Endocrine

Royal College Exam Preparation

Dr. Josephine Ho

March 8, 2018

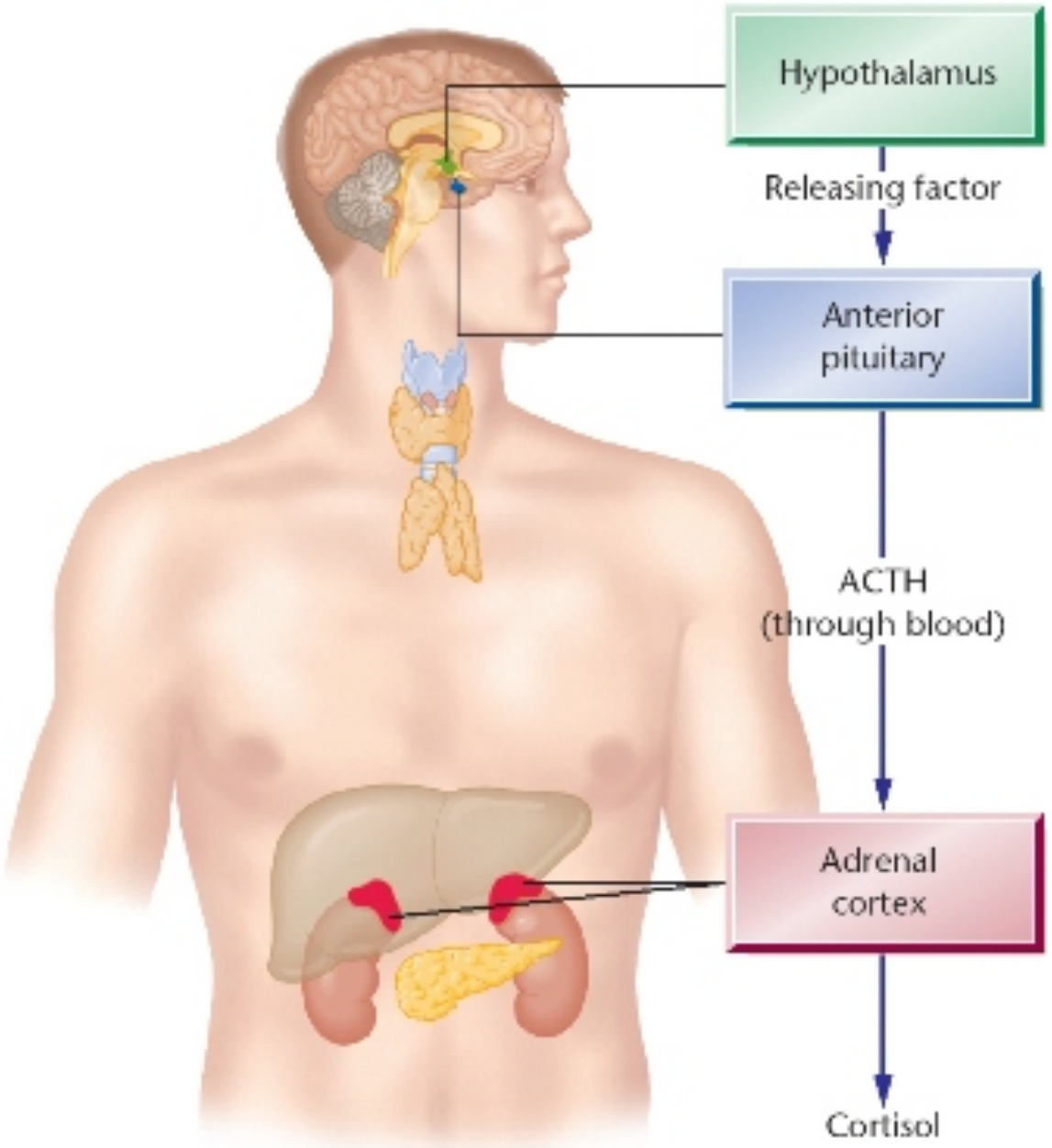
Adrenal Insufficiency

- Teenage girl with **pigmented tongue, hyponatremia.** What is the best way to make a definitive diagnosis?
- a. ACTH level
- b. AM cortisol
- c. ACTH stim test
- d. 17 OHP

Answer: C

- **This question brought up another question of indications for AM cortisol vs. ACTH stim-test?**

- JHO: I would pick C



Primary

http://www.stolaf.edu/depts/cis/wp/winslowj/web/HPA_pic.jpg

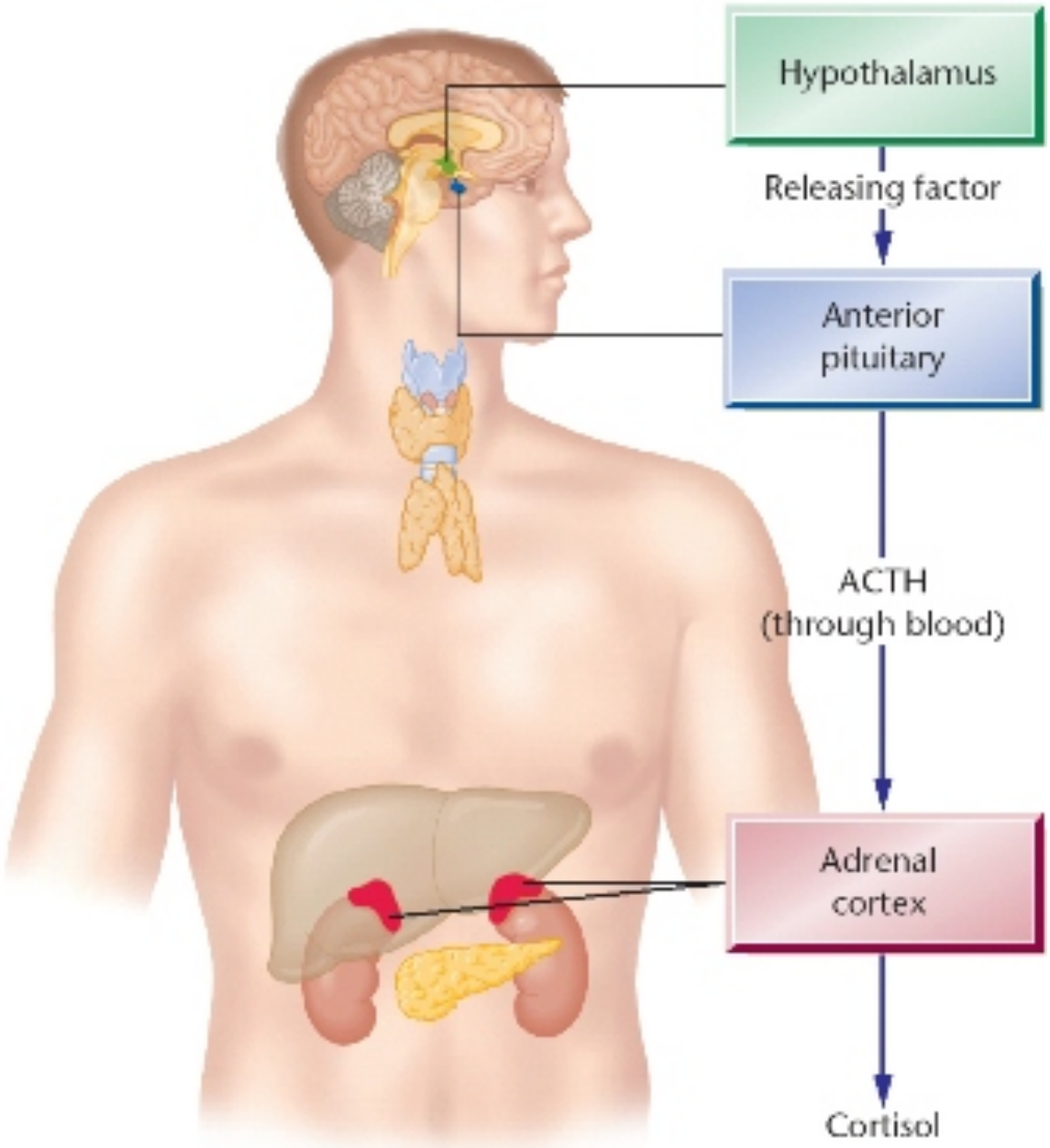
Primary Adrenal Insufficiency (Adrenal Gland)

- Steroidogenesis disorders
  - CAH: 21 hydroxylase deficiency, 11 B hydroxylase deficiency, etc.
  - Multiple enzyme defects have been reported

- Damage to otherwise normal glands
  - Hemorrhage
  - Auto-immunity: AIRE mutation, Addison's
  - Infection: TB, fungus, HIV
  - Drugs: ketoconazole

Primary Adrenal Insufficiency (Adrenal Gland)

- Peroxisomal defects
  - Adrenoleukodystrophy
  - Zellweger syndrome
- Abnormal adrenal development
  - X-linked adrenal hypoplasia congenita (AHC)- DAX1 gene mutation
  - Adrenal hypoplasia due to steroidogenic factor mutation (SF-1 gene)
- Unresponsive to ACTH
  - Allgrove syndrome



Secondary

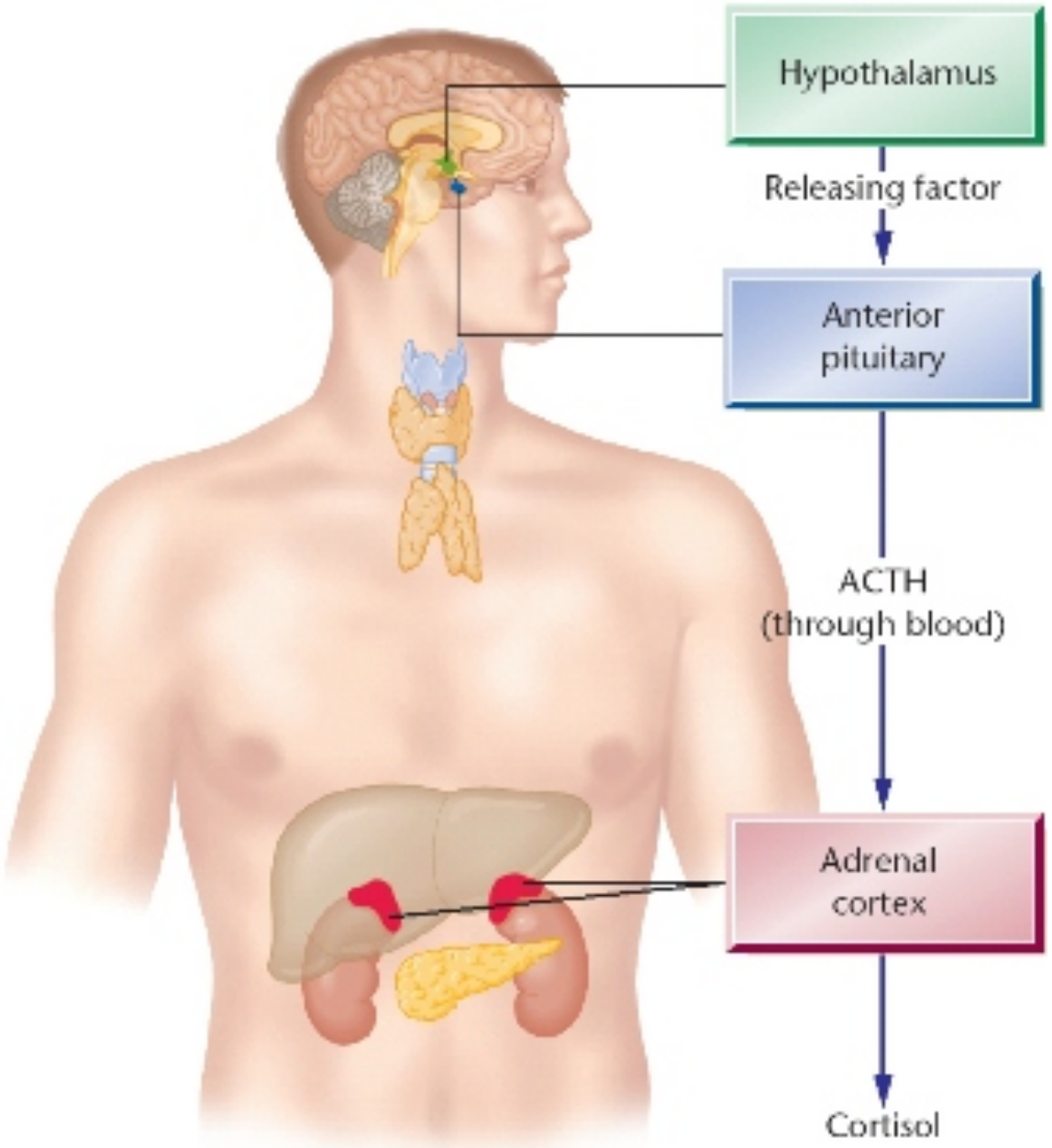
http://www.stolaf.edu/depts/cis/wp/winslowj/web/HPA_pic.jpg

Secondary Adrenal Insufficiency (Pituitary)

- Congenital
  - Mutations: PROP-1, PIT-1, T-Pit, POMC
  - Isolated idiopathic ACTH deficiency
  - Midline defects: eg. septo-optic dysplasia

- Acquired
  - Tumour
  - Hemorrhage
  - Surgery
  - Cranial radiation

- Infiltrative diseases
  - Hemochromatosis
  - Sarcoidosis
  - Langerhans histiocytosis



Tertiary

http://www.stolaf.edu/depts/cis/wp/winslowj/web/HPA_pic.jpg

Tertiary Adrenal Insufficiency (Hypothalamus)

- Congenital
  - Mutations: CRH gene defect, CRH receptor mutation
  - Midline defects: eg. septo-optic dysplasia

- Acquired
  - Tumour
  - Hemorrhage
  - Surgery
  - Cranial radiation

- Infiltrative diseases
  - Hemochromatosis
  - Sarcoidosis
  - Langerhans histiocytosis

Tertiary Adrenal Insufficiency (Hypothalamic **Suppression**)

- Cessation of ***supraphysiologic*** doses of glucocorticoid
  - If greater than **14 days** of therapy, consider patient to be at potential risk of adrenal insufficiency during acute stress
- Resection of cortisol secreting tumour
- Resection of ACTH secreting tumour

What is a **supraphysiologic** dose?

- Baseline production is:
  - Hydrocortisone 6-8 mg/m^2/day
- Anything above this amount is *supraphysiologic*, which is roughly equivalent to:
  - Prednisone 1- 1.5 mg/m^2/day
  - Dexamethasone 0.2 – 0.3 mg/m^2/day
- Typically a therapeutic dose of steroid is MUCH greater than the physiologic dose

Example

- 5 year old boy with height 110 cm (50^{th}%) and weight 18 kg (50^{th}%)
- Body surface area = $\sqrt{(ht \times wt)} / 3600$
- BSA = 0.74 m^2
- The following doses would be ***supraphysiologic*** in this child:
  - Prednisone greater than 1.5 mg once a day
  - Dexamethasone greater than 0.3 mg once a day

Avoiding Adrenal Insufficiency

- Tapering of ***supraphysiologic doses*** should be based on underlying disease symptoms being treated
  - eg. arthritis symptoms, respiratory distress, Crohn flare, etc.
- Once at a ***physiologic replacement*** dose, gradual tapering to facilitate symptom free recovery of HPA axis
- May need “stress” dose steroids if acute stress

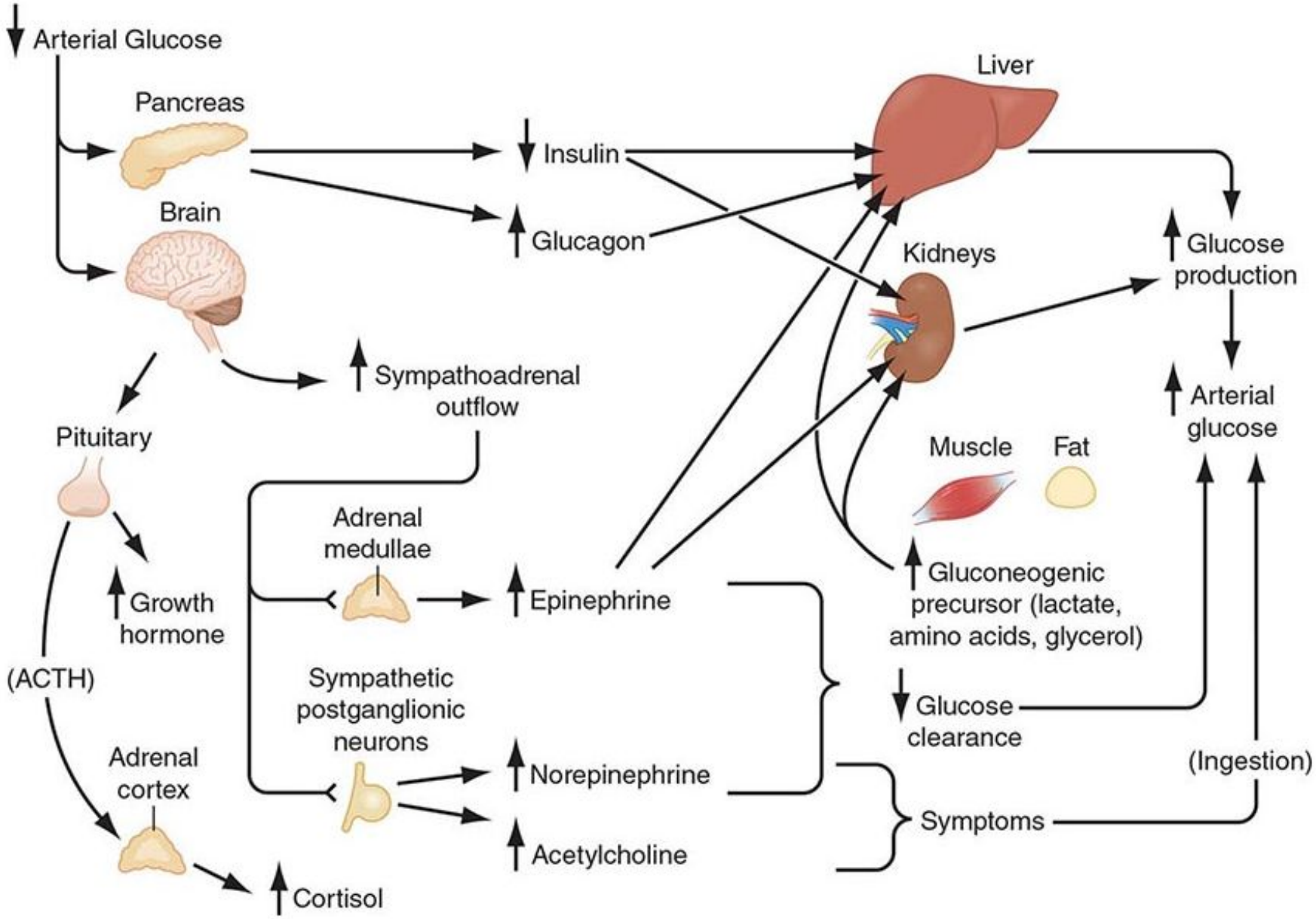
Hypoglycemia

- A **5 month old** boy who has been unwell for 48 hours (not feeding, lethargic) presents with **glucose 0.8, metabolic acidosis, no urine ketones**. Glucagon is given and raises the blood sugar to 1.2. What is the most likely diagnosis?

  - A. Glycogen storage disease
  - B. Fatty acid oxidation disorder
  - C. Hyperinsulinism

- **Answer: C**

- We chose C however, as it seems most likely and the BG did go up after glucagon we had read that glucagon does not cause BG to go up above 2.2mmolL then it is not hyperinsulinism…?



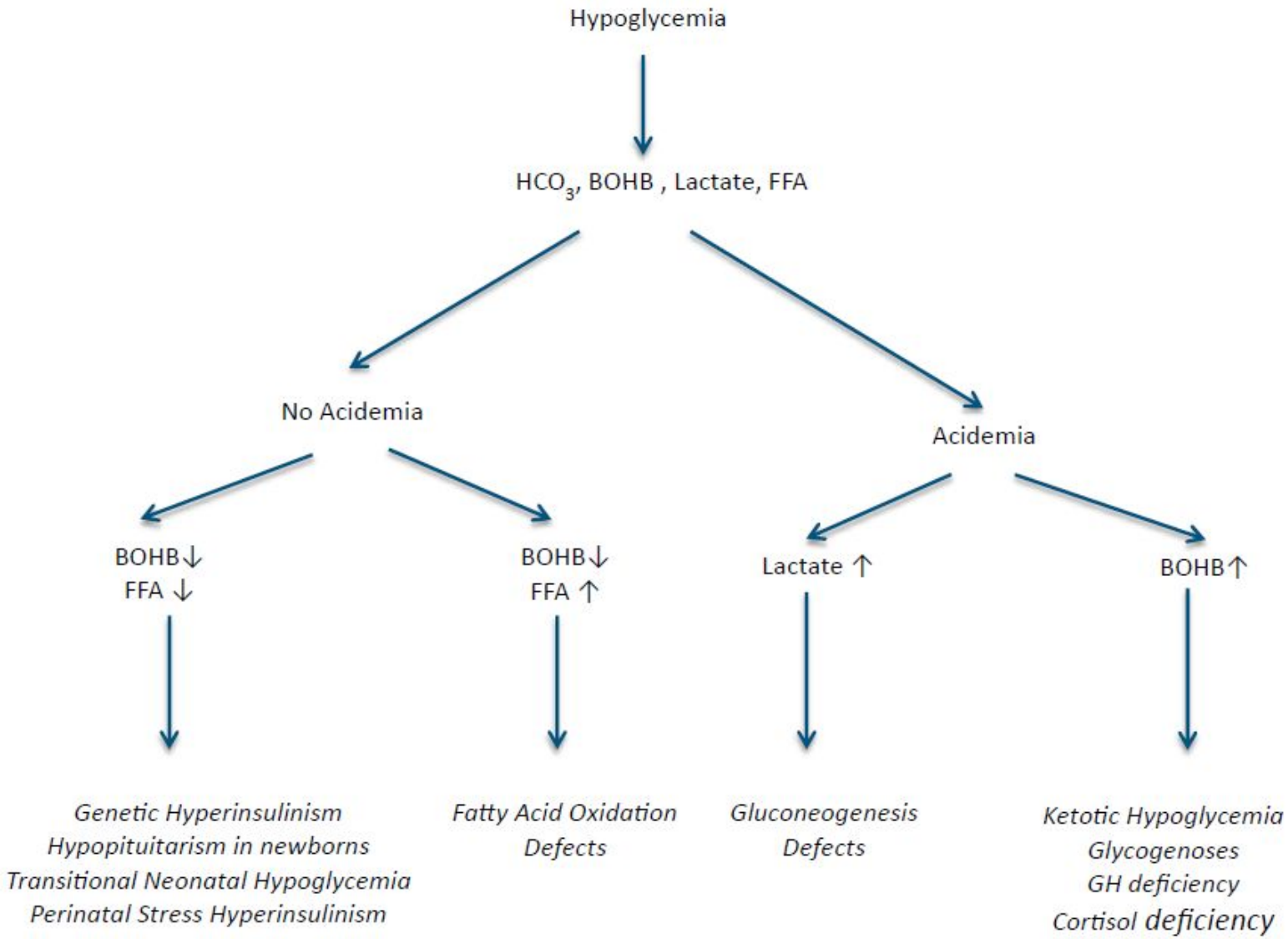
https://basicmedicalkey.com/wp-content/uploads/2016/11/image12436-2.jpeg

THE JOURNAL OF PEDIATRICS • www.jpeds.com

Recommendations from the Pediatric Endocrine Society for Evaluation and Management of Persistent Hypoglycemia in Neonates, Infants, and Children

Paul S. Thornton, MB, BCh[1], Charles A. Stanley, MD[2], Diva D. De Leon, MD, MSCE[2], Deborah Harris, PhD[3], Morey W. Haymond, MD[4], Khalid Hussain, MD, MPH[5], Lynne L. Levitsky, MD[6], Mohammad H. Murad, MD, MPH[7], Paul J. Rozance, MD[8], Rebecca A. Simmons, MD[9], Mark A. Sperling, MBBS[10], David A. Weinstein, MD, MMSc[11], Neil H. White, MD[12], and Joseph I. Wolfsdorf, MB, BCh[13]

Metabolic Clues to Hypoglycemia Diagnosis



For suspected hyperinsulinism, the fasting test can be terminated when the PG concentration is <50 mg/dL (<2.8 mmol/L) with administration of glucagon (1 mg IV, intramuscularly, or subcutaneously) to evaluate the glycemic response. An exaggerated glycemic response (>30 mg/dL [>1.7 mmol/L]) is nearly pathognomonic of hyperinsulinism.[33] Because plasma insulin concentration is sometimes not above the lower limit of detection,[34] it is important to include the following tests when assessing the possibility of hypoglycemia due to hyperinsulinism: plasma BOHB and FFA (both inappropriately low; BOHB <1.5 mmol/L [<15 mg/dL] and FFA <1.0-1.5 mmol/L [<28-42 mg/dL]), and an increased glycemic response to glucagon. Based on

Type 2 Diabetes

- The **parents of an 8 year old child** present to you to ask about **screening for Diabetes Mellitus type 2. Both parents have DMII** and they would like to know **when their child should be screened?**

- a. now
- b. at 10 years
- c. at puberty
- d. only if he develops symptoms suggestive of DMII

- Answer: ?? B

- JHO: I would pick D

DIABETES CANADA
CLINICAL PRACTICE GUIDELINES
The Canadian Diabetes Association has become Diabetes Canada*

3. Screening for type 2 diabetes should be performed every 2 years using an FPG test in children with any of the following:

    I. ≥3 risk factors in nonpubertal or ≥2 risk factors in pubertal children [Grade D, Consensus]

        a. Obesity (BMI ≥95th percentile for age and gender) [Grade D, Level 4 (2)]

        b. Member of a high-risk ethnic group (e.g. Aboriginal, African, Asian, Hispanic or South Asian descent) [Grade D, Level 4 (2)]

        c. Family history of type 2 diabetes and/or exposure to hyperglycemia in utero [Grade D, Level 4 (2)]

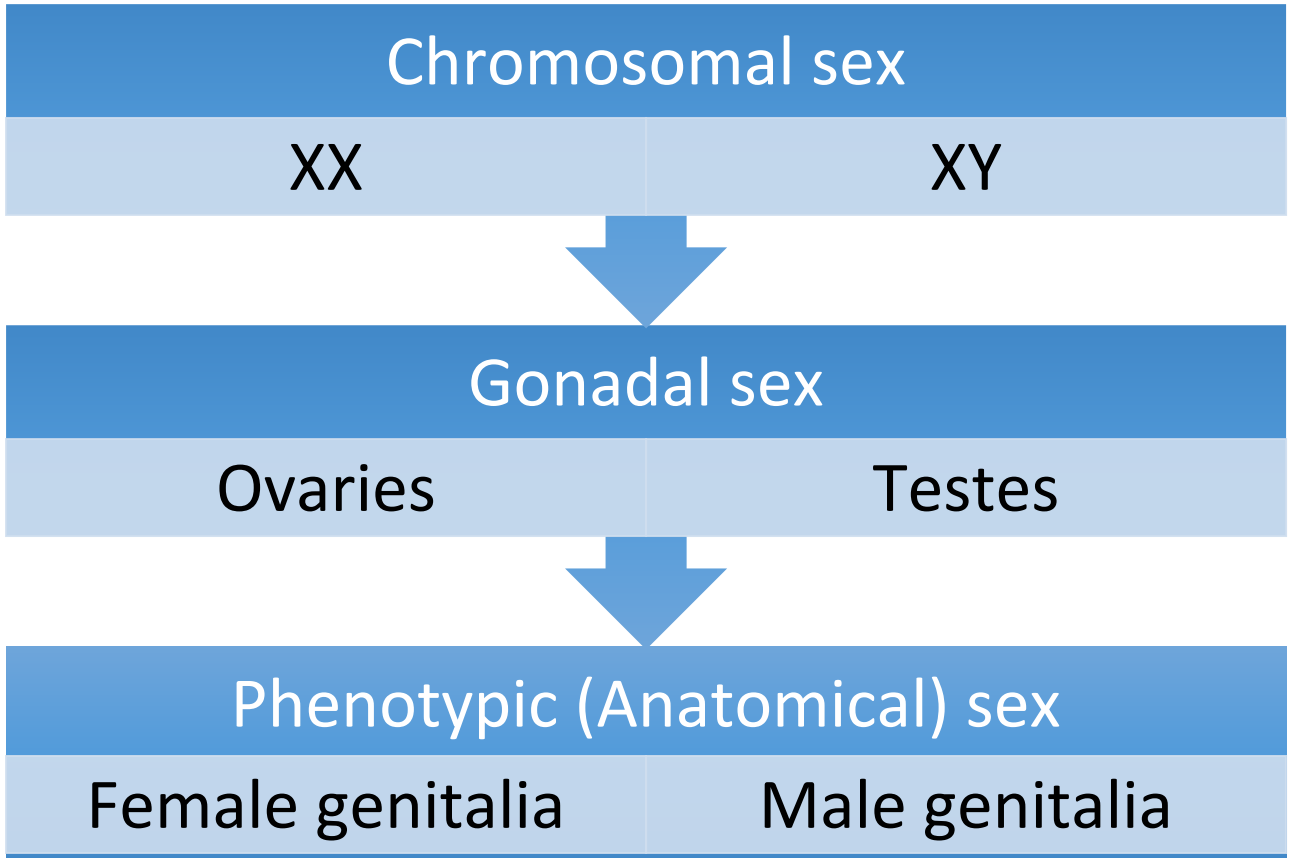
        d. Signs or symptoms of insulin resistance (including acanthosis nigricans, hypertension, dyslipidemia, NAFLD [ALT >3X upper limit of normal or fatty liver on ultrasound], PCOS) [Grade D, Level 4 (2)]

    II. Impaired fasting glucose or impaired glucose tolerance [Grade D, Consensus]

    III. Use of atypical antipsychotic medications [Grade D, Consensus]

http://guidelines.diabetes.ca/browse/chapter35#sec3

Ambiguous genitalia


Chromosomal sex
XX
XY
Gonadal sex
Ovaries
Testes
Phenotypic (Anatomical) sex
Female genitalia
Male genitalia

Sex ≠ Gender

- Biologic sex is made up of genetic/hormonal/physiologic components
- Gender is the individuals internal sense of being male or female (whether they identify as male or female)
- Individual markers of biologic sex can be associated with a range of gender outcomes
- Gender assignment:
  - individual's gender may not match their biologic sex

Review of Sexual Development

- Genetic sex - 46XX or 46XY

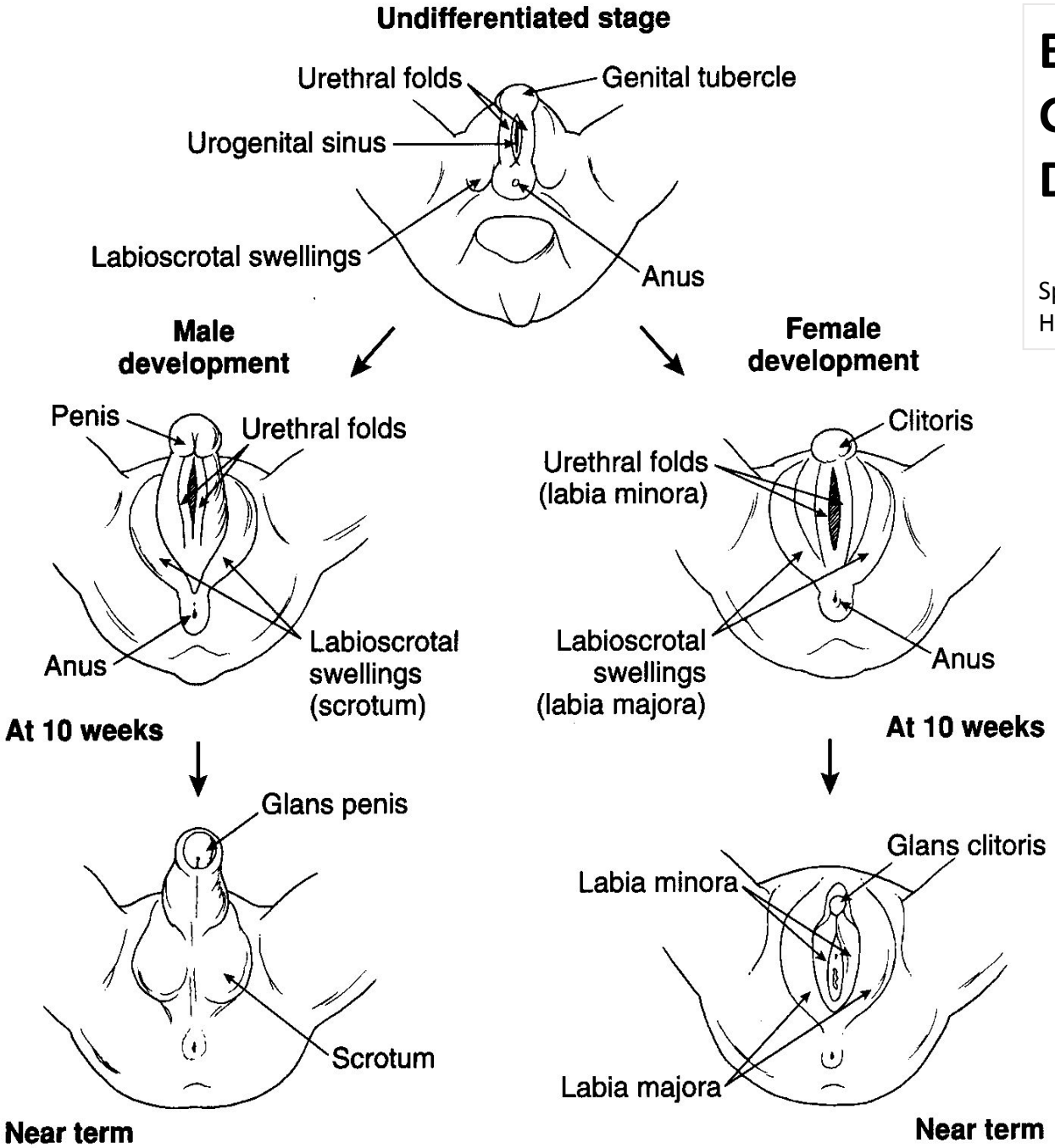
- Gonadal sex – SRY gene
  - Testes determining factor- stimulates undifferentiated gonad to become testis

- Genital duct structures
  - Leydig cells- testosterone maintains Wolffian structures
  - Sertoli cells – MIF (AMH) causes regression of Mullerian structures

- External genitalia
  - DHT causes virilization

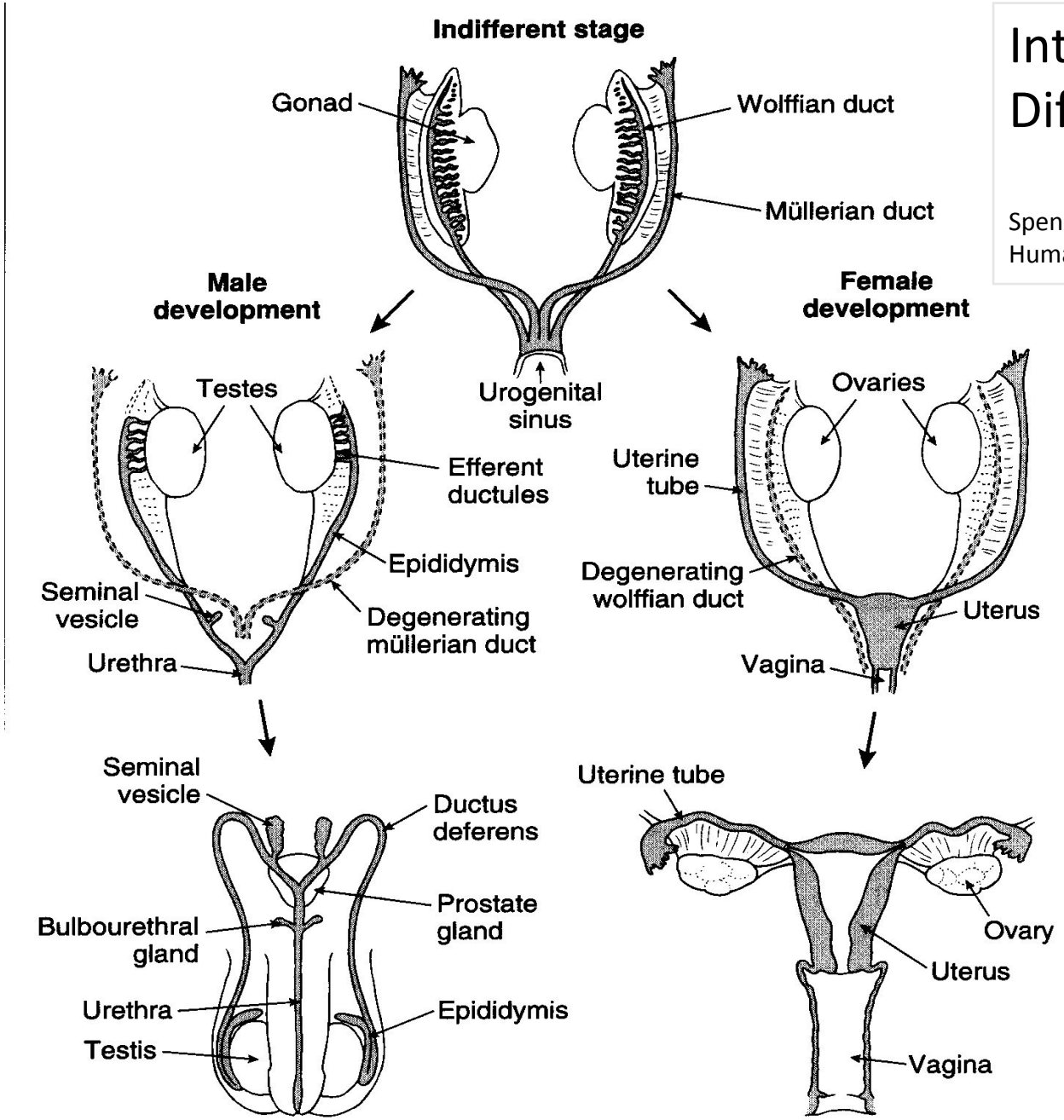
External Genital Differentiation

Spence AP, Mason EB. 1987
Human Anatomy & Physiology



Internal Genital Differentiation

Spence AP, Mason EB. 1987
Human Anatomy and Physiology



Definition of DSD

- Congenital conditions in which development of the chromosomal, gonadal or anatomical sex is atypical

Consensus Statement on Management of Intersex Disorders
Pediatrics 2006; 118; e488-500.

What's in a name?

- PES/ESPE International Consensus Conference on Intersex held in 2005
- Existing terminology "intersex", "pseudohermaphroditism", "hermaphroditism", "sex reversal"
- Controversial and confusing
- Proposal for revised nomenclature

Consensus Statement on Management of Intersex Disorders
Pediatrics 2006; 118; e488-500.

Classification of DSD

Sex Chromosome DSD	• 45,X, 45,X/46,XY • 47,XXY • 46,XX/46,XY
46,XY DSD Undervirilized XY	• Disorders of gonadal development • Disorders of androgen synthesis or action
46,XX DSD Virilized XX	• Disorders of gonadal development • Disorders of androgen excess • Other

Consensus Statement on Management of Intersex Disorders
Pediatrics 2006; 118; e488-500.

Prader Staging For Degree of External Virilization

Prader 0: Normal female external genitalia.

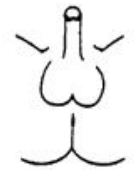
Prader 1: Female external genitalia with clitoromegaly.

Prader 2: Clitoromegaly with partial labial fusion forming a funnel-shaped urogenital sinus.

Prader 3: Increased phallic enlargement. Complete labioscrotal fusion forming a urogenital sinus with a single opening.

Prader 4: Complete scrotal fusion with urogenital opening at the base or on the shaft of the phallus.

Prader 5: Normal male external genitalia.

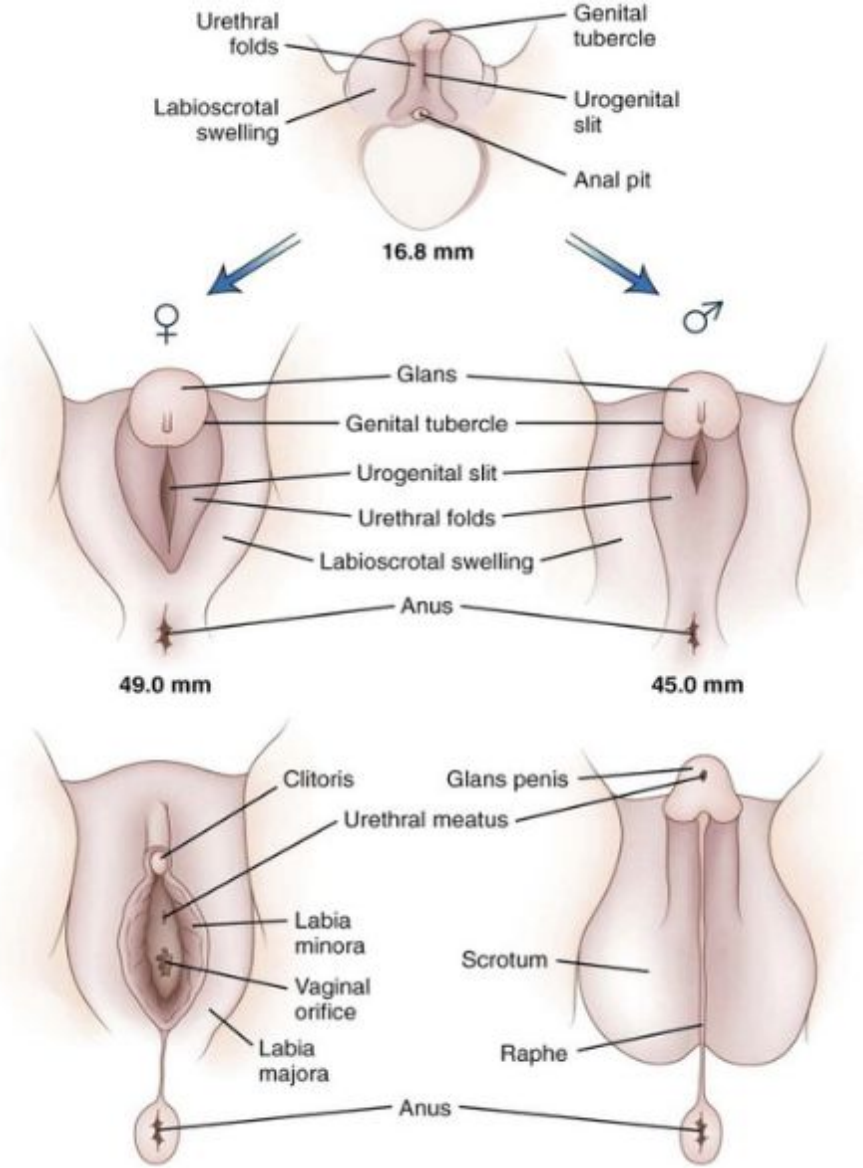


(Prader Von, A. (1954). "Der genitalbefund beim Pseudohermaproditismus femininus des kongenitalen adrenogenitalen Syndroms. Morphologie, Hausfigkeit, Entwicklung und Vererbung der verschiedenen Genitalformen." *Helv. Pediatr. Acta.* 9: 231-248.)

First steps with the family

- Engage parents while examining baby

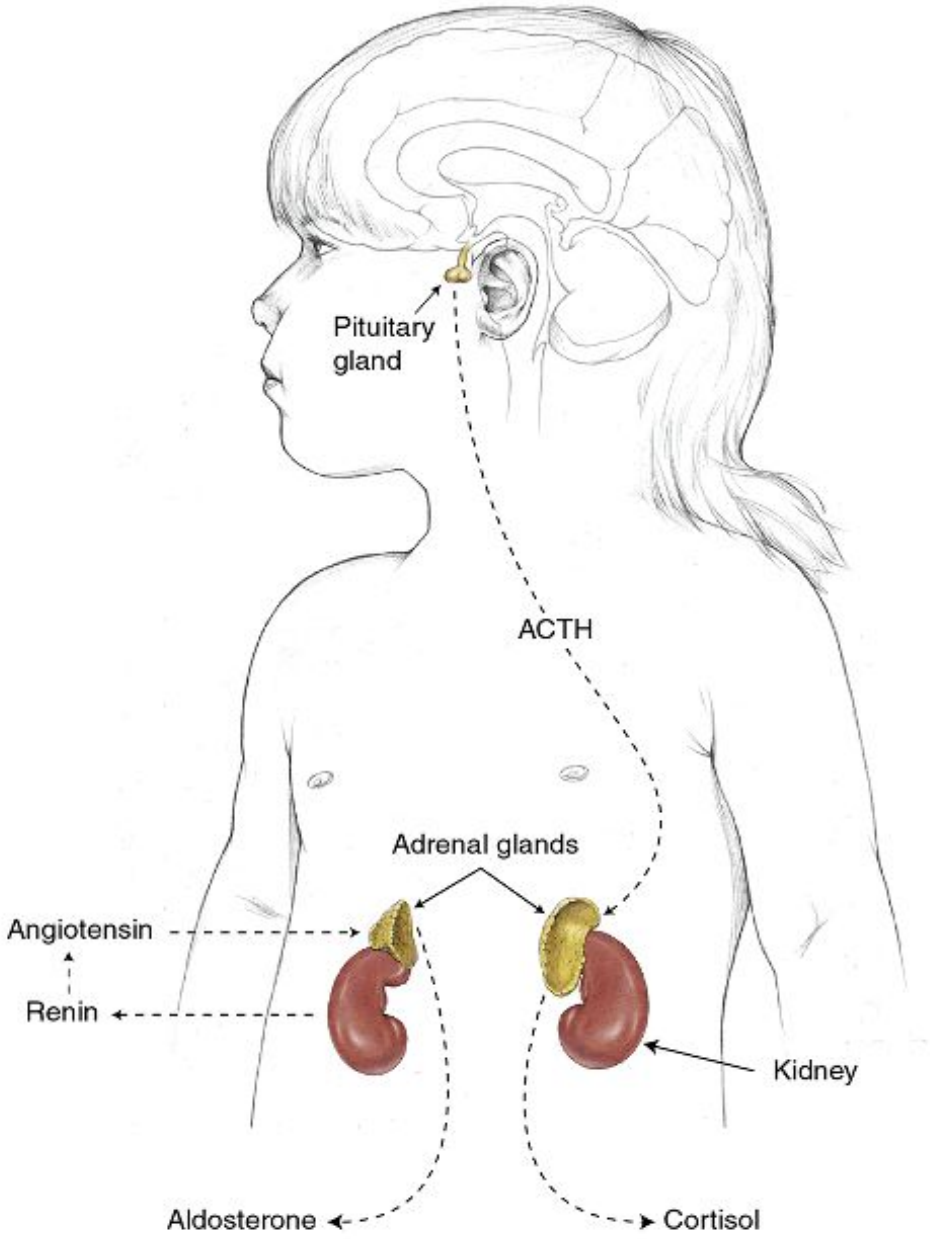
- Use gender-neutral terms t describe anatomy
  - Phallus
  - Single opening/two openings
  - Labioscrotal folds
  - Gonads



46XX DSD (Virilized 46XX)

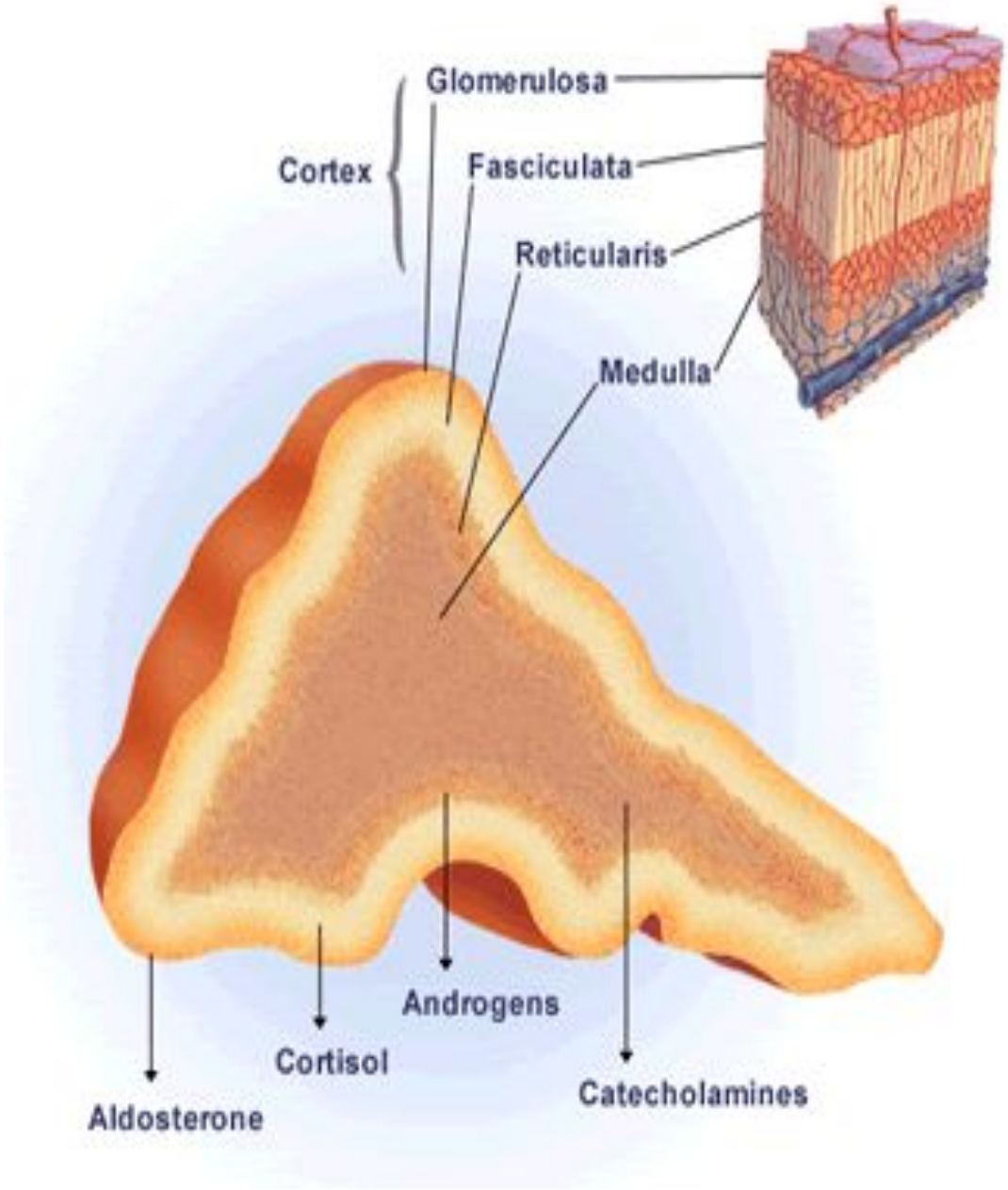
- Endogenous **fetal** androgen
  - Congenital adrenal hyperplasia
  - Ovarian or adrenal neoplasm (rare)
- Transplacental **maternal** androgen
  - Exogenous
    - Maternal exogenous androgens
  - Endogenous
    - Congenital adrenal hyperplasia
    - Ovarian or adrenal neoplasm

Hypothalamic-Pituitary-Adrenal Axis

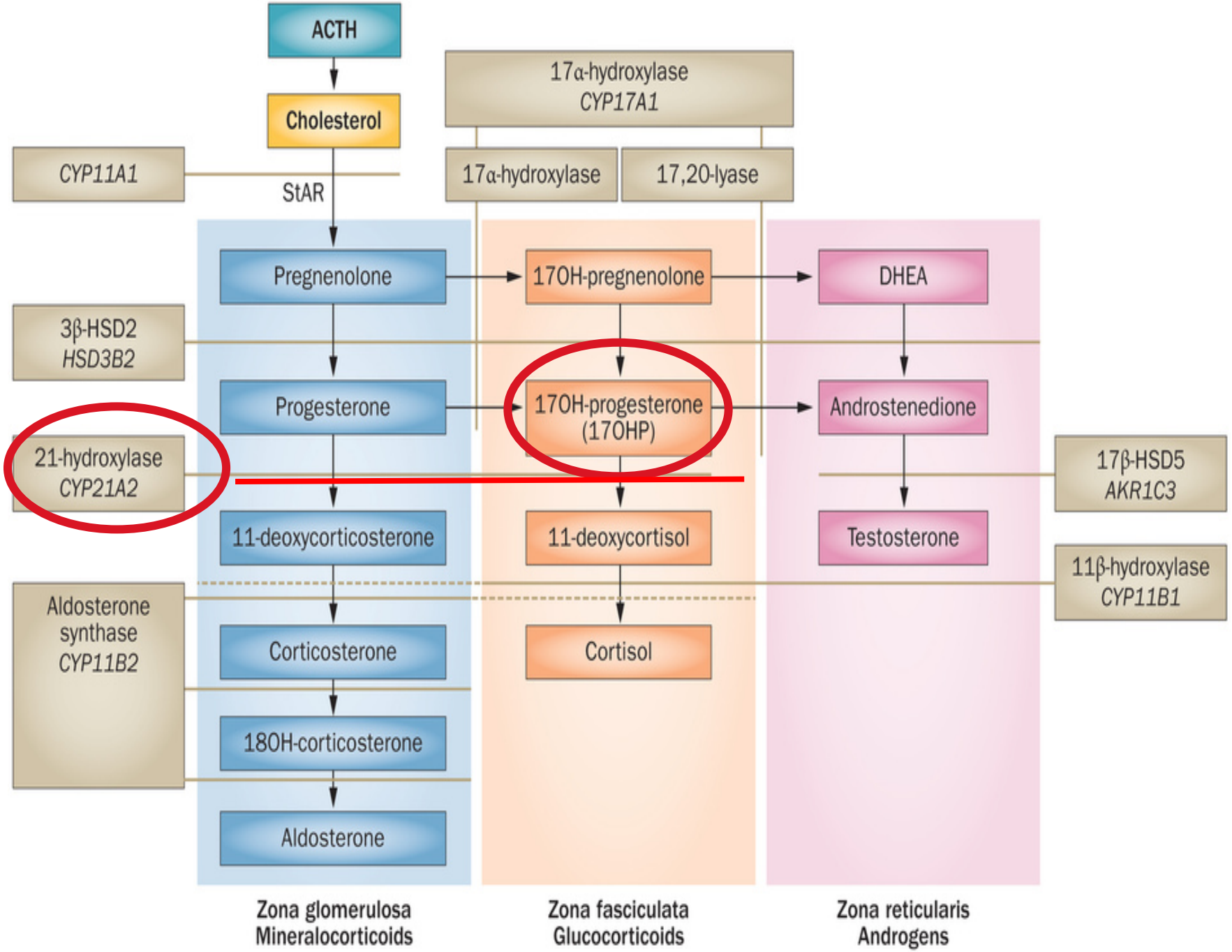


http://www.hopkinschildrens.org/cah/images/fig1.gif

Adrenal Gland Hormone Production



http://www.lotusgyn.com/images/Adrenalglanddetails_000.gif



http://www.nature.com/nrendo/journal/v10/n2/images/nrendo.2013.239-f2.jpg

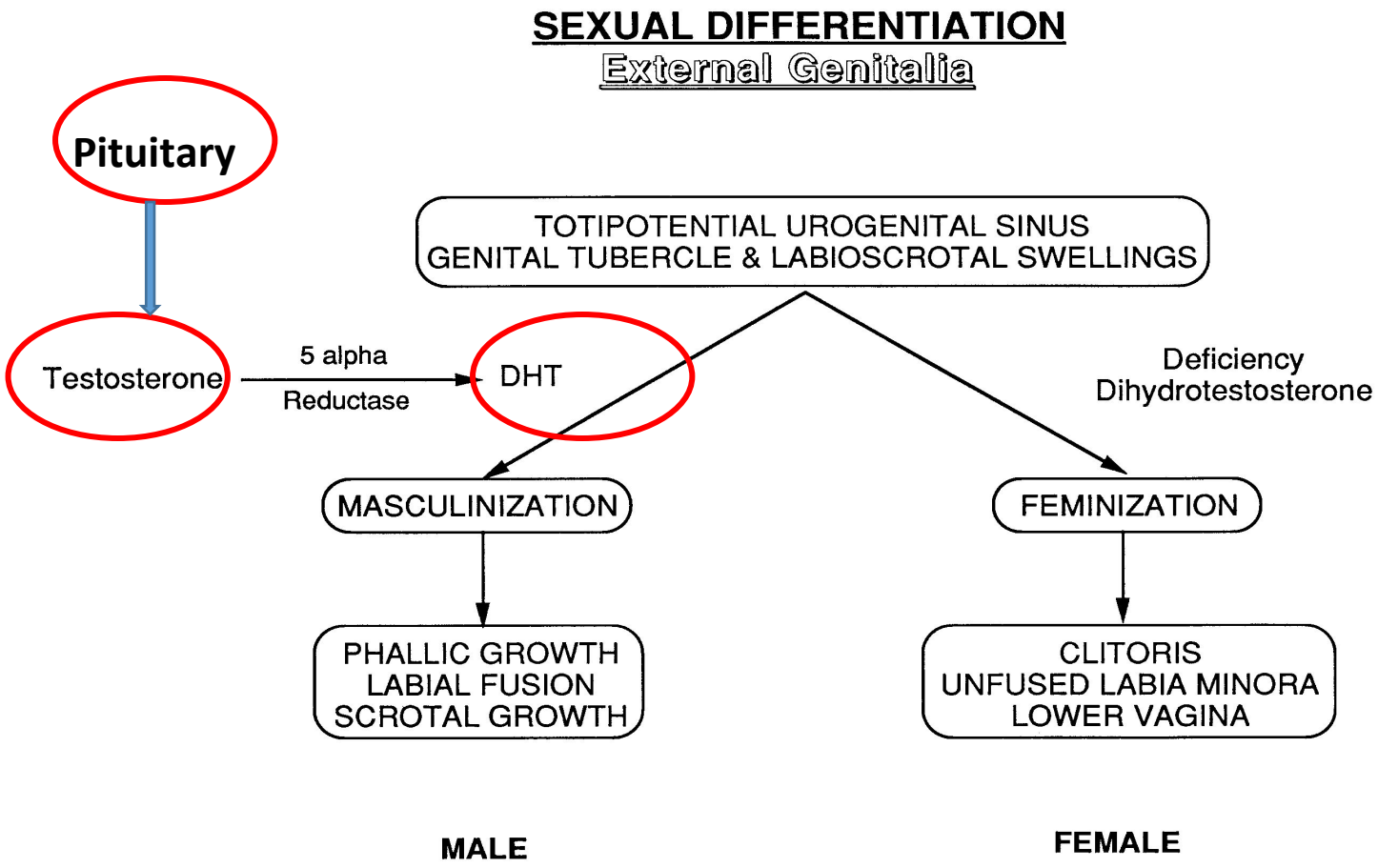
	Female Phenotype ♀	CAH in Female	Male Phenotype ♂
Karyotype	XX	XX	XY
Gonads	Ovaries	Ovaries	Testes
Androgen	No	Yes (Adrenal)	Yes
Wolffian Ducts	Regress	Regress	Develop
AMH	No	No	Yes
Mullerian Ducts	Develop	Develop	Regress
External Genitals	Female	Ambiguous	Male
Puberty	Feminize	Feminize*	Masculinize

* Requires glucocortioid +/- mineralcorticoid replacement

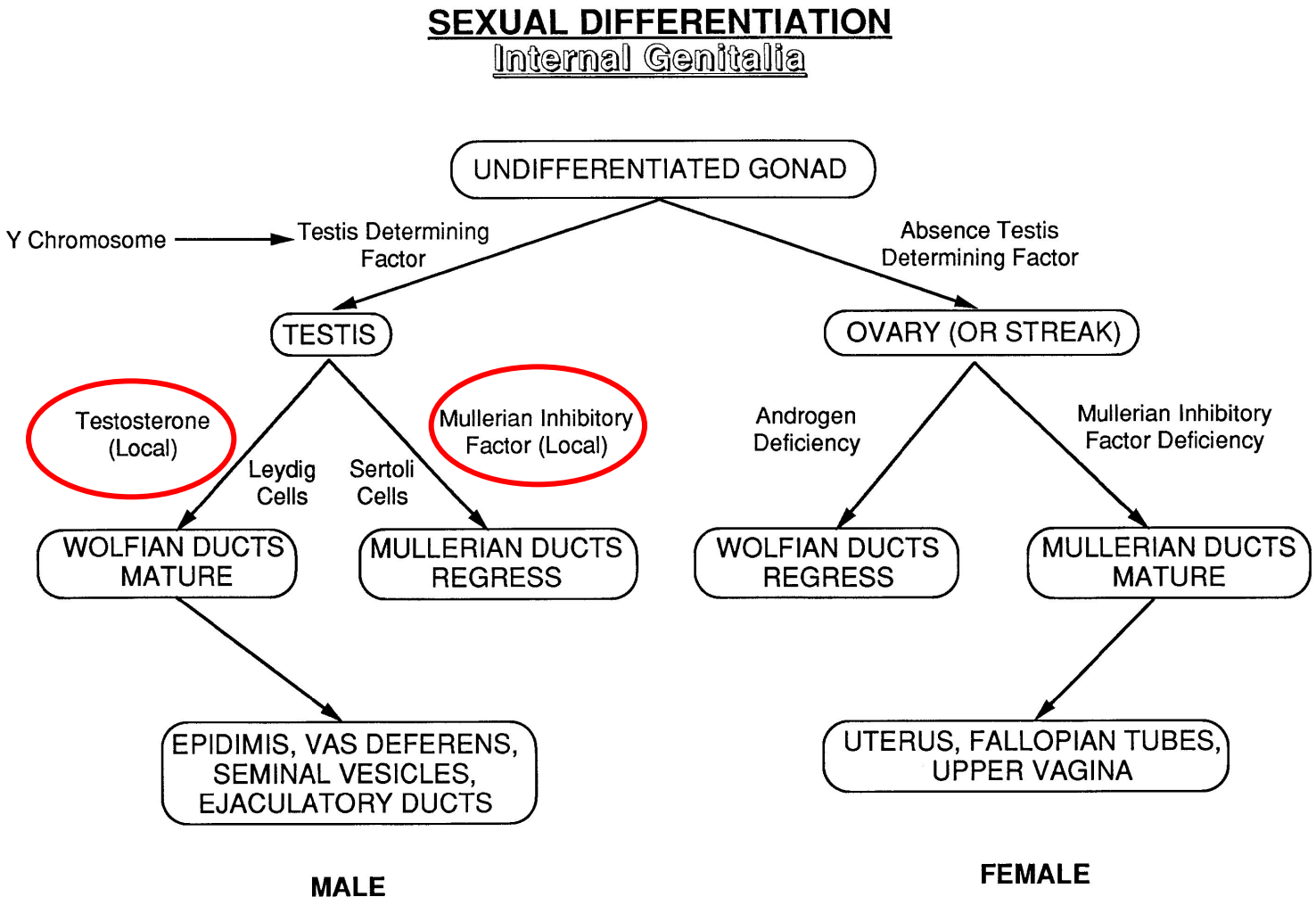
46 XY DSD (Undervirilized 46XY)

- 1. Inadequate androgen production
- 2. Defect of testosterone biosynthesis
- 3. Androgen receptor defect
- 4. Anti-mullerian hormone deficiency

46 XY DSD


SEXUAL DIFFERENTIATION
External Genitalia
Pituitary
TOTIPOTENTIAL UROGENITAL SINUS
GENITAL TUBERCLE & LABIOSCROTAL SWELLINGS
Testosterone
5 alpha
Reductase
DHT
Deficiency
Dihydrotestosterone
MASCULINIZATION
FEMINIZATION
PHALLIC GROWTH
LABIAL FUSION
SCROTAL GROWTH
CLITORIS
UNFUSED LABIA MINORA
LOWER VAGINA
MALE
FEMALE

46 XY DSD


SEXUAL DIFFERENTIATION
Internal Genitalia
UNDIFFERENTIATED GONAD
Y Chromosome
Testis Determining Factor
Absence Testis Determining Factor
TESTIS
OVARY (OR STREAK)
Testosterone (Local)
Mullerian Inhibitory Factor (Local)
Leydig Cells
Sertoli Cells
Androgen Deficiency
Mullerian Inhibitory Factor Deficiency
WOLFIAN DUCTS MATURE
MULLERIAN DUCTS REGRESS
WOLFIAN DUCTS REGRESS
MULLERIAN DUCTS MATURE
EPIDIMIS, VAS DEFERENS, SEMINAL VESICLES, EJACULATORY DUCTS
UTERUS, FALLOPIAN TUBES, UPPER VAGINA
MALE
FEMALE

	Phenotypic Female ♀	Testicular Dysgenesis	Phenotypic Male ♂
Karyotype	XX	XY	XY
Gonads	Ovaries	Streak	Testes
Androgen	No	Variable	Yes
Wolffian Ducts	Regress	Incomplete	Develop
AMH	No	Variable	Yes
Mullerian Ducts	Develop	Incomplete	Regress
External Genitals	Female	Ambiguous	Male
Puberty	Feminize	*	Masculinize

Feminize with estrogen; Masculinize with testosterone

	Phenotypic Female ♀	Testosterone Biosynthetic Defect	Phenotypic Male ♂
Karyotype	XX	XY	XY
Gonads	Ovaries	Testes	Testes
□Androgen	No	No	Yes
Wolffian Ducts	Regress	Regress	Develop
AMH	No	Yes	Yes
Mullerian Ducts	Develop	Regress	Regress
External Genitals	Female	Female	Male
Puberty	Feminize	*	Masculinize

Feminize with estrogen; Masculinize with testosterone

	Phenotypic Female ♀	Androgen Insensitivity (Complete)	Phenotypic Male ♂
Karyotype	XX	XY	XY
Gonads	Ovaries	Testes	Testes
Androgen	No	Yes (No effect)	Yes
Wolffian Ducts	Regress	Regress	Develop
AMH	No	Yes	Yes
Mullerian Ducts	Develop	Regress	Regress
External Genitals	Female	Female	Male
Puberty	Feminize	Feminize	Masculinize

	Phenotypic Female ♀	AMH Deficiency in Males	Phenotypic Male ♂
Karyotype	XX	XY	XY
Gonads	Ovaries	Testes	Testes
Androgen	No	Yes	Yes
Wolffian Ducts	Regress	Develop	Develop
AMH	No	No	Yes
Mullerian Ducts	Develop	Develop	Regress
External Genitals	Female	Male	Male
Puberty	Feminize	Masculinize	Masculinize

	Phenotypic Female ♀	Sex Chromosome DSD (45,X)	Phenotypic Male ♂
Karyotype	XX	45,X	XY
Gonads	Ovaries	Streak	Testes
Androgen	No	No	Yes
Wolffian Ducts	Regress	Regress	Develop
AMH	No	No	Yes
Mullerian Ducts	Develop	Develop	Regress
External Genitals	Female	Female	Male
Puberty	Feminize	Feminize	Masculinize

	Phenotypic Female ♀	Sex Chromosome DSD (46,XY)	Phenotypic Male ♂
Karyotype	XX	46,XY (SRY-ve)	XY
Gonads	Ovaries	Streak	Testes
Androgen	No	No	Yes
Wolffian Ducts	Regress	Regress	Develop
AMH	No	No	Yes
Mullerian Ducts	Develop	Develop	Regress
External Genitals	Female	Female	Male
Puberty	Feminize	Feminize	Masculinize

- A question describing a baby with ambiguous genitalia, palpable gonads. Which is most likely?

- a. CAH
- b. Partial androgen insensitivity
- c. 5 alpha reductase deficiency
- d. pseudohermaphrodism

- Answer: B vs. C?

- Newborn with penile-scrotal hypospadias, short phallus and no palpable gonads. Diagnosis?

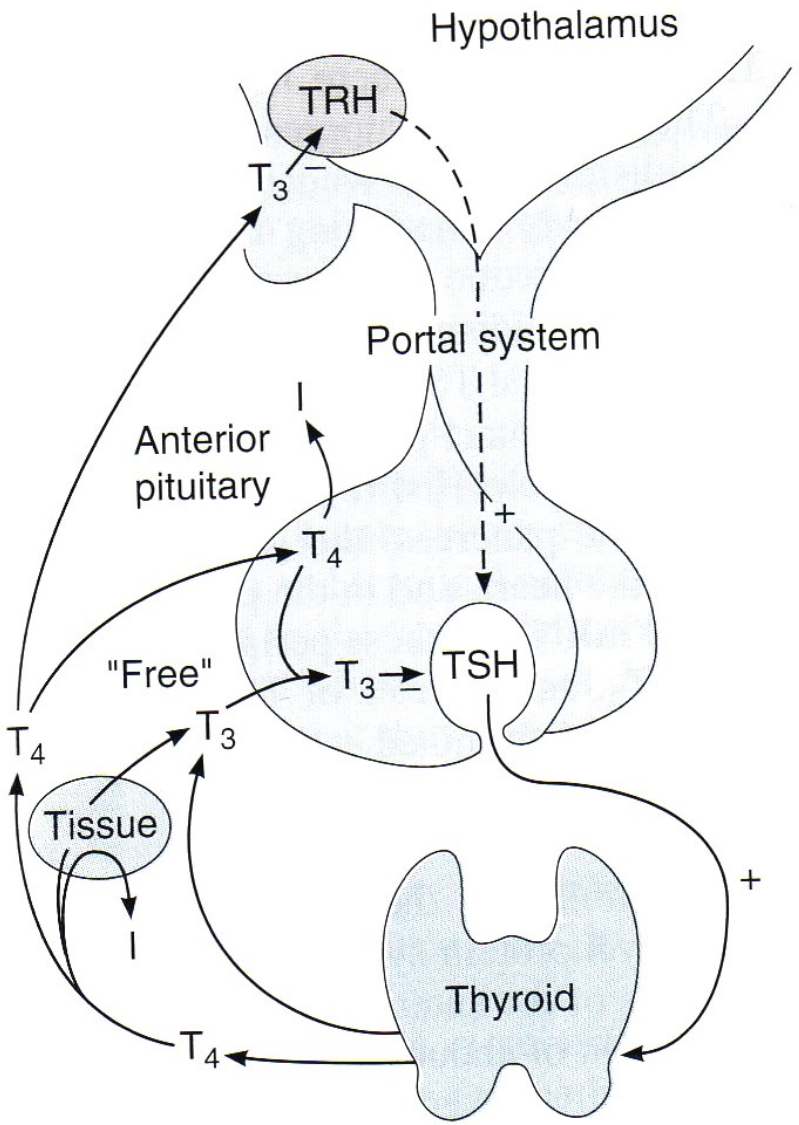
- a. Male pseudohermaphrodism with partial AIS
- b. 5 alpha reductase resistance (deficiency?)
-

- Answer: A vs. B?

- A physical examination of a 1 day old infant reveals no palpable gonads with a mid penile proximal hypospadias .Which of the following is appropriate initial management :
- A) measurement of serum cortisol (Yes-- concern is undervirilized male vs virlized female (most common is 21 hydroxylase def CAH)-- with no gonads palpable this is most concerning....so cortisol, 17OHP, lytes, karyoptype, ultrasound would all be useful . JHO)
- B) measurement of serum electrolyte (May not see salt wasting until later eg day 5-7)
- C) observation and assessment in one month (NO-- too late. JHO)
- D) karyotype (Yes-- important to do. JHO)
-
- * We are stuck between B and D. How soon after birth should we check electrolytes on a baby suspected of having CAH? If we can only choose one, do we take lytes first, or karyotype? Furthermore, if 17-OHP was an option for this question, in what order should we do our investigations (17-OHP vs. lytes vs. karyotype)?
- (I am wondering for this question if it was supposed to be an EXCEPT question? I would then pick C as the answer...all you have suggested I would do EXCEPT for C? We tend to follow all at same time so hard to pick one or the other first--- if I could pick one-- I would do 17-OHP to start and then karyoptype and then lytes a few days later? JHO)

Thyroid

Thyroid Physiology



From : Greenspan, 6th ed, 2001

- Child has autoimmune thyroiditis, want to monitor therapeutic treatment of levo, how do you do this?
- a) TSH
- b) FT4
- c) T4
- d) Thyroid peroxisome
- **Answer: A?**
- **We wondered about this one as Nelsons says stmt should be monitored by measuring serum fT4 and TSH q4-6 months**

- Girl who is non-symptomatic, with firm homogeneous enlarged thyroid, with normal skin and hair, no cold intolerance, normal school, normal growth, normal TSH (4.6); what to do?
- a. thyroid ultrasound
- b. refer to endocrinology
- c. follow-up 6 months
- **Answer: C**
- With this question, it brought up a question of how one gets a goiter if you're euthyroid?

- What is best test to determine initial dose of thyroid replacement in Hashimoto’s
- a. TSH
- b. T4
- c. fT4
-

  Answer: A

- Which is used to determine the initial dose of replacement therapy in lymphocytic thyroiditis:
- a) TSH
- b) T3
- c) T4
- d) free T4
- e) thyroid antibodies

- JH: I would choose TSH (ie. antibodies can be present in patient before they clinically have hypothyroidism, FT4 can be normal but I would still treat if TSH > 10, same for total T4 and total T3 (we don't really use))
- I agree with TSH for same reason. Would treat if TSH >10 with low normal FT4.

- What is the best way to monitor effectiveness of thyroid replacement in autoimmune thyroiditis?
- a. T4
- b. free T4
- c. T3
- d. TSH
- e. antibody

- JH: Same as previous question (would titrate based on TSH)
- Agree with TSH.

- A neonate’s newborn screen shows a TSH of 45. What is the NEXT step in management?
- a. Book a visit for a physical exam
- b. Order a TSH + free T4*
- c. Order a radionuclide thyroid scan
- So a couple questions regarding this. We know that you can get falsely positive TSH screens if taken too early. So we thought you would repeat the test (B. TSH and free T4) to get a true value. However- if there was an option to: "Start treatment" would you do that first? b/c you can abate the cognitive effects the sooner you treat? Would the order of things be:
- Order TSH + fT4 --> Start treat
- OR
- Start treatment --> Order TSH/fT4
-
- We all understand that you would do both likely! But the Royal College seems to LOVE "What is your NEXT step..." type questions. So although its all silly details, these type of questions come up all the time!
- And with a screen of 45 you would start treatment BEFORE finding out the RESULT of the repeat, correct? It didn't seem likely that you would wait for the results (that isn't even an option here- just making sure I understand the sequence of things)
- Also- what is a TRUE positive on newborn screen? We have heard different numbers. Some say >30, some say >40, etc.
- We didn't pick physical exam- b/c its seems that most babes have normal physical exams in the neonatal period, and the real urgent thing is to confirm and treat!

Growth

(*J Clin Endocrinol Metab* 93: 4210–4217, 2008)

SPECIAL FEATURE

Consensus Statements

Consensus Statement on the Diagnosis and Treatment of Children with Idiopathic Short Stature: A Summary of the Growth Hormone Research Society, the Lawson Wilkins Pediatric Endocrine Society, and the European Society for Paediatric Endocrinology Workshop

P. Cohen, A. D. Rogol, C. L. Deal, P. Saenger, E. O. Reiter, J. L. Ross, S. D. Chernausek, M. O. Savage, and J. M. Wit on behalf of the 2007 ISS Consensus Workshop participants

Department of Pediatric Endocrinology (P.C.), Mattel Children's Hospital at University of California, Los Angeles, Los Angeles, California 90095; Department of Pediatrics (A.D.R.), University of Virginia, and ODR Consulting, Charlottesville, Virginia 22911; Endocrinology Service (C.L.D.), Sainte-Justine Hospital, Montreal, Quebec, Canada H3T 1C5; Department of Pediatrics (P.S.), Albert Einstein College of Medicine, Bronx, New York 10467; Baystate Children's Hospital (E.O.R.), Tufts University School of Medicine, Springfield, Massachusetts 01199; Department of Pediatrics (J.L.R.), Thomas Jefferson University, Philadelphia, Pennsylvania 19107; Department of Pediatrics (S.D.C.), University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma 73104; Centre for Endocrinology (M.O.S.), the London School of Medicine and Dentistry, London E1 2AD, United Kingdom; and Department of Pediatrics (J.M.W.), Leiden University Medical Center, 2300 RC Leiden, The Netherlands

- Conditions where there is a discrepancy between chronologic age and bone age
-
- a. chronic granulomatous disease
- b. failure to thrive
- c. psychosocial deprivation
- d. malnutrition

- JH: I think all could present with a delay in bone age
- If I had to pick one, I would pick chronic granulomatous disease as chronic disease often results in delayed puberty and delayed bone ages.

- In which population would growth hormone studies be considered:

- a. children with height <3rd %ile
- b. short children with tall parents
- c. children with growth velocity of 6 cm/yr
- d. children with height >3 SD below the mean (this is <0.3%ile)

- Answer: B vs. D

- JHO: I would pick D

- A mother comes into your office because she is concerned about her 10-year old daughter’s decreased rate of growth. She is otherwise completely healthy.

- a. growth hormone stimulation testing
- b. karyotype
- c. the growth rate is likely to increase soon

- Answer: C

- JHO: C

- **9 yo female** with **menarche**, parents want to know about **final height;** what do you tell them?
- a. Expect another 5 cm (as per endo)
- b. Do bone age (as per concensus)
- c. Calculate mid parental height

- Answer: A

JHO: B

- Boy presents with pubic hair at 8y of age. What would you do?
- a) observe
- b) testicular US
- c) karyotype
- d) image head

- JH: For me, there is not enough detail to decide-- eg. a few fine soft hairs, no other signs of puberty and no risk factors for early puberty, no exogenous exposure, etc -- I would observe and may consider bone age. I wish bone age were an option since I think that is the first test I would pick.
- If question said testicular enlargement, I would pick 'image head' as he has central precocious puberty which is more concerning for a CNS tumor in boys vs. girls. If he had + virilization and prepubertal testes, I would worry about a peripheral source of testosterone and pick testicular US. Based on info provided, I would observe. If bone age was there, or 17-OHP for late onset CAH, I would pick these.

- 6 y.o. female with 6 month history of pubic hair development. No other secondary sexual characteristics. Bone age is 6 yr 6 months. Urine ketosteroids markedly increased. Urine hydroxysteroids normal. Serum gonadotropins, testosterone, 17-hydroxyprogesterone and ketosteroids normal. No change with dexamethasone challenge. Most likely diagnosis:
- a. CAH - normal 17-OHP rules this out
- b. adrenal tumour what does the dexamethasone challenge do? - would not expect normal testosterone. In terms of dex challenge - from up to date:
- "Although the specific approach differs among endocrinologists, we favor the dexamethasone androgen-suppression test (DAST) as the next diagnostic step if a virilizing disorder is suspected [42]. The primary goal of this test is to distinguish a virilizing tumor (in which dexamethasone fails to suppress one or more adrenal androgens) from other forms of virilization, including CAH and exaggerated adrenarche (in which androgens are suppressed) (algorithm 1)."
- c. physiologic adrenarche - this is not physiologic as it is premature (normal age for girls after 8 years, for boys after 9 years)
- d. undisclosed exogenous source of steroids- would not expect normal testosterone
- e. Cushing's high blood levels of cortisol and other glucocorticoids - does not really make sense except for fact that there was no change with dex challenge
- f. Premature pubarche - we don't measure urine steroids and so I think this question is very old. I would be aware of the typical features of premature pubarche, and I think this will be adequate to answer a question about this condition.
- g. Hyperthyroidism - does not present like this
- ** We're confused. This sounds like premature pubarche... but why would there be urine ketosteroids? And why are blood ketosteroids normal?
-
- JH: not sure if this question makes sense? Typically a 1 mg dexamethasone suppression is to rule out Cushing-- so no change means high cortisol after dexamthasone challenge-- which fits Cushing.
- I think this question is missing information or remembered incorrectly. I also think it is an old question. I put my comments directly beside the options. I think it will be difficult to figure out the answer to this question in the manner it was remembered.

Obesity

J Clin Endocrinol Metab, March 2017, 102(3):709–757

CLINICAL PRACTICE GUIDELINE

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

Dennis M. Styne,[1] Silva A. Arslanian,[2] Ellen L. Connor,[3] Ismaa Sadaf Farooqi,[4] M. Hassan Murad,[5] Janet H. Silverstein,[6] and Jack A. Yanovski[7]

[1]University of California Davis, Sacramento, California 95817; [2]University of Pittsburgh, Pittsburgh, Pennsylvania 15224; [3]University of Wisconsin, Madison, Wisconsin 53792; [4]University of Cambridge, Cambridge CB2 0QQ, United Kingdom; [5]Mayo Clinic, Rochester, Minnesota 55905; [6]University of Florida, Gainesville, Florida 32607; and [7]National Institutes of Health, Bethesda, Maryland 20892

Cosponsoring Associations: The European Society of Endocrinology and the Pediatric Endocrine Society. This guideline was funded by the Endocrine Society.

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report

EXPERT PANEL ON INTEGRATED GUIDELINES FOR CARDIOVASCULAR HEALTH AND RISK REDUCTION IN CHILDREN AND ADOLESCENTS

Pediatrics 2011;128;S213; originally published online November 14, 2011;
DOI: 10.1542/peds.2009-2107C

- Adolescent who is obese and referred for increased LDL and total cholesterol. Father died of MI at age 38.
-
- a. weight reduction
- b. dietary changes
- c. start bile acid sequestrant
- d. start statin
- e. start statin, lifestyle changes

- I assume its lifestyle choices first, and then visit medication options as second line. But I don't have any good resource!

- JHO: Lifestyle

- 11 yo male who is **obese**. His **father had a myocardial infarction at the age of 38 years.** His **total cholesterol is 6.3 and his LDL is 3.8.** What is the **best management?**

- a. lifestyle modification
- b. lifestyle modification and low-fat diet
- c. lifestyle modification and bile acid sequestrant
- d. lifestyle modification and statin
-

- Answer: A vs. B?

- JHO: B first then needs D

- Features of childhood obesity include all EXCEPT:
- a) 50% chance of being obese if one parent is obese, 80% if both parents are obese (this sounds true-- I looked online and these are numbers quoted. JHO)
- b) premorbid psychological problems predate the onset of obesity (this also sounds true-- we see this clinically ie autism,depression, adjustment disorder, anxiety, etc... JHO)
- c) increased incidence in lower socioeconomic class (this is true-- increased obesity with low SES. JHO)
- d) associated with decreased exercise (this is true-- JHO) They all sound true to me??? JHO
-
- * We are stuck between B and C. Is it true that obesity actually has a higher incidence in the higher socioeconomic class?

- 9 year old obese kid. Dad MI at 38. History of high cholesterol in child with increased total and LDL. Mgmt?

- a. lifestyle change (increase activity, wt loss)
- b. lifestyle change as above + low fat diet
- c. lifestyle change + bile sequesterant
- d. lifestyle change + HMG Co reductase

- JHO: B to start

- 10 y.o with metabolic syndrome. What is the best measure of adiposity to follow?
- a. BMI
- b. Hip-to-waist circumference ratio
- c. Waist circumference
- d. Triceps fat fold thickness
-

  Answer: A??

- **JHO: A- not great but most practical**

Type 1 Diabetes

Helpful Websites

- Canadian Diabetes Association:
  - **www.diabetes.ca**

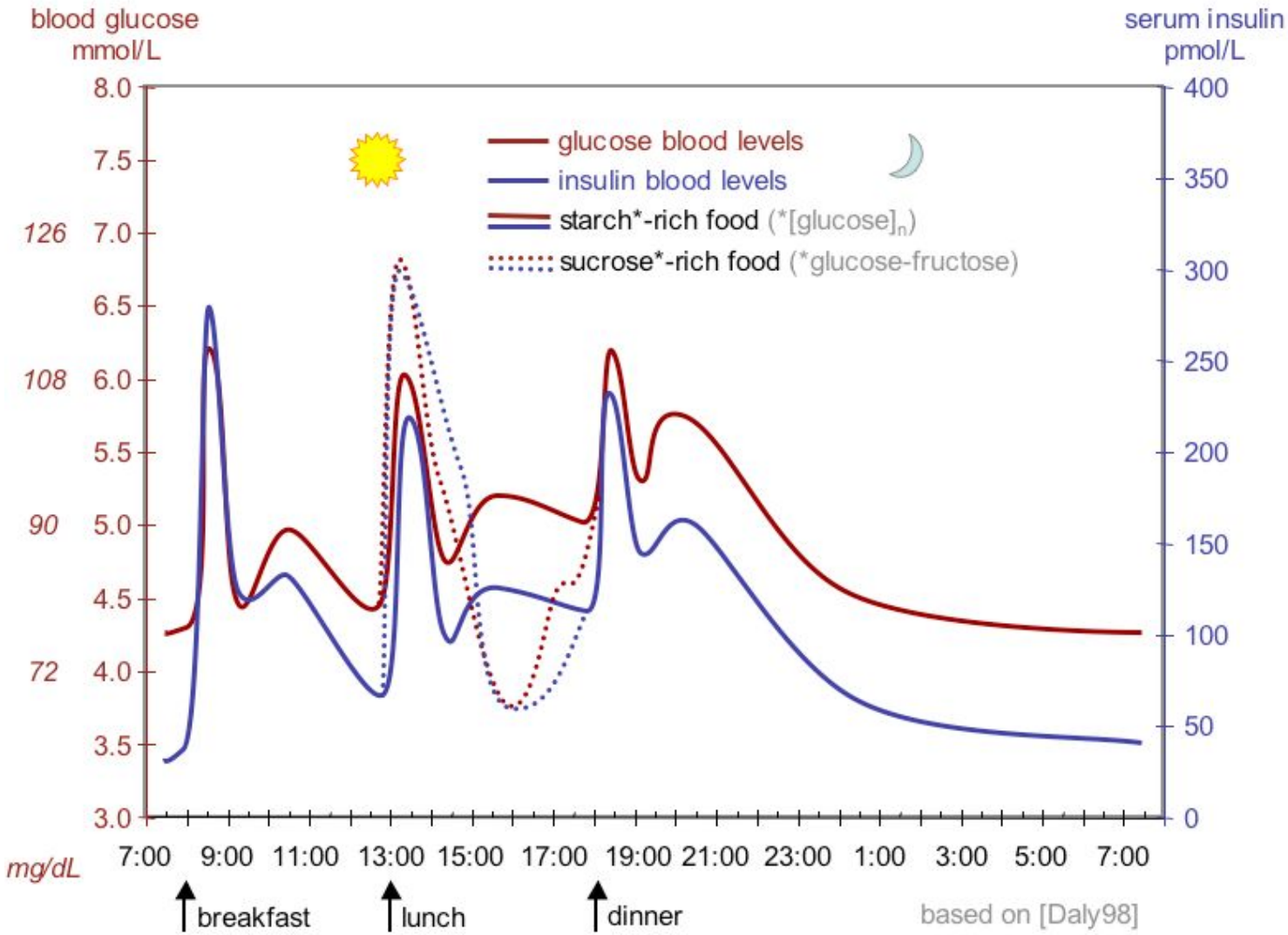
- International Society for Pediatric and Adolescent Diabetes:
  - **www.ispad.org**

Basaglar
Toujeo

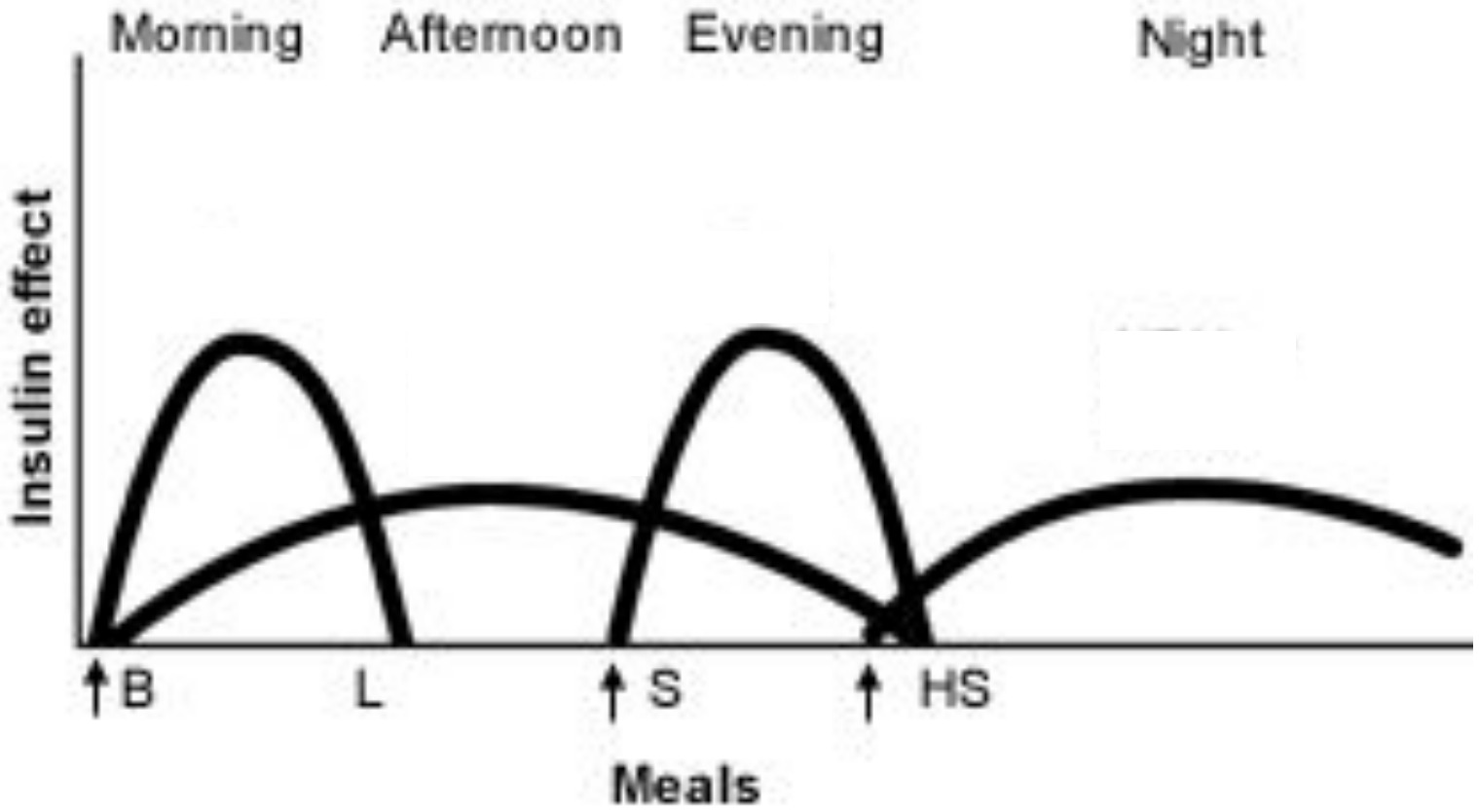
Insulin Preparations

Drug (brand)	Onset time[a]	Peak time[a]	Duration[a]	Comments
Rapid-acting				
Insulin aspart (NovoLog)	10-20 min	1-3 hr	3-5 hr	Administer within 15 min before or immediately after meals
Insulin glulisine (Apidra)	25 min	45-48 min	4-5 hr	
Insulin lispro (Humalog)	15-30 min	0.5-2.5 hr	3-6.5 hr	
Short-acting				
Insulin regular (Novolin R, Humulin R)	30-60 min	1-5 hr	6-10 hr	Administer 30 min before meals
Intermediate-acting				
Insulin NPH (Novolin N, Humulin N)	1-2 hr	6-14 hr	16-24+ hr	Cloudy appearance
Long-acting				
Insulin detemir (Levemir)	1.1-2 hr	3.2-9.3 hr	5.7-24 hr (dose-dependent)	Do not mix with other insulins
Insulin glargine (Lantus)	1.1 hr	None	24 hr	
Premixed				
70% Insulin aspart protamine/30% insulin aspart (NovoLog Mix 70/30)	10-20 min	1-4 hr	24 hr	Cloudy appearance Administer within 15 min before meals
75% Insulin lispro protamine/25% insulin lispro protamine (Humalog Mix 75/25)	15-30 min	2 hr	22 hr	
50% Insulin lispro protamine/50% insulin lispro protamine (Humalog Mix 50/50)	15-30 min	2 hr	22 hr	
70% Insulin NPH/30% insulin regular (Humulin 70/30, Novolin 70/30)	30 min	1.5-12 hr	24 hr	Cloudy appearance Administer within 30 min before meals
50% Insulin NPH/50% insulin regular (Humulin 50/50)	30-60 min	1.5-4.5 hr	7.5-24 hr	

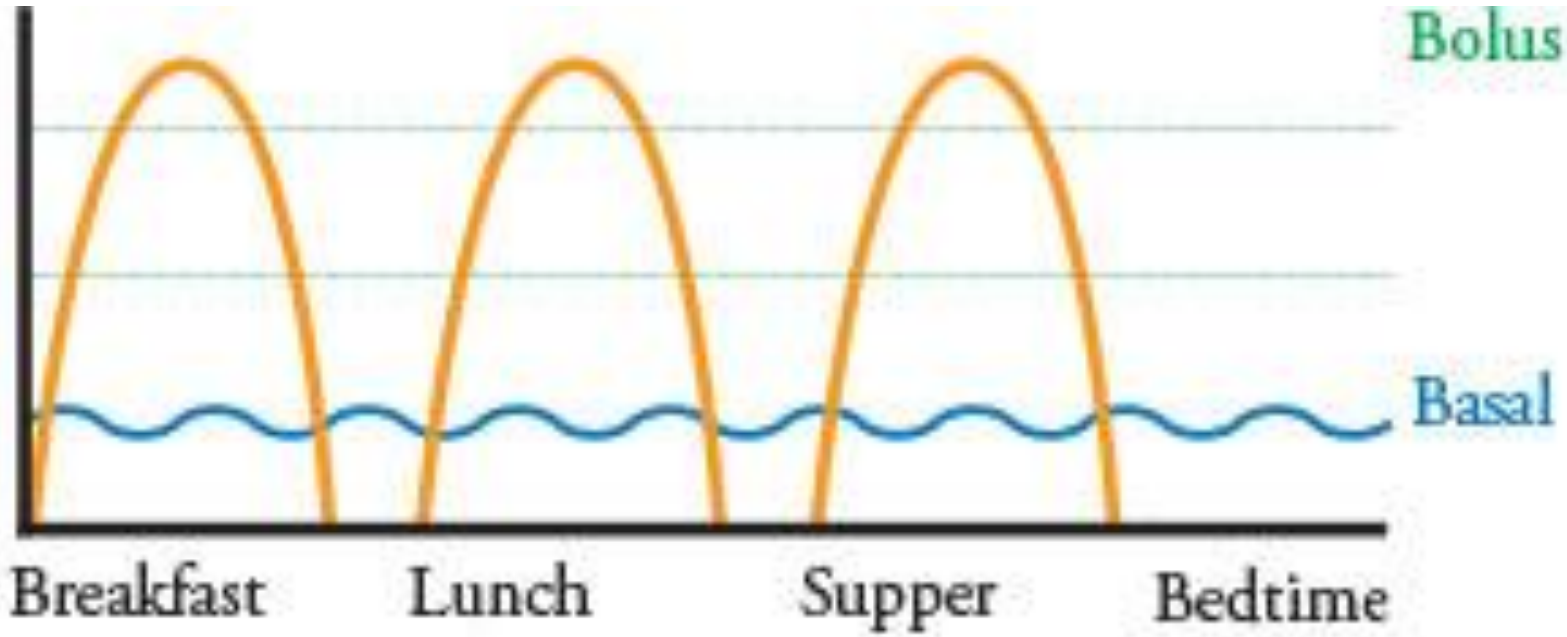
Normal Variation in Insulin Secretion



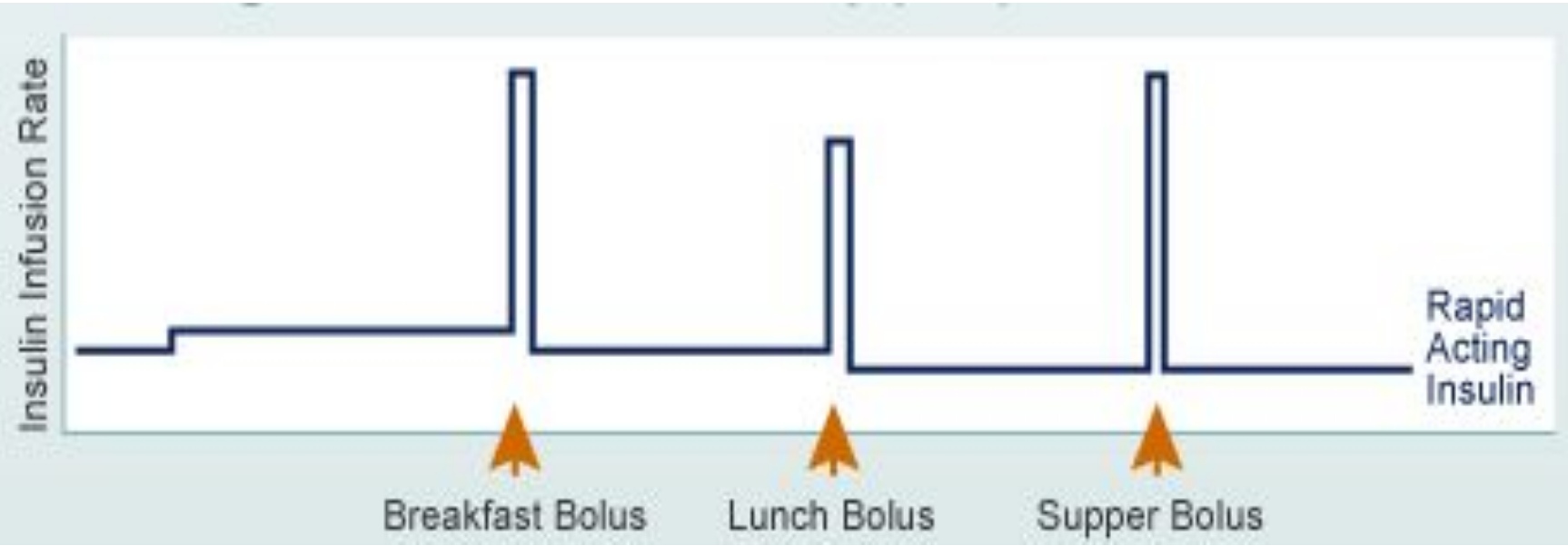
TID Regimen


Morning
Afternoon
Evening
Night
Insulin effect
B
L
S
HS
Meals

Basal-Bolus



Pump


Insulin Infusion Rate
Rapid Acting Insulin
Breakfast Bolus
Lunch Bolus
Supper Bolus

Guide to Insulin Total Daily Doses

- In the honeymoon phase:
  - 0.2 to 0.5 units/kg/day
- Children beyond the honeymoon phase:
  - 0.7 to 1 unit/kg/day
- Adolescents:
  - up to 1.5 units or more/kg/day.

Insulin dose calculations…

- These are rough guidelines for what you might commonly see on the wards
- Often individualized and may vary depending on circumstances eg BID insulin in some cases
- If you have any questions, please page endocrine on-call and we are always happy to review !

Calculation of TID Insulin Dose

- Starting dose = 0.5-0.7 units/kg/day

- 2/3 insulin in morning
  - 2/3 of this as intermediate acting
  - 1/3 of this as rapid acting

- 1/3 insulin in evening
  - 2/3 of this as intermediate acting
  - 1/3 of this as rapid acting

- Breakfast- intermediate and rapid acting
- Supper- rapid acting
- Bedtime- intermediate acting

Calculation of Basal – Bolus Dose

- Total daily dose= 0.5-0.7 units/kg/day:
  - 50% basal insulin
  - 50% bolus insulin

- Breakfast- rapid acting insulin
- Lunch- rapid acting insulin
- Supper- rapid acting insulin
- Bed- long acting insulin

Insulin Sensitivity Factor

- ISF= 100 / Total Daily Dose of insulin
- Each 1 unit of rapid insulin is expected to decrease the BG by “x” mmol/L
- Eg. For a child with a TDD insulin= 10
  - ISF= 100 / 10 = 10
  - 1 unit rapid insulin will decrease BG by 10 mmol/L

Insulin Sensitivity Factor: “Sliding Scale”

- Eg. ISF = 10

- **BG insulin**

15-20	0.5 units
> 20	1.0 units

- Eg. ISF = 2

- **BG insulin**

10-12	1 unit
12-14	2 units
14-16	3 units
16-18	4 units
18-20	5 units
>20	6 units

Insulin Sensitivity Factor: “Correction Formula”

$$\frac{\text{Actual Glucose - Target Glucose}}{\text{Insulin Sensitivity Factor}} = \text{dose}$$

If ketones are positive:

Please call physician if ketones positive (increase correction doses and monitoring until ketones cleared)

**multiply correction x 1.5 if ketones positive

Insulin to Carbohydrate Ratios

- Estimate based on 50% of TDD and “standard” carb amounts from initial food trays
  - Total meal carb divided by 50% of TDD

- Or

- Estimate by:
  - Insulin: CHO ratio = 500 / Total Daily Dose Insulin
  - Eg. A 50 kg child on 50 units of insulin/day
  - 500 / 50 = 10
  - I unit of rapid acting insulin for each 10 g of carbohydrate ingested

- SAQ -- Child with Type 1 DM. Ate supper but missed pre-supper insulin (5R and 8N). About to take evening snack. Glucose 23.5. Mom calling for advice.

- * We said:
- - Check urine for ketones (YES- JHO)
- - Give 8N now (YES- JHO)
- - Give Rapid insulin using patient's correction sliding scale (YES-with extra if ketones. JHO)
- - Check chemstrip overnight (YES- to be specific I would check about 3 hours after correction with rapid. JHO)

- Is that okay? Or should we be more specific about how much R to give? Should we say a specific percentage of Rapid to give? (I don't think you can be too specific without knowing the am doses of insulin to calculate an ISF? and not knowing if there are ketones or not? JHO)

- A mother calls because her child with type 1 is sick but has good oral intake. The child's glucose is 15 and ketones are moderate. Its now supper. Her baseline short acting insulin is 3 U but according to her sliding scale she should receive 5. Her morning rapid is 4 U morning NPH is 5 U and night NPH is 8 U.
- 1) How much insulin should she get now?
- 2) What advice for further management?

- TDD= 20
- therefore ISF= 5
- which makes sense because "usual scale" would mean she gets base of 3 units plus 2 for correction = 5 units now
- However, with ketones, we would multiply usual correction x 1.5 ....so instead of 2 for correction I would give 3 units since they are more resistant.
- So would give now base of 3 plus 3 to correct = 6 units short acting
- check again in 2 hours-3 hours
- if BG still above 14 mmol/L would check for ketones and give another correction and check again in 2-3 hours.

- An adolescent girl with diabetes for the last ten years is seen in diabetes follow up clinic. Her HbA1c is 7.6%. She is a straight A student. She has no complaints. Her weight has dropped from the 25th to the 5th percent. What is the most likely cause of her symptoms?
- 1) Eating disorder
- 2) Celiac disease
- 3) Hypothyroidism

- JHO: could be eating disorder or celiac--- not enough info to decide?
- Based on the statement that she is a straight A student, I would pick eating disorder. But it could also be celiac disease which is often asymptomatic. I think this question has more detail on the exam (I remember it from my exam), which made it easier to decide on the answer.

Questions?

josephine.ho@ahs.ca