene mutation (responsible for water reabsorption in response to ADH, autosomal recessive (affect both boys and girls)

GOOD LUCK