ENDOCRINE PEARLS: ACP 2017

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CONFLICT OF INTEREST: NONE
No FDA unapproved drugs will be endorsed

Question: 1

- 24 years old while male is life-flighted from Moab on ventilator
- According to mom – went into difficulty in breathing 5 days ago, was seen in ER, treated for asthma, no improvement became unresponsive and was moved to ICU
- Treated off and on for bipolar illness, healthy otherwise, was cleaning 18 wheeler containers and killed mice in the process
- Leading diagnosis – Hanta Virus infection

Lab studies

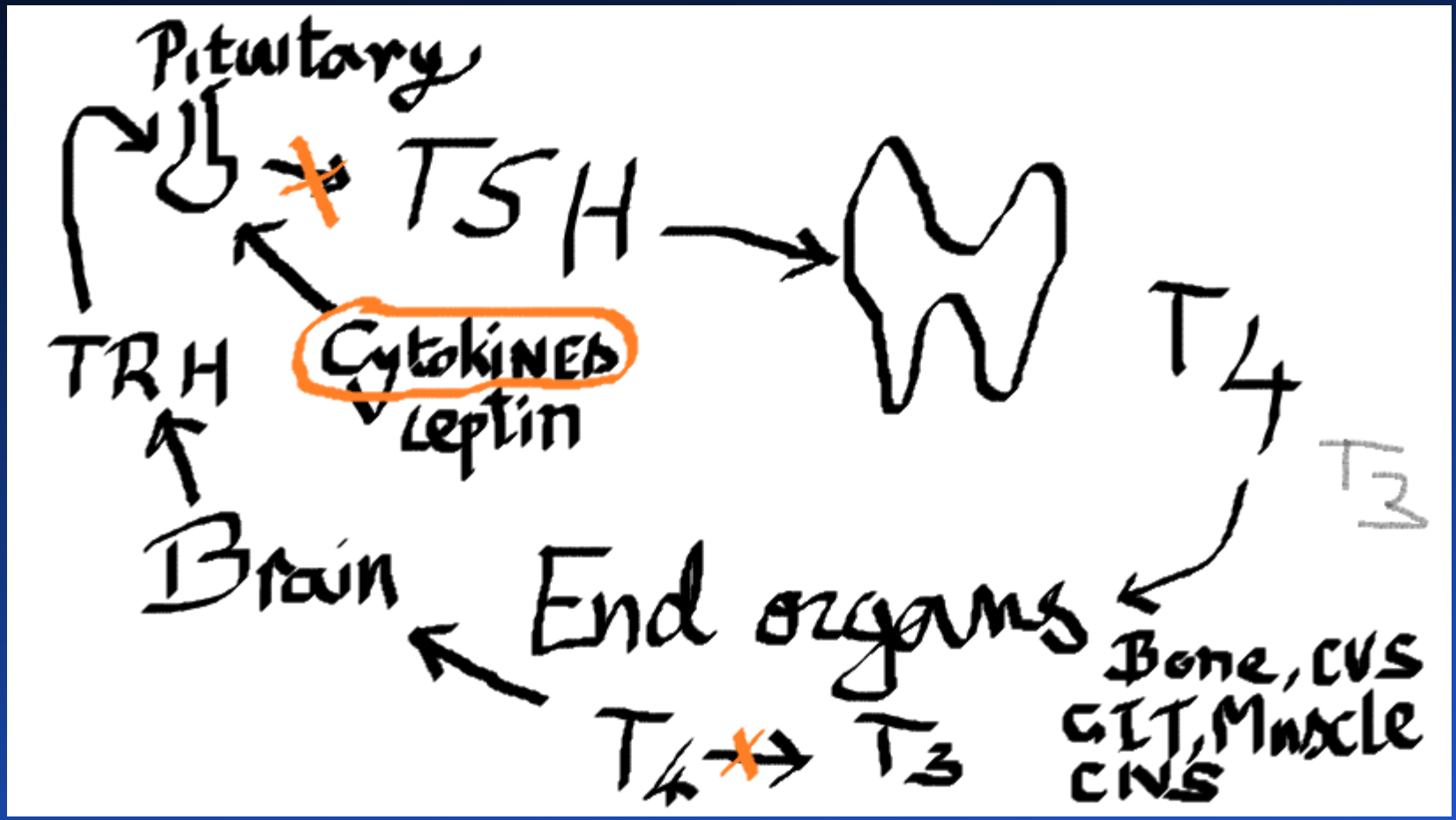
- CBC – HCT – 45, WBC 15, normal platelets
- AST 306, ALT 443, Hep C, B, A serology negative
- TSH <0.01, Free T_4 5.6 (0.8-1.8), T_3 by RIA – 298 (70-200)
- Mom with history of Hashimoto's thyroiditis
- Difficult to feel thyroid – no eye or nail changes

One of the following is the most likely diagnosis…

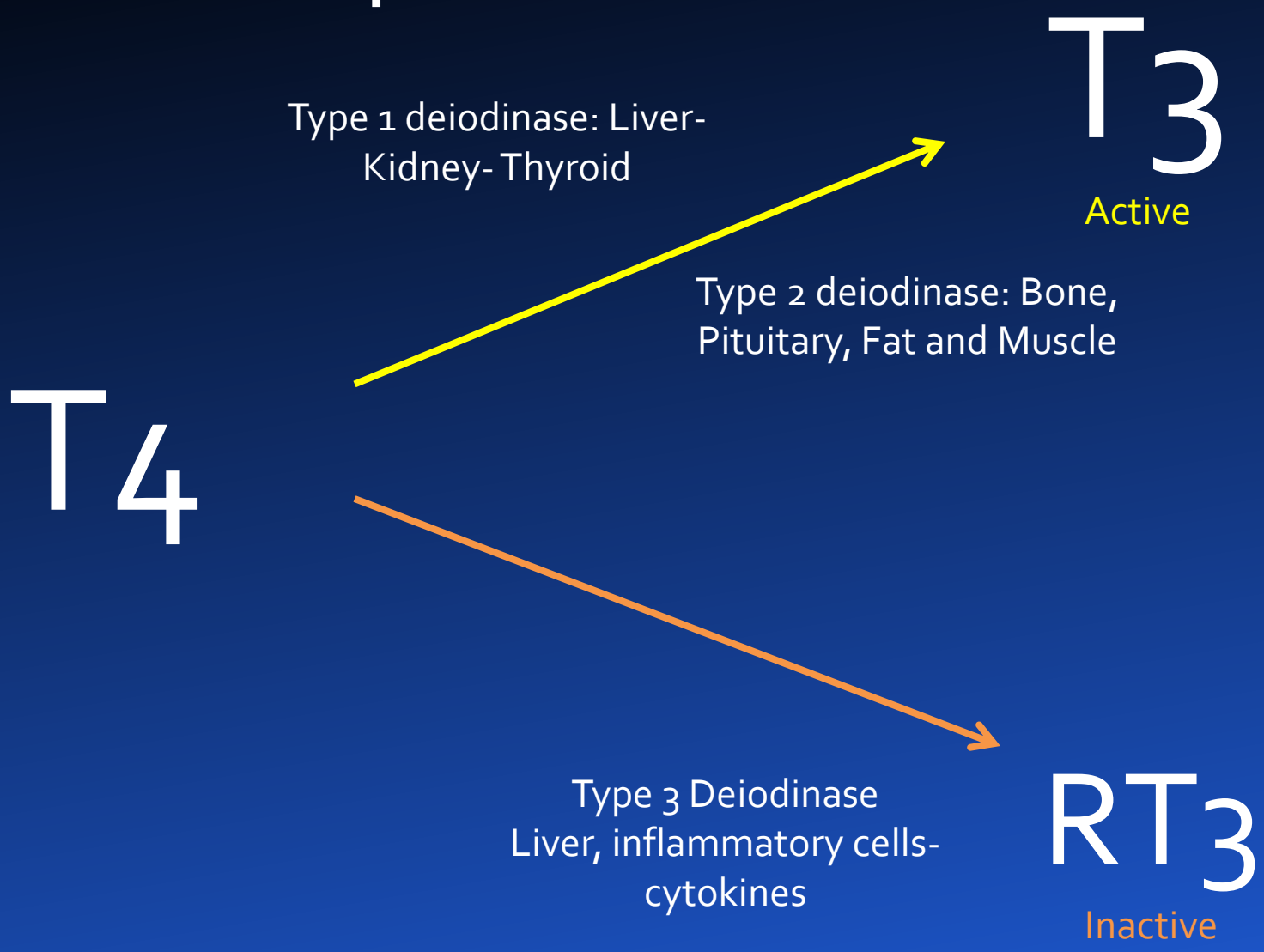
a. Possible hypothyroid, therefore, place patient on thyroxine
b. Graves disease of thyroid with crisis due to elevation of T_4 and T_3
c. Sick-Euthyroid syndrome, as evidenced by low TSH
d. Lithium toxicity, with associated thyroid dysfunction
e. Possible pituitary apoplexy, perform MRI

Etiology	TSH	FT_4	RAI uptake	Thyroid scan	Therapy
Graves disease	↓	↑	↑	Diffuse	RAI, Med, Surgery
Sub acute Thyroiditis	↓	↑	↓	No image	Prednisone
M NG	↓	↑	↑	Patchy	RAI or surgery
TOXIC ADENOMA	↓	↑	↑	Hot nodule	Surgery, RAI, ETOH
Exogenous	↓	↑	↓	No image	Counseling
TSH secreting pituitary tumor	↑	↑	↑	Diffuse	Pituitary surgery
Sick euthyroid	Low t_3, low TSH, low free T_4 – Low FT_4 is associated with poor outcome				

Sick euthyroid state – non thyroidal illness : Low TSH, Low Free T4, low T3 - seen in very ill individuals



Fate of T4


Type 1 deiodinase: Liver- Kidney- Thyroid
T3
Active
Type 2 deiodinase: Bone, Pituitary, Fat and Muscle
T4
Type 3 Deiodinase Liver, inflammatory cells- cytokines
RT3
Inactive

Changes following acute illness

- First change is drop in T_3 level – few hours
- This is due to conversion to RT_3
- The next change is drop in T_4 level
- Despite drop in T_4 and T_3 levels, there is no compensatory increase in TSH
- Dopamine, glucocorticoids and leptin (low) also regulate (lower) TSH secretion in illness

The following clues point towards primary thyroid illness:

- Low TSH prior to illness
- High normal T_3 levels during illness
- Complete suppression of TSH
- Elevated TPO, TRAB
- Clinical findings: Unexplained tachycardia (elevated or upper normal T_3), hypothermia or bradycardia (usually Free T_4 will be very low)

Treatment of acute severe hyperthyroidism

- PTU (added benefit- blocks T_3 formation), Methimazole
- Beta blockers
- Dexamethasone (blocks T_4 to T_3 conversion)
- Oral Cholestyramine
- i.v iodine (caution)
- surgery (usually not possible)
- Once recovered - RAI

Question: 2

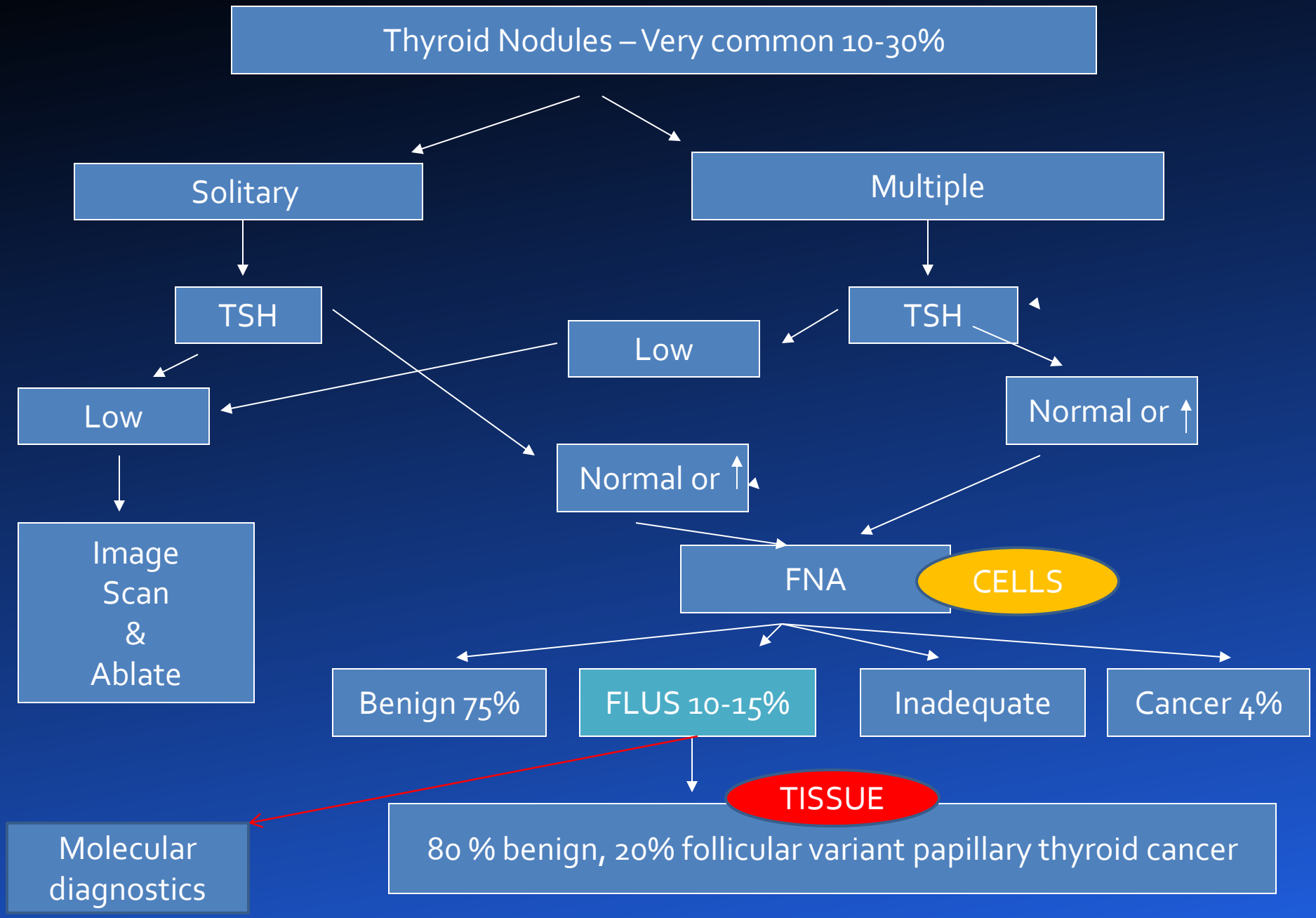
- 30 years old female is brought from the Utah State Prison for a nodule in her thyroid gland
- She reports no symptoms, but carries a diagnosis of ADD in her child hood and bipolar disorder as adult and has been on lithium and Ritalin for 10 yrs
- She also feels best when using marijuana
- No family history of thyroid disease
- No exposure to radiation
- No monthly cycles for 1 year

Clinical exam and laboratory studies...

- Thin lady with no tremors or proximal muscle weakness, 3 cm right thyroid nodule
- TSH 0.01 (normal 0.34 – 4)
- Free T_4 – 1.8 (normal 0.8 – 1.8)
- TRAB / TPO negative

What evaluation or testing would you do next?

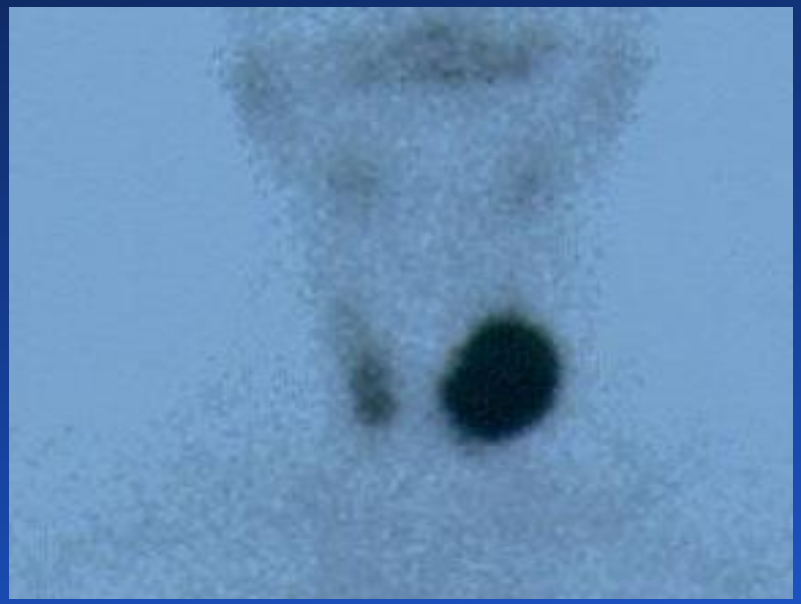
a. Biopsy of the nodule to rule out malignancy
b. Nuclear thyroid uptake and scan
c. Excision biopsy of the nodule
d. NSAID and prednisone 20 mg per day and repeat test in 6 months.

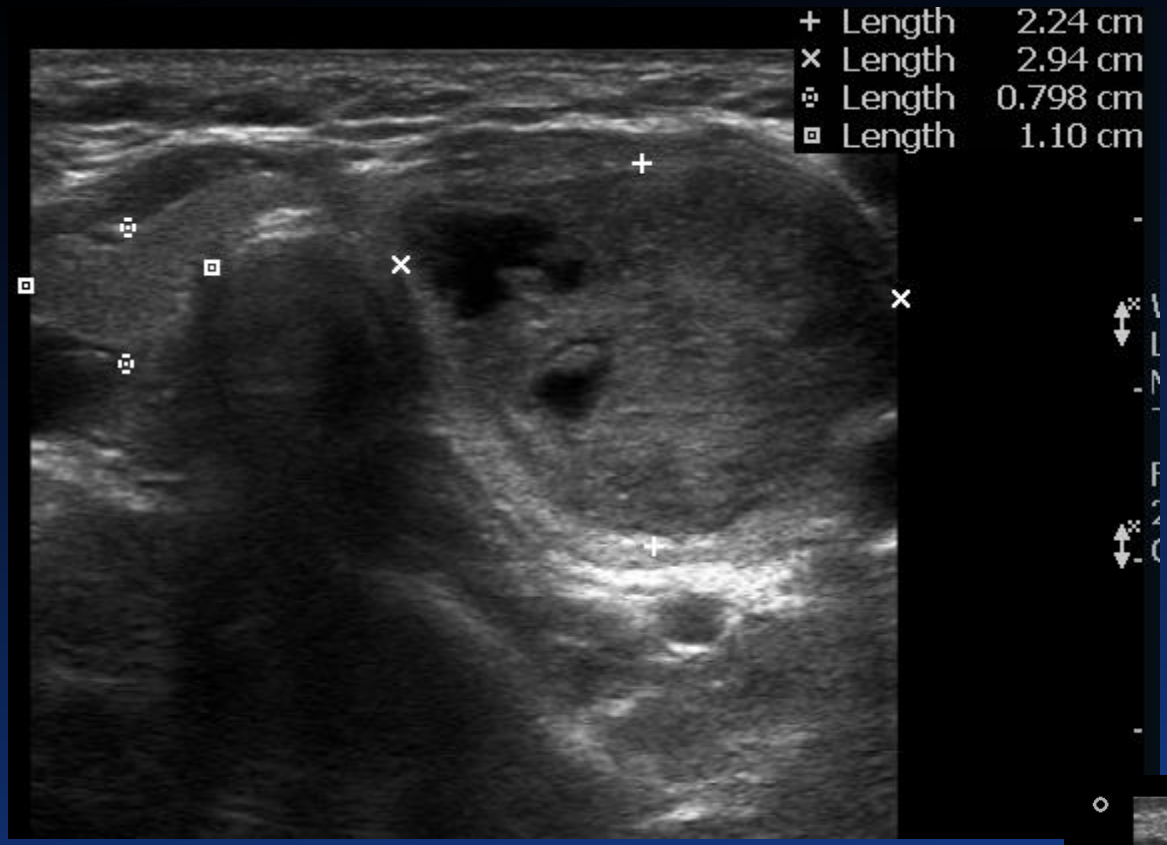

Thyroid Nodules – Very common 10-30%
Solitary
Multiple
TSH
TSH
Low
Low
Normal or
Normal or
Image
Scan
&
Ablate
FNA
CELLS
Benign 75%
FLUS 10-15%
Inadequate
Cancer 4%
TISSUE
Molecular
diagnostics
80 % benign, 20% follicular variant papillary thyroid cancer

Disorders of thyroid over-activity

Back to our patient…

- What test will you perform?
- Thyroid scan and uptake

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× Length 2.94 cm
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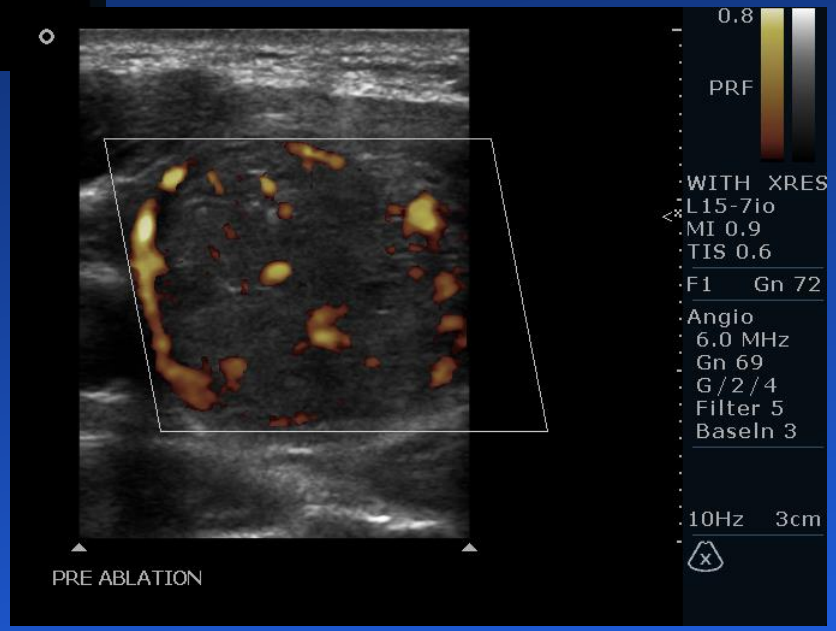

0.8
PRF
WITH XRES
L15-7io
MI 0.9
TIS 0.6
F1 Gn 72
Angio
6.0 MHz
Gn 69
G/2/4
Filter 5
Baseln 3
10Hz 3cm
PRE ABLATION

Question: 3

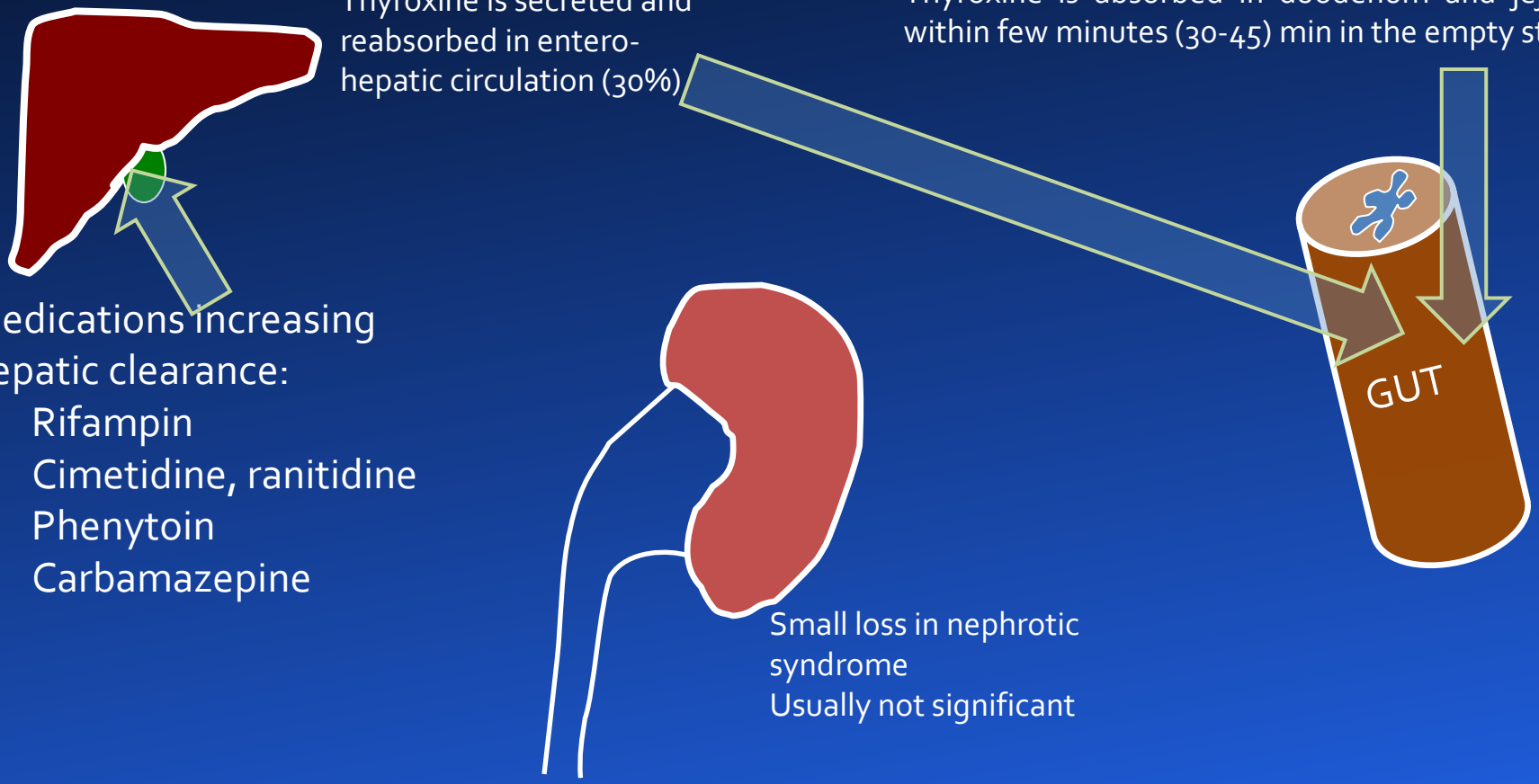
- 34 years old admin assistant presents for evaluation of hypothyroidism
- persistent elevation of TSH
- Diagnosed 10 years ago, she weighs 128 lbs, 5ft 6 inches tall, takes on empty stomach -30-45 minutes prior to eating
- Strong family history of underactive thyroid
- Her present dose of levothyroxine 175 mcg
- TSH 34
- Free T_4 0.7

Which one of the following is the next best step?

a) Commonest cause of elevation of tsh is noncompliance, therefore, ask her to download med minder app and follow smartphone reminders
b) Take levothyroxine on empty stomach and wait for 2 hours before eating
c) Tissue-trans-glutaminase ab estimation
d) MRI brain to rule out pituitary tumor
e) Possible interfering TSH heterophile antibody, use a different TSH testing lab

1) Non compliance is the commonest cause of elevation of TSH
2) Supervised administration also helps
3) Typical weight based dose 1.4-1.8 mcg per kg

1. Interference- food – calcium, iron
2. Mucosal disease – Regional ileitis, celiac
3. GI fistulation – biliary fistula, loss of bile
4. Bowel resection
5. Bowel irradiation



Medications increasing hepatic clearance:

1. Rifampin
2. Cimetidine, ranitidine
3. Phenytoin
4. Carbamazepine

Role for T3 or Armour thyroid?

- As for as literature stands, there in no apparent benefit in double blind controlled studies…
- Case by case basis, we use it meet patient expectations

How to treat patients with elevated TSH despite adequate weight based t4 replacement?

- Counseling
- Give more t4 until TSH is normalized
- Rule out celiac sprue and other disorders
- Correct answer: TTG measurement to rule out celiac sprue

Hypothyroidism and pregnancy

- Trimester specific TSH
- <2.5 – 1st Trimester
- <3 – 2nd & 3rd Trimesters

- 4 weeks TSH checks or following dose change during 1st trimester – At least once every trimester – 6-8 weeks

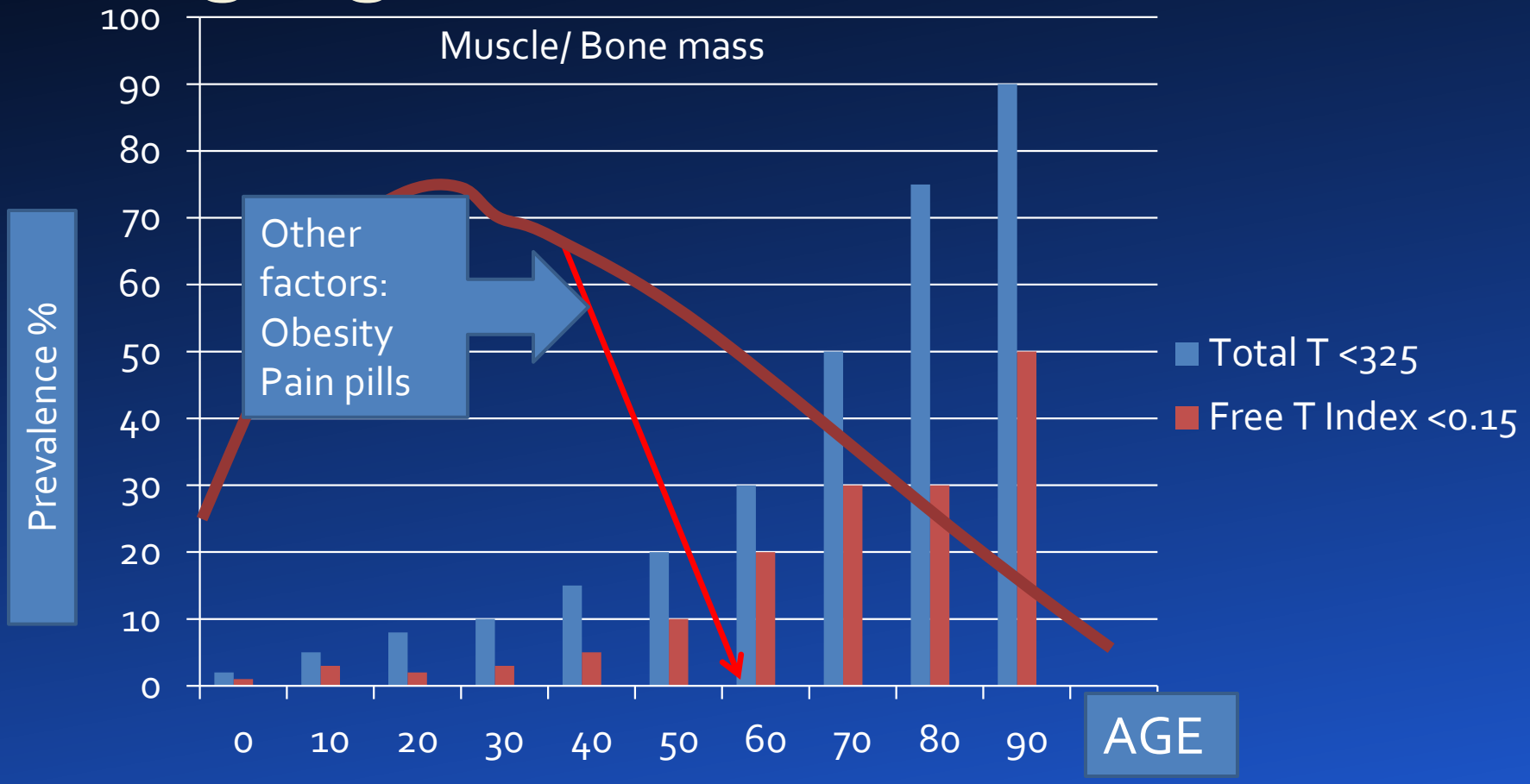
Question 4:

- A 61 years old middle school basketball coach presents for the evaluation of suspected testosterone deficiency. He reports of lack of erection sufficient enough for sexual intercourse despite intact desire.
- He also observes that he has less energy on the court during coaching sessions. Past medical history is relevant for remote history of smoking, concurrent treatment for essential hypertension and type 2 diabetes. His medication includes Lisinopril, HCTZ, metformin and glipizide,
- Physical examination reveals an overweight but cheerful appearing man with mild plethora. Normal axillary hair, normal facial hair and testicular volume, rectal examination reveals enlarged – non indurated prostate. Mild enlargement of breasts bilaterally.
- Pulse – 83 bpm, regular, BP 136/ 88 mm hg, intact peripheral pulses and normal sensation of extremities without peripheral edema – BMI 34
- HCT – 50%, Creatinine – 1.3, A1c – 6.9%, LDL – 124, HDL – 38, TGL – 205
- Testosterone total – 264 ng per dl

One of the following is the next best step to determine his testosterone status:

a) Early am free testosterone measurement on two different days by available analog assay
b) Serum LH and FSH estimation
c) Serum prolactin
d) SHBG estimation and calculate free testosterone level
e) Sellar imaging by CT or MRI

Reduction of T related to aging

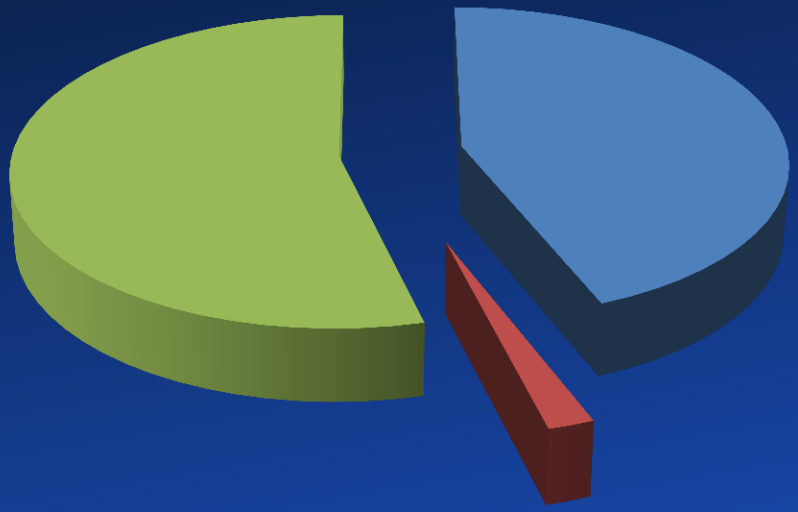


Harman et al JCEM 86 724-731 2001

Diagnosis: accurate T measurement

- 8 am Testosterone
- Multiple measurements – in borderline situations
- FSH and LH will aid in differentiating primary vs secondary disorders
- Prolactin, TSH, Estrogen etc in special situations

Testosterone binding…calculated testosterone is more accurate than analog assay



Total Testosterone

- SHBG bound T 44%
- Free T 2%
- Albumin Bound T 54%

Bio available T

Factors that influence SHBG levels and Testosterone binding …

- Elevated Total T and SHBG
  - Hepatitis
  - HIV
  - Hyperthyroidism
  - Estrogens
  - Cirrhosis
- Low Total T and Low SHBG
  - Morbid obesity
  - Nephrotic syndrome
  - Acromegaly
  - Untreated hypothyroid
  - Glucocorticoids

Free & Bioavailable Testosterone calculator

These calculated parameters more accurately reflect the level of bioactive testosterone than does the sole measurement of total serum testosterone. Testosterone and dihydrotestosterone (DHT) circulate in plasma unbound (free approximately 2 - 3%) ,bound to specific plasma proteins (sex hormone-binding globulin SHBG) and weakly bound to nonspecific proteins such as albumin. The SHBG-bound fraction is biologically inactive because of the high binding affinity of SHBG for testosterone. Free testosterone measures the free fraction, bioavailable testosterone includes free plus weakly bound to albumin.

Albumin	4.3	g/dL	Calculate	Explanation and examples
SHBG		nmol/L		
Testosterone		ng/dL		

Free Testosterone	
Bioavailable Testosterone	

Disclaimer: Results from this calculator should NOT be solely relied upon in making (or refraining from making) any decision in any case/ circumstances without the prior consultation of experts or professional persons. No responsability whatsoever is assumed for its correctness or suitability for any given purpose.

WARNING! The calculated free and bioavailable testosterone are reliable in most clinical situations, but should not be relied upon in situations with potential massive interference by steroids binding to SHBG; e.g. in women during pregnancy, in men during treatment inducing high levels of DHT (e.g. transdermal DHT, oral testosterone) or mesterolon

This calculator was developed at the Hormonology department, University Hospital of Ghent, Belgium. If you have suggestions to improve this calculator, or for further questions or help contact us Dr. Tom Fiers or Prof. Dr. J.M. Kaufman

When to perform cranial imaging?

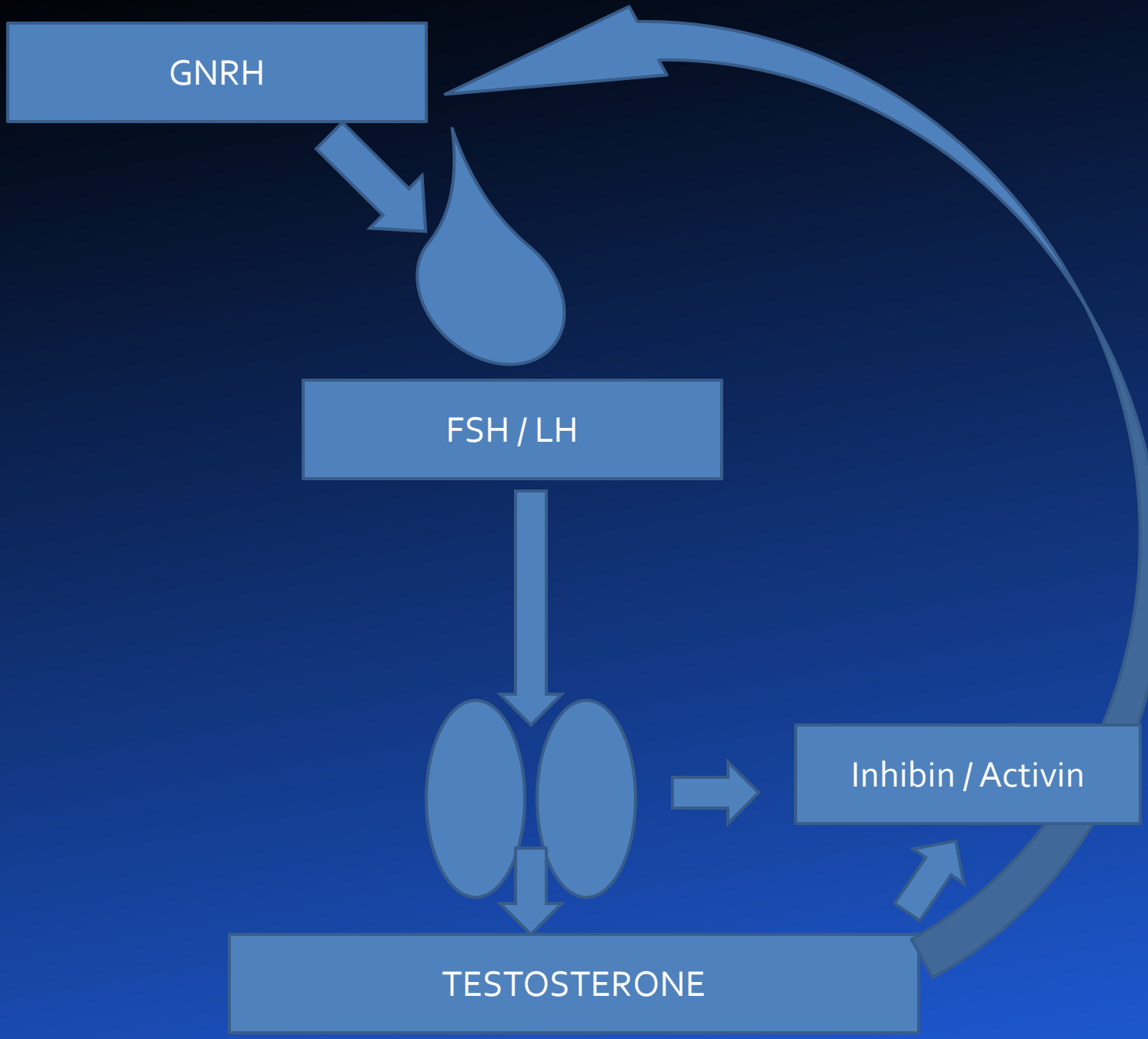
- All young males with secondary hypogonadism <45 – 50 years…
- Massively obese, young individuals with slight reduction – follow closely
- Most men (except >65) with significant reduction of testosteorone (<150 - 200 ng/dl)
- Most men with abrupt reduction (outside of acute illnesses)
- In general men >65 do not need imaging unless: HA, Vision, Galactorrhea, other signs of HP axis problem

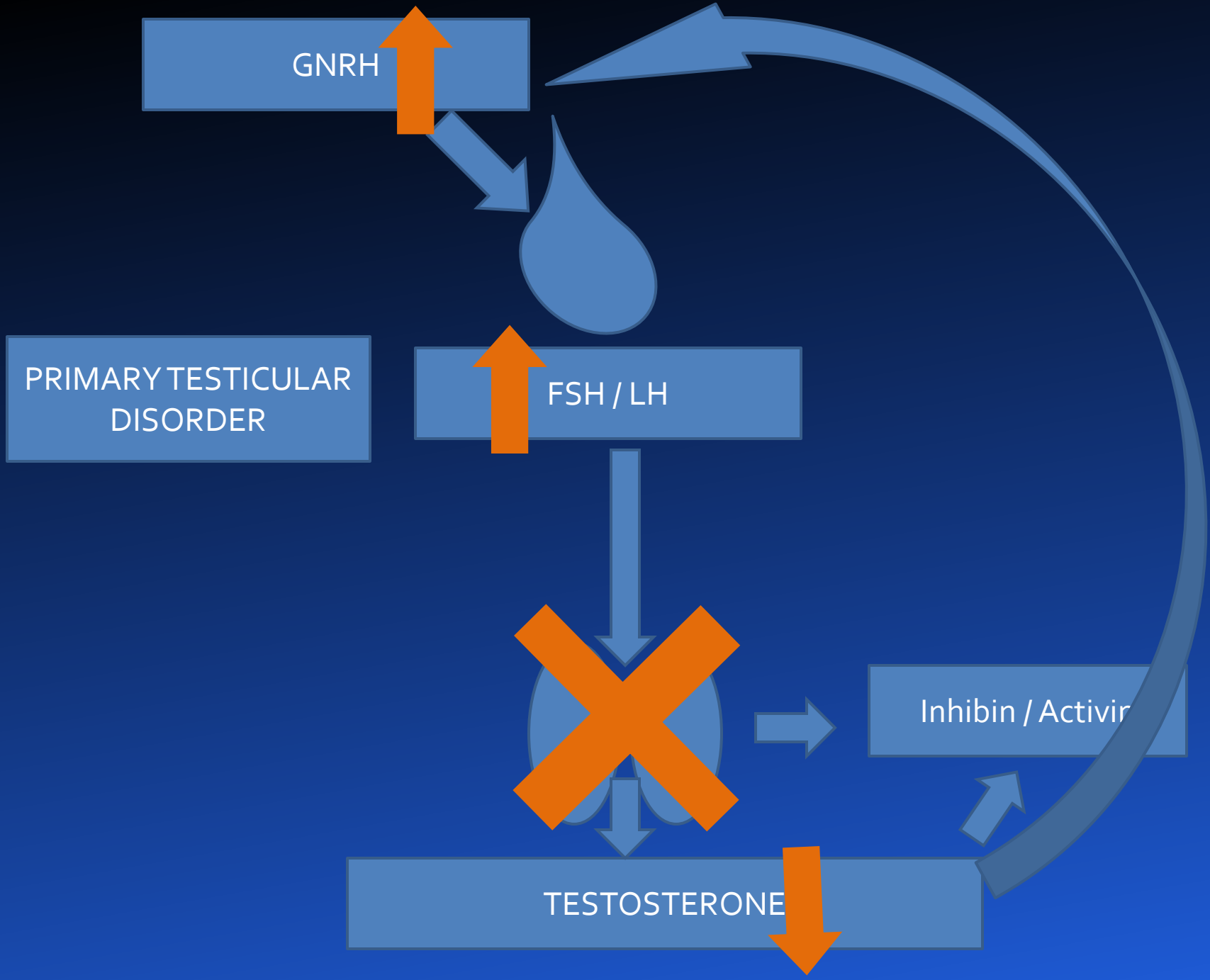
Question 5: 22 years old white male … no sexual function

- Presents for the evaluation of lack of maturation: Accompanied by dad and mom
- No hot flashes
- Ht – 5ft 11 inches, 155 lbs
- Upper segment to lower segment ratio - <1
- Testicles – 10 mm – no distinct masses
- No development of phallus, genital hair or upper body musculature
- Total Testosterone 50 ng /dl (300-900 ng/dl)
- FSH – 94 (1-13 mIu/ml)

One of the following is the next best step…

a. Replace testosterone- parenterally with testosterone cipionate or undeconate
b. Perform Karyotype analysis
c. Pituitary MRI to rule out pituitary tumor
d. Repeat testosterone and FSH estimation in one week at 8 am
e. Estrogen estimation


GNRH
FSH / LH
Inhibin / Activin
TESTOSTERONE


GNRH
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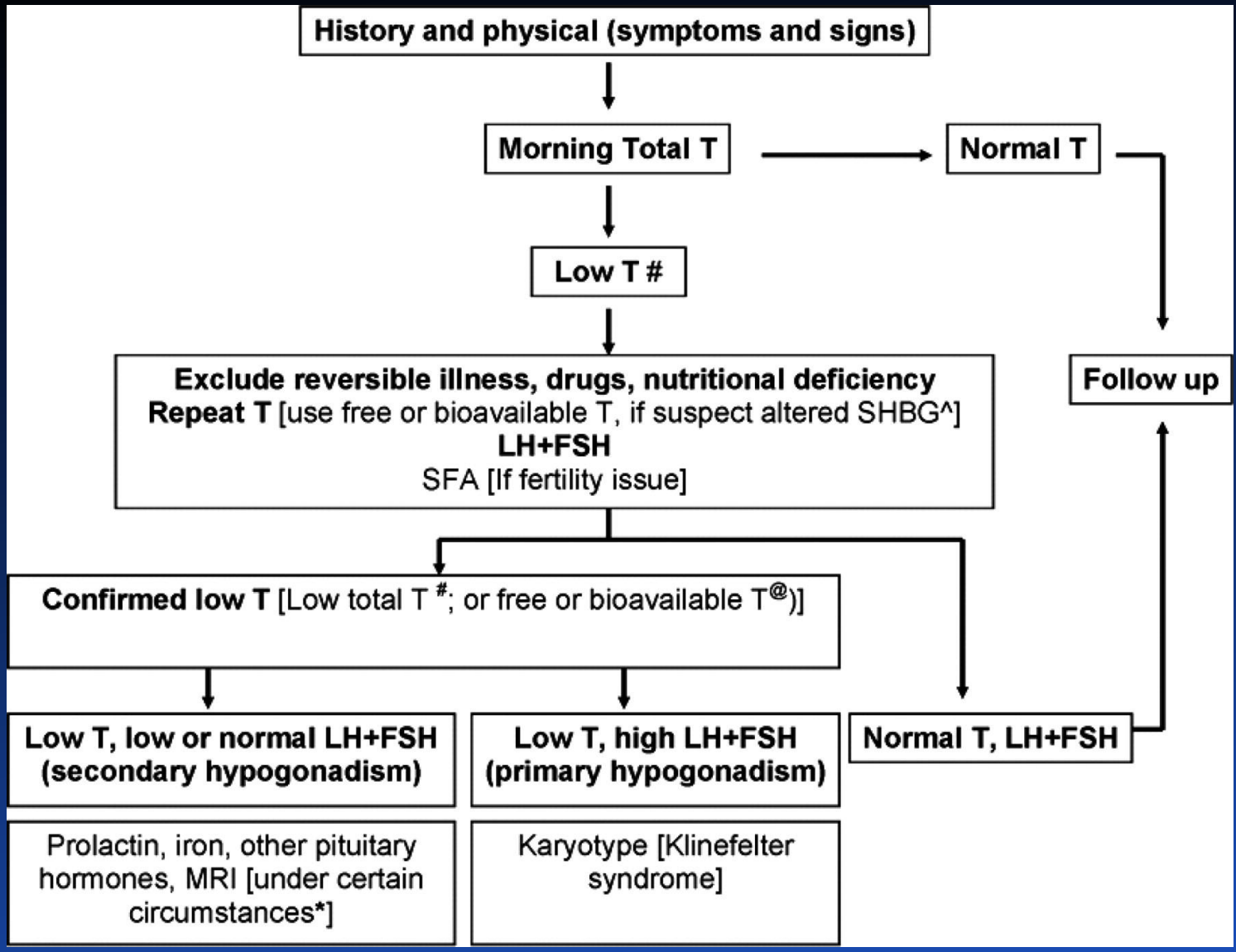
FSH / LH
Inhibin / Activir
TESTOSTERONE



An approach for the diagnostic evaluation of adult men suspected of having androgen deficiency

Published in: Shalender Bhasin; Glenn R. Cunningham; Frances J. Hayes; Alvin M. Matsumoto; Peter J. Snyder; Ronald S. Swerdloff; Victor M. Montori; *The Journal of Clinical Endocrinology & Metabolism* **2010,** 95, 2536-2559.
DOI: 10.1210/jc.2009-2354

ENDOCRINE SOCIETY

Case 6: 58 years old male

- Diagnosed with idiopathic hypogonadism, he has been placed on parenteral and dermal preparations for more than 25 years.
- He has developed LUTS for the past 2 years off and on. His PSA is 2.0 and he has been placed on tamsulosin 0.4 mg per day, after DRE. This led to partial resolution of prostate symptoms.
- He was then placed on dutasteride, he returned in 6 months with reports of worsening of his prostate symptoms. PSA – 1.4

One of the following is the next best step…

a. Discontinue testosterone and revaluate in 6 months
b. PSA is stable therefore, reassure patient and increase alfa blockers
c. Referral for urological evaluation as soon as possible
d. Discontinue testosterone and try DHEA instead

Archived Content

The content on this page is provided for reference purposes only. This content has not been altered or updated since it was archived.

Search Archive

Safety

5-alpha reductase inhibitors (5-ARIs): Label Change - Increased Risk of Prostate Cancer

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

Drugs in the 5-ARI class include finasteride and dutasteride. These drugs are marketed under the brand-names Proscar, Propecia, Avodart, and Jalyn

[Posted 06/09/2011]

AUDIENCE: Urology, Family Medicine, Internal Medicine

ISSUE: FDA notified healthcare professionals that the Warnings and Precautions section of the labels for the 5-alpha reductase inhibitor (5-ARI) class of drugs has been revised to include new safety information about the increased risk of being diagnosed with a more serious form of prostate cancer (high-grade prostate cancer).

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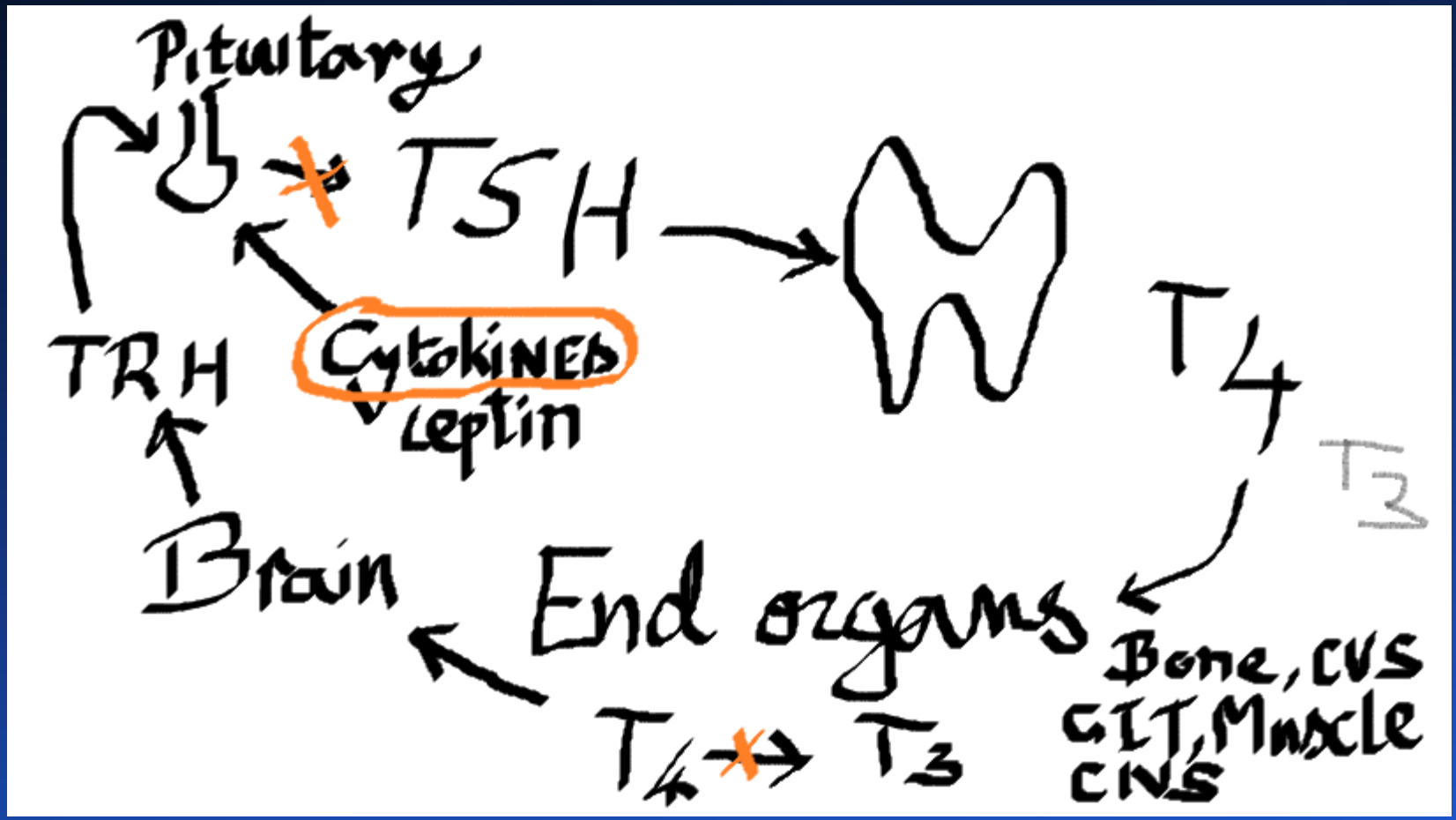
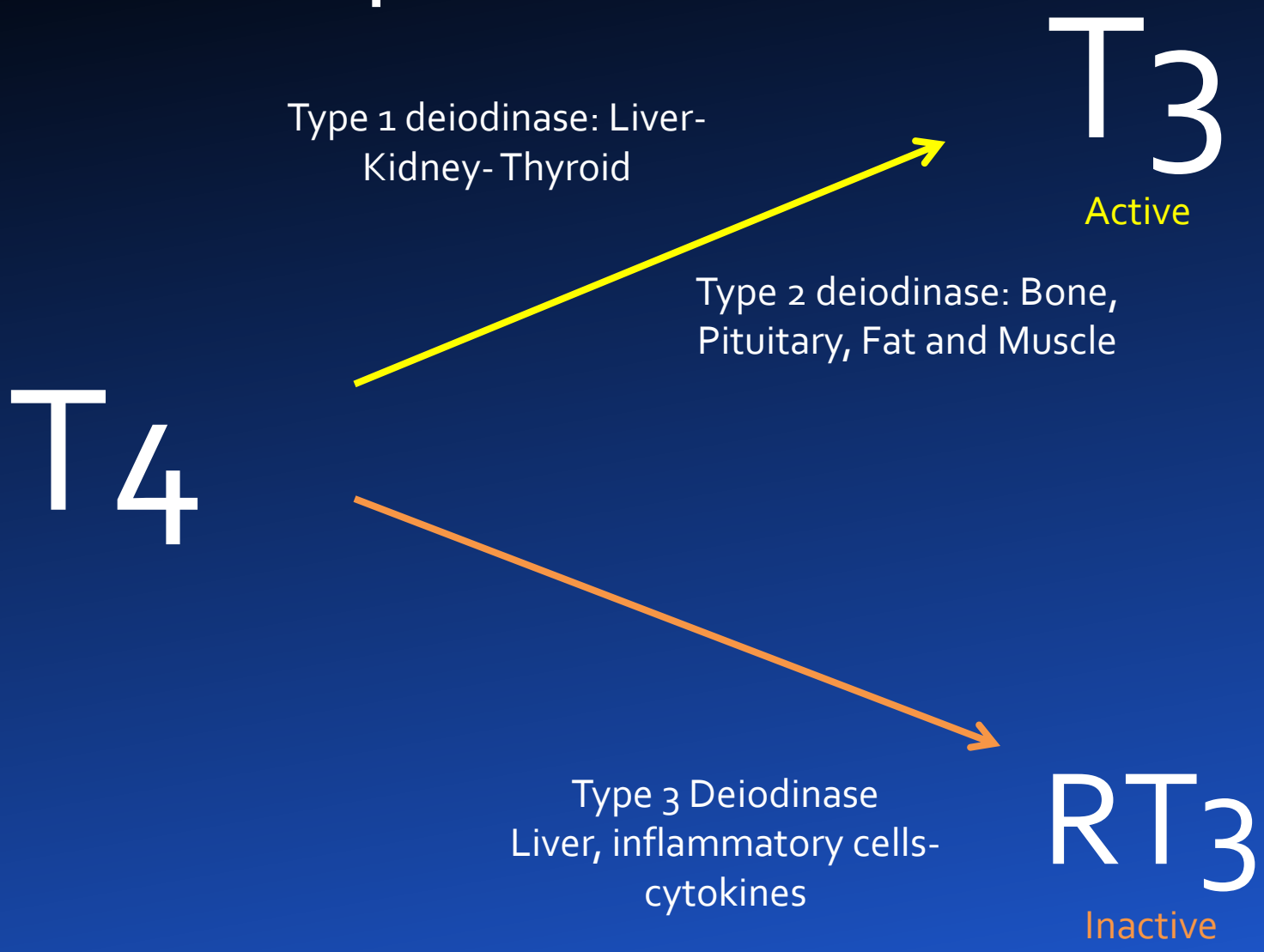


Fate of T4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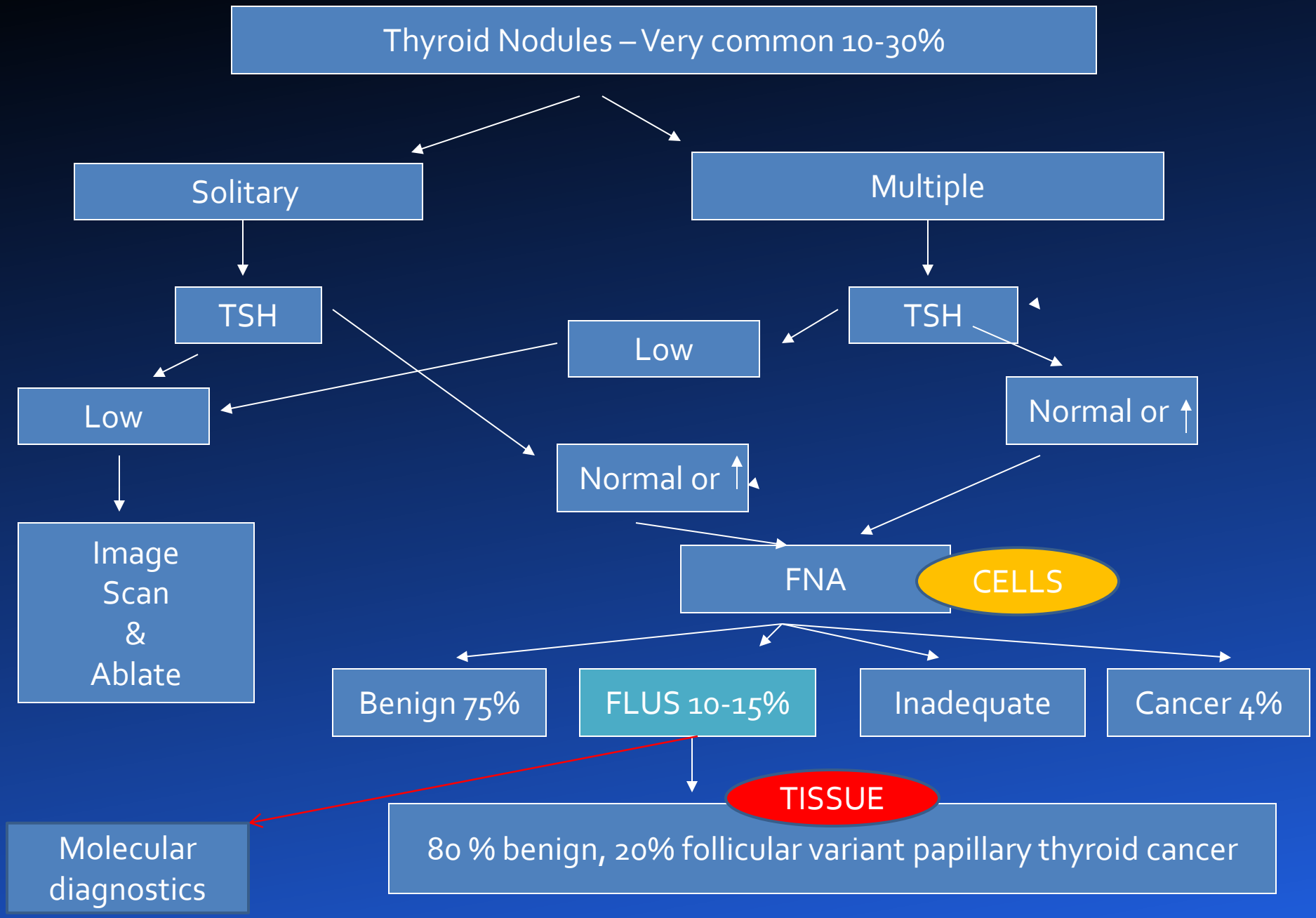
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FLUS 10-15%
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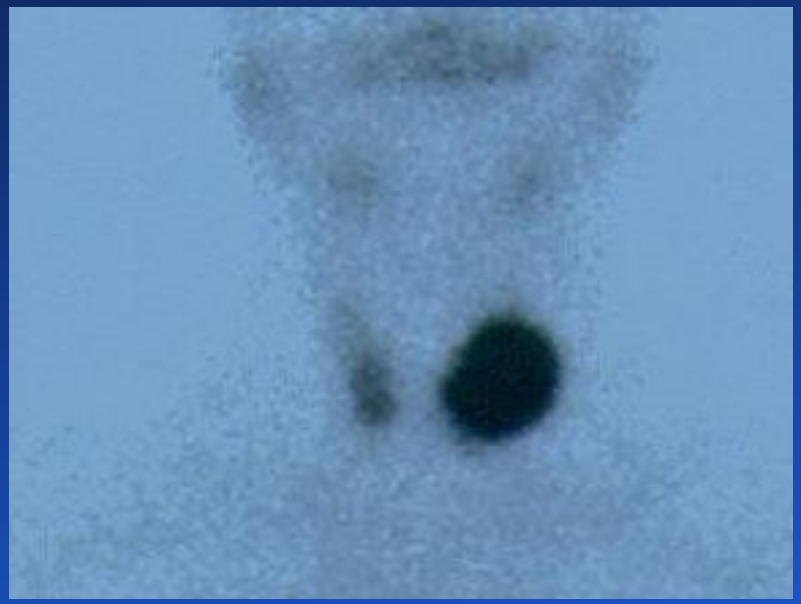

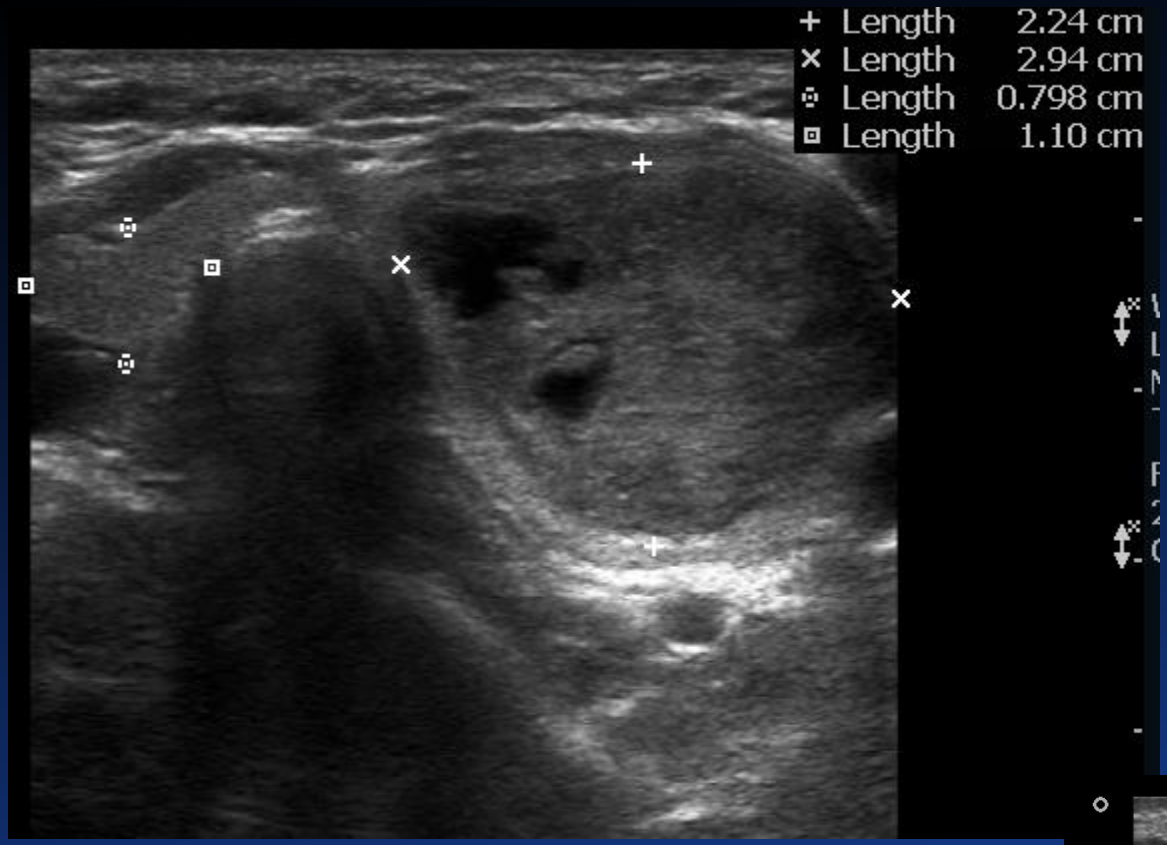
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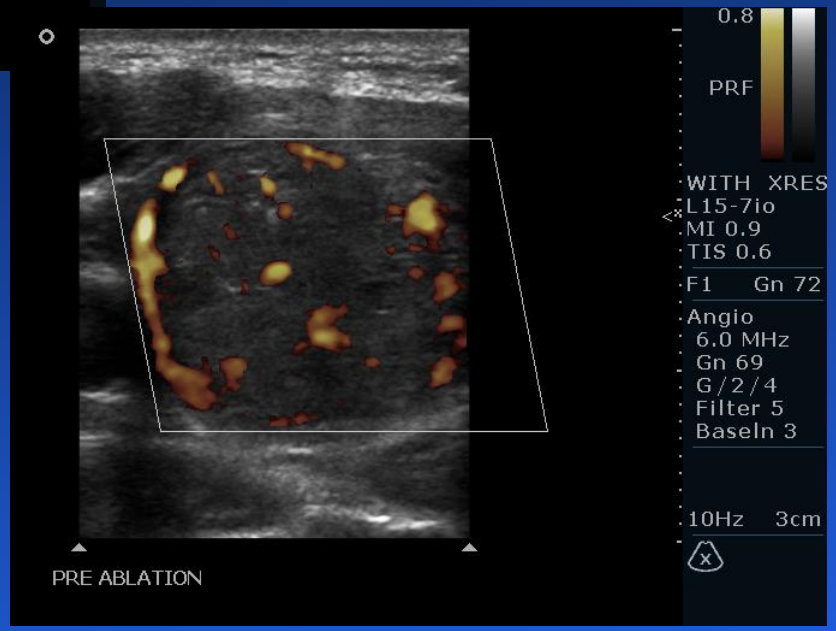
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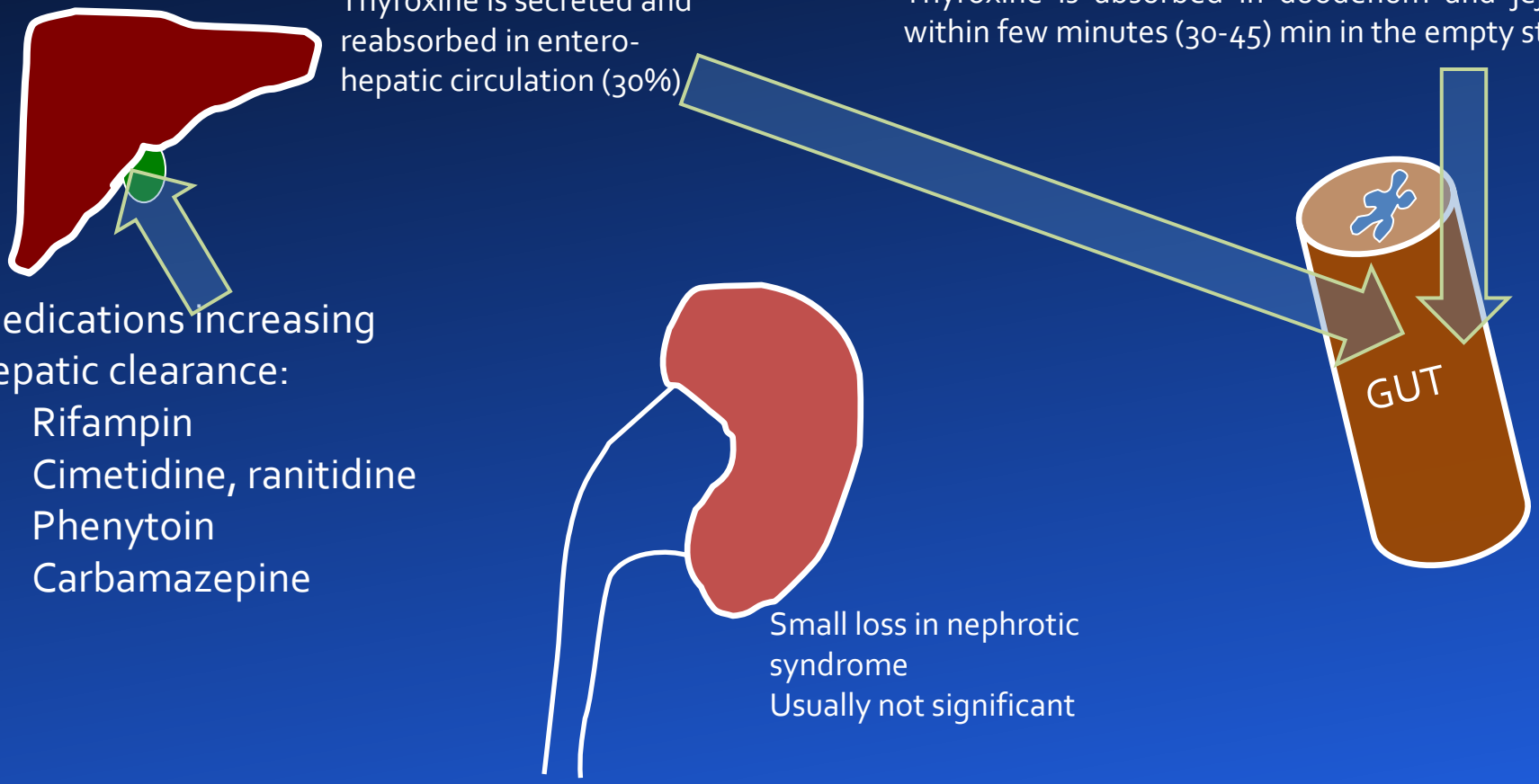

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- 4 weeks TSH checks or following dose change during 1st trimester – At least once every trimester – 6-8 weeks

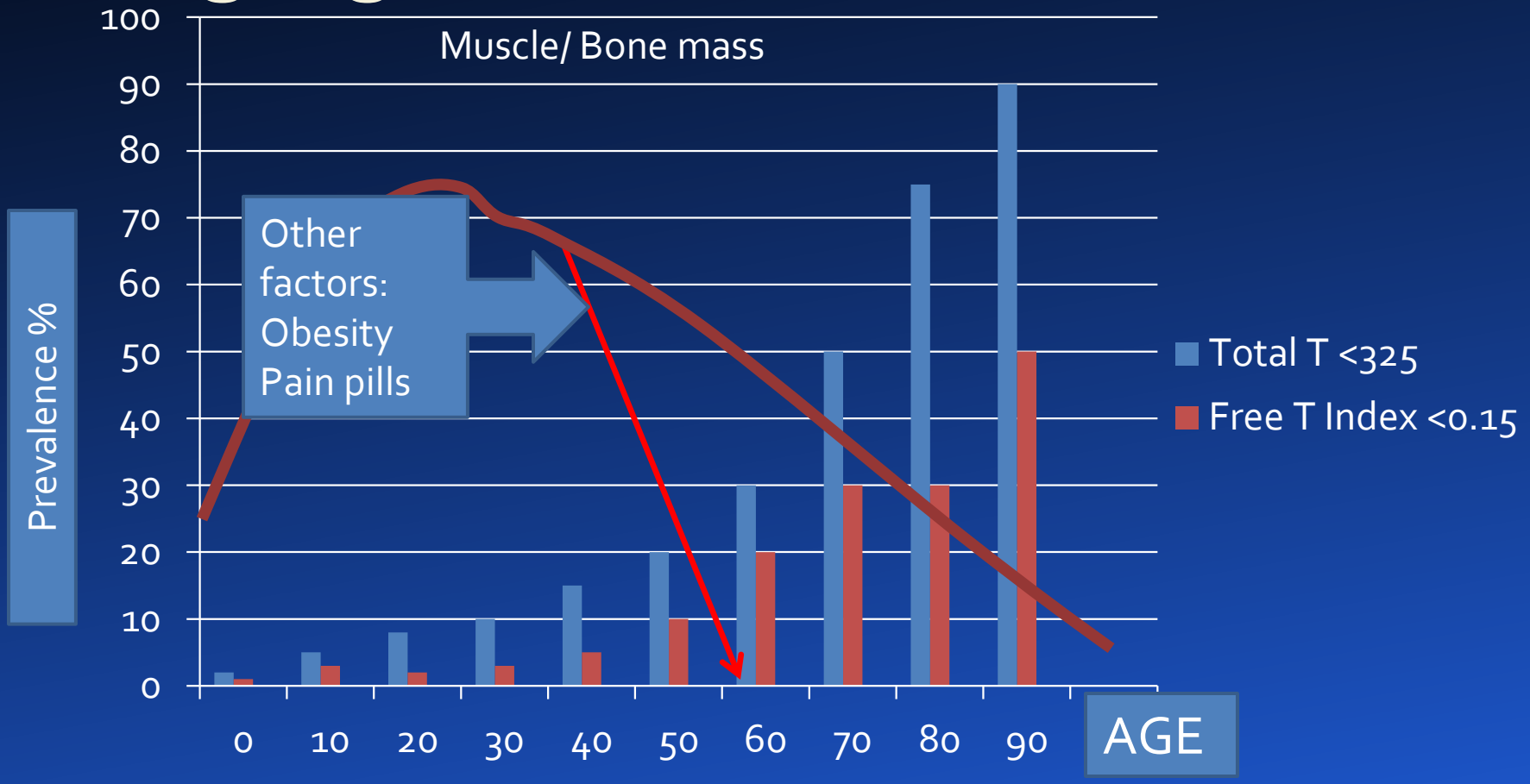
Question 4:

- A 61 years old middle school basketball coach presents for the evaluation of suspected testosterone deficiency. He reports of lack of erection sufficient enough for sexual intercourse despite intact desire.
- He also observes that he has less energy on the court during coaching sessions. Past medical history is relevant for remote history of smoking, concurrent treatment for essential hypertension and type 2 diabetes. His medication includes Lisinopril, HCTZ, metformin and glipizide,
- Physical examination reveals an overweight but cheerful appearing man with mild plethora. Normal axillary hair, normal facial hair and testicular volume, rectal examination reveals enlarged – non indurated prostate. Mild enlargement of breasts bilaterally.
- Pulse – 83 bpm, regular, BP 136/ 88 mm hg, intact peripheral pulses and normal sensation of extremities without peripheral edema – BMI 34
- HCT – 50%, Creatinine – 1.3, A1c – 6.9%, LDL – 124, HDL – 38, TGL – 205
- Testosterone total – 264 ng per dl

One of the following is the next best step to determine his testosterone status:

a) Early am free testosterone measurement on two different days by available analog assay
b) Serum LH and FSH estimation
c) Serum prolactin
d) SHBG estimation and calculate free testosterone level
e) Sellar imaging by CT or MRI

Reduction of T related to aging

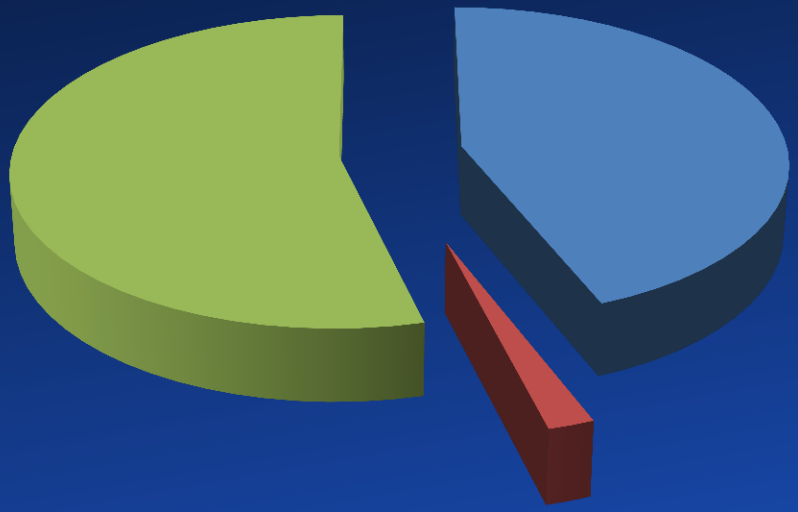


Harman et al JCEM 86 724-731 2001

Diagnosis: accurate T measurement

- 8 am Testosterone
- Multiple measurements – in borderline situations
- FSH and LH will aid in differentiating primary vs secondary disorders
- Prolactin, TSH, Estrogen etc in special situations

Testosterone binding…calculated testosterone is more accurate than analog assay



Total Testosterone

- SHBG bound T 44%
- Free T 2%
- Albumin Bound T 54%

Bio available T

Factors that influence SHBG levels and Testosterone binding …

- Elevated Total T and SHBG
  - Hepatitis
  - HIV
  - Hyperthyroidism
  - Estrogens
  - Cirrhosis
- Low Total T and Low SHBG
  - Morbid obesity
  - Nephrotic syndrome
  - Acromegaly
  - Untreated hypothyroid
  - Glucocorticoids

Free & Bioavailable Testosterone calculator

These calculated parameters more accurately reflect the level of bioactive testosterone than does the sole measurement of total serum testosterone. Testosterone and dihydrotestosterone (DHT) circulate in plasma unbound (free approximately 2 - 3%) ,bound to specific plasma proteins (sex hormone-binding globulin SHBG) and weakly bound to nonspecific proteins such as albumin. The SHBG-bound fraction is biologically inactive because of the high binding affinity of SHBG for testosterone. Free testosterone measures the free fraction, bioavailable testosterone includes free plus weakly bound to albumin.

Albumin	4.3	g/dL	Calculate	Explanation and examples
SHBG		nmol/L		
Testosterone		ng/dL		

Free Testosterone	
Bioavailable Testosterone	

Disclaimer: Results from this calculator should NOT be solely relied upon in making (or refraining from making) any decision in any case/ circumstances without the prior consultation of experts or professional persons. No responsability whatsoever is assumed for its correctness or suitability for any given purpose.

WARNING! The calculated free and bioavailable testosterone are reliable in most clinical situations, but should not be relied upon in situations with potential massive interference by steroids binding to SHBG; e.g. in women during pregnancy, in men during treatment inducing high levels of DHT (e.g. transdermal DHT, oral testosterone) or mesterolon

This calculator was developed at the Hormonology department, University Hospital of Ghent, Belgium. If you have suggestions to improve this calculator, or for further questions or help contact us Dr. Tom Fiers or Prof. Dr. J.M. Kaufman

When to perform cranial imaging?

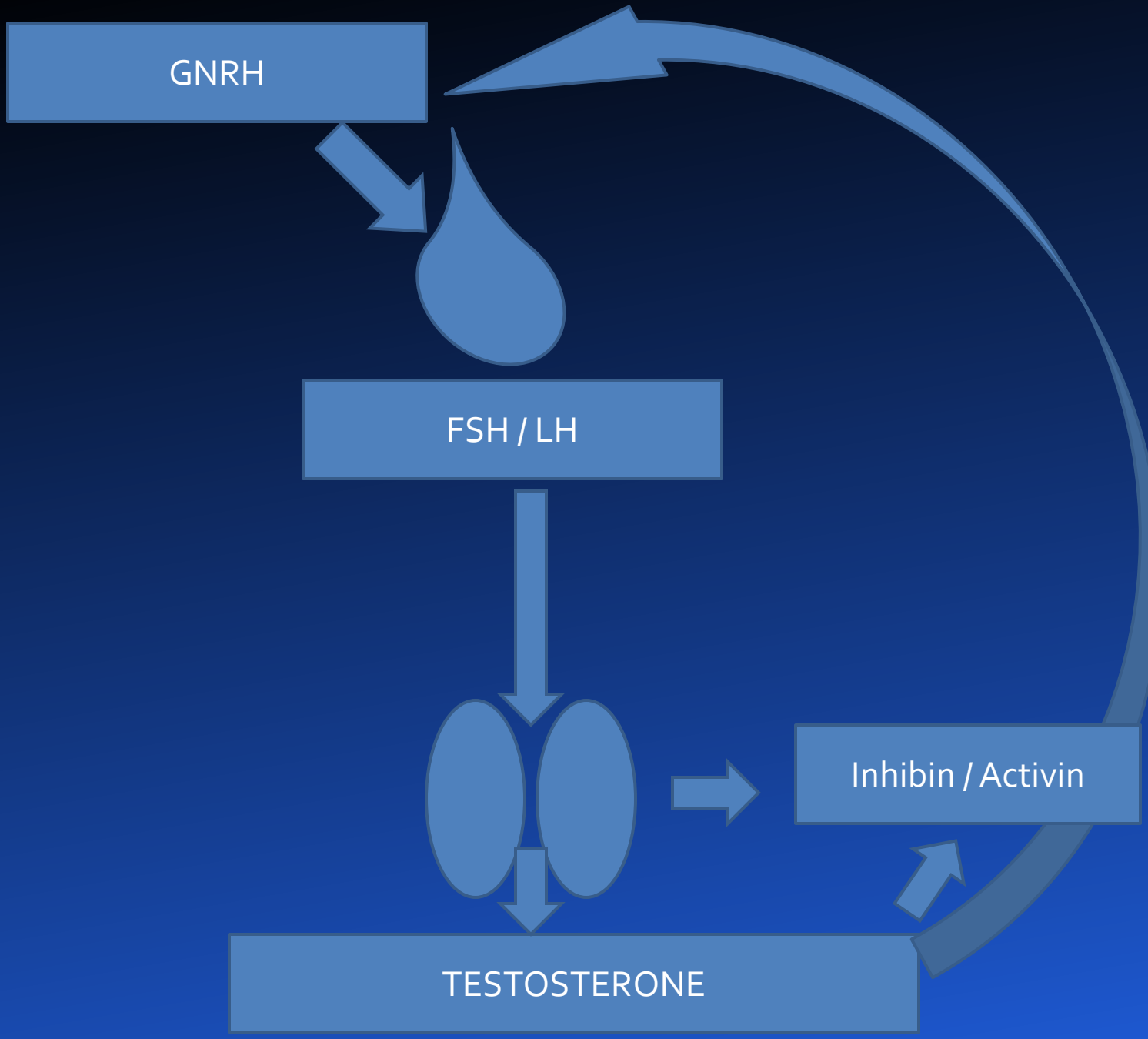
- All young males with secondary hypogonadism <45 – 50 years…
- Massively obese, young individuals with slight reduction – follow closely
- Most men (except >65) with significant reduction of testosteorone (<150 - 200 ng/dl)
- Most men with abrupt reduction (outside of acute illnesses)
- In general men >65 do not need imaging unless: HA, Vision, Galactorrhea, other signs of HP axis problem

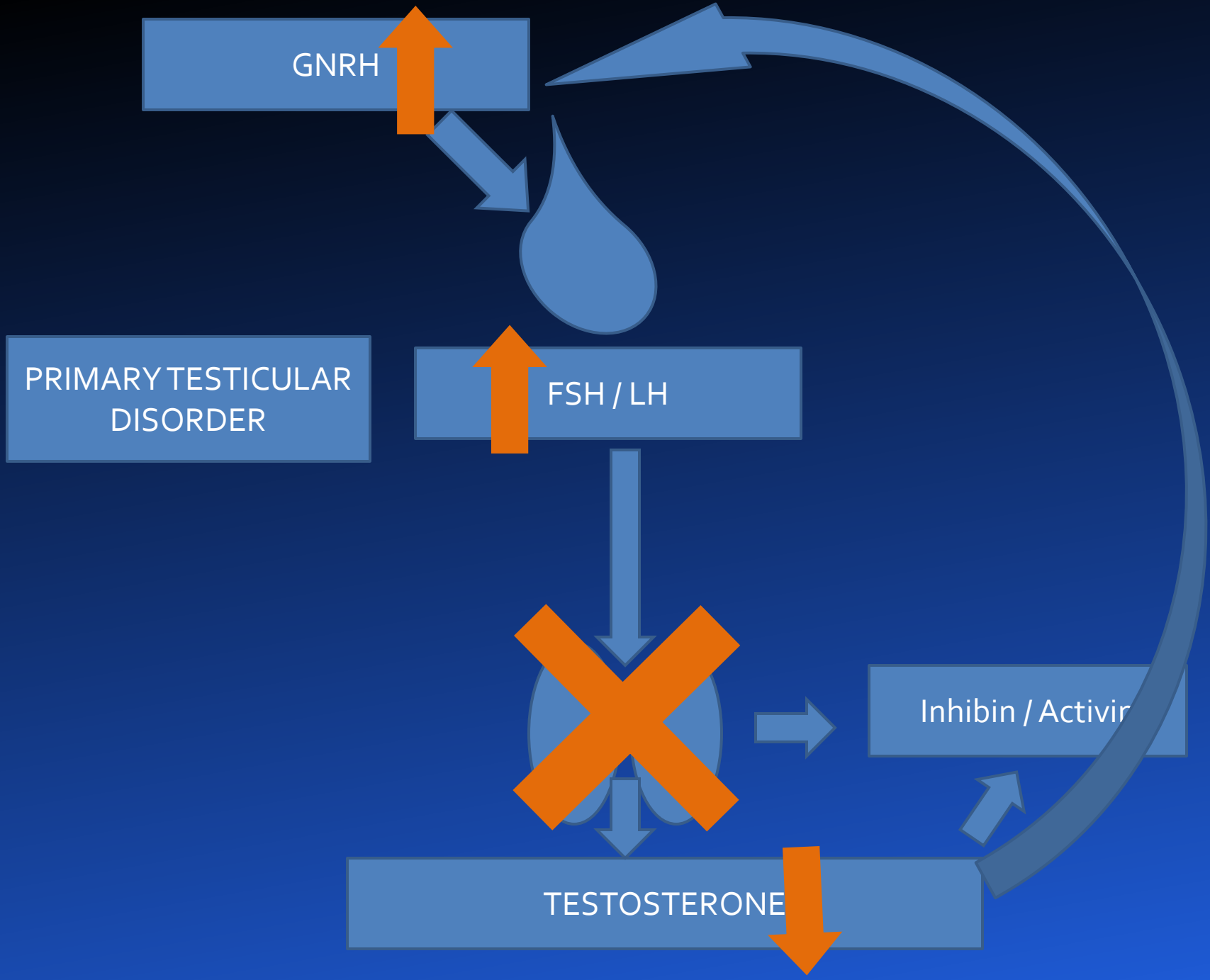
Question 5: 22 years old white male … no sexual function

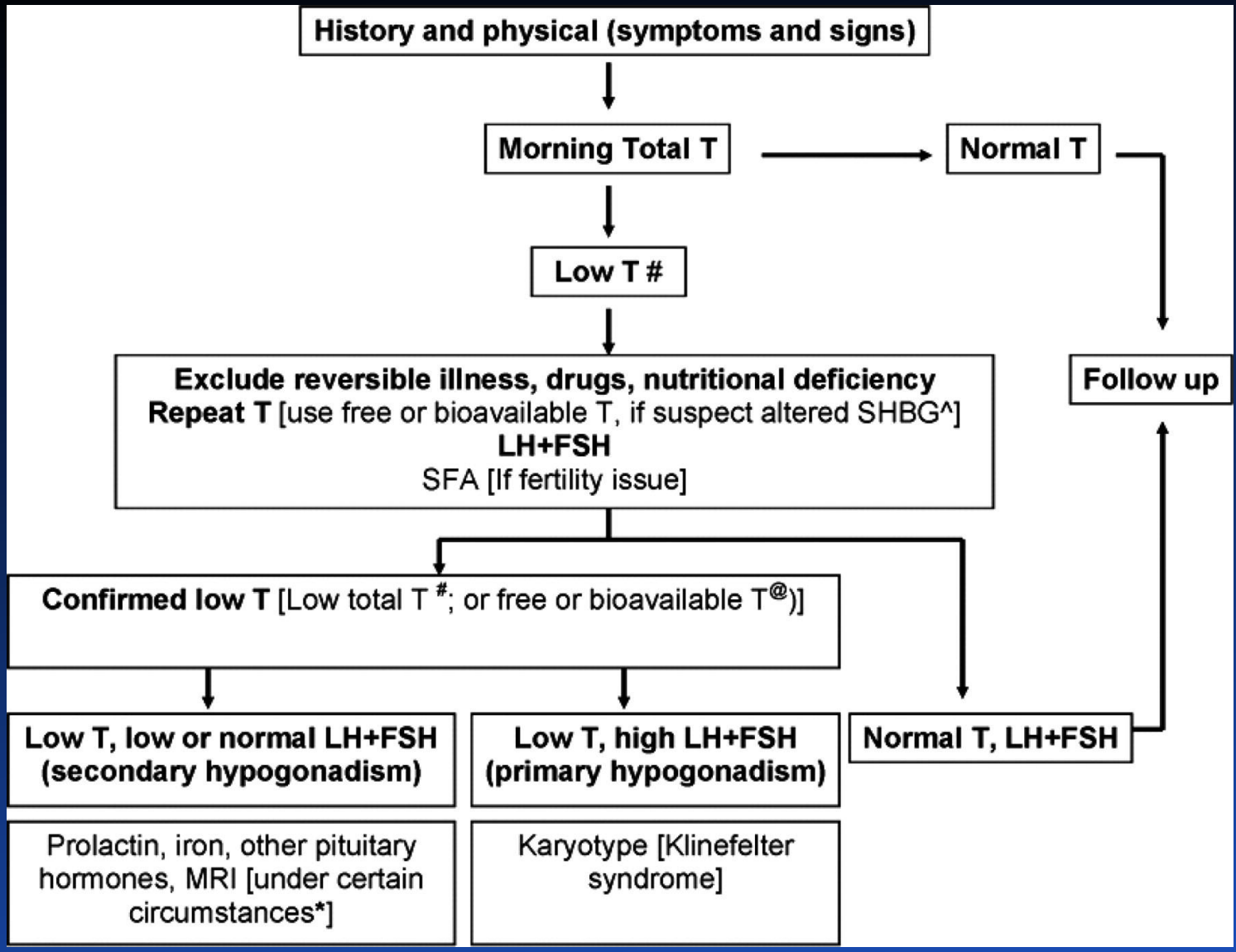
- Presents for the evaluation of lack of maturation: Accompanied by dad and mom
- No hot flashes
- Ht – 5ft 11 inches, 155 lbs
- Upper segment to lower segment ratio - <1
- Testicles – 10 mm – no distinct masses
- No development of phallus, genital hair or upper body musculature
- Total Testosterone 50 ng /dl (300-900 ng/dl)
- FSH – 94 (1-13 mIu/ml)

One of the following is the next best step…

a. Replace testosterone- parenterally with testosterone cipionate or undeconate
b. Perform Karyotype analysis
c. Pituitary MRI to rule out pituitary tumor
d. Repeat testosterone and FSH estimation in one week at 8 am
e. Estrogen estimation


GNRH
FSH / LH
Inhibin / Activin
TESTOSTERONE


GNRH
PRIMARY TESTICULAR DISORDER
FSH / LH
Inhibin / Activir
TESTOSTERONE



An approach for the diagnostic evaluation of adult men suspected of having androgen deficiency

Published in: Shalender Bhasin; Glenn R. Cunningham; Frances J. Hayes; Alvin M. Matsumoto; Peter J. Snyder; Ronald S. Swerdloff; Victor M. Montori; *The Journal of Clinical Endocrinology & Metabolism* **2010,** 95, 2536-2559.
DOI: 10.1210/jc.2009-2354

ENDOCRINE SOCIETY

Case 6: 58 years old male

- Diagnosed with idiopathic hypogonadism, he has been placed on parenteral and dermal preparations for more than 25 years.
- He has developed LUTS for the past 2 years off and on. His PSA is 2.0 and he has been placed on tamsulosin 0.4 mg per day, after DRE. This led to partial resolution of prostate symptoms.
- He was then placed on dutasteride, he returned in 6 months with reports of worsening of his prostate symptoms. PSA – 1.4

One of the following is the next best step…

a. Discontinue testosterone and revaluate in 6 months
b. PSA is stable therefore, reassure patient and increase alfa blockers
c. Referral for urological evaluation as soon as possible
d. Discontinue testosterone and try DHEA instead

Archived Content

The content on this page is provided for reference purposes only. This content has not been altered or updated since it was archived.

Search Archive

Safety

5-alpha reductase inhibitors (5-ARIs): Label Change - Increased Risk of Prostate Cancer

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Drugs in the 5-ARI class include finasteride and dutasteride. These drugs are marketed under the brand-names Proscar, Propecia, Avodart, and Jalyn

[Posted 06/09/2011]

AUDIENCE: Urology, Family Medicine, Internal Medicine

ISSUE: FDA notified healthcare professionals that the Warnings and Precautions section of the labels for the 5-alpha reductase inhibitor (5-ARI) class of drugs has been revised to include new safety information about the increased risk of being diagnosed with a more serious form of prostate cancer (high-grade prostate cancer).