Common Thyroid & calcium Disorders in Children

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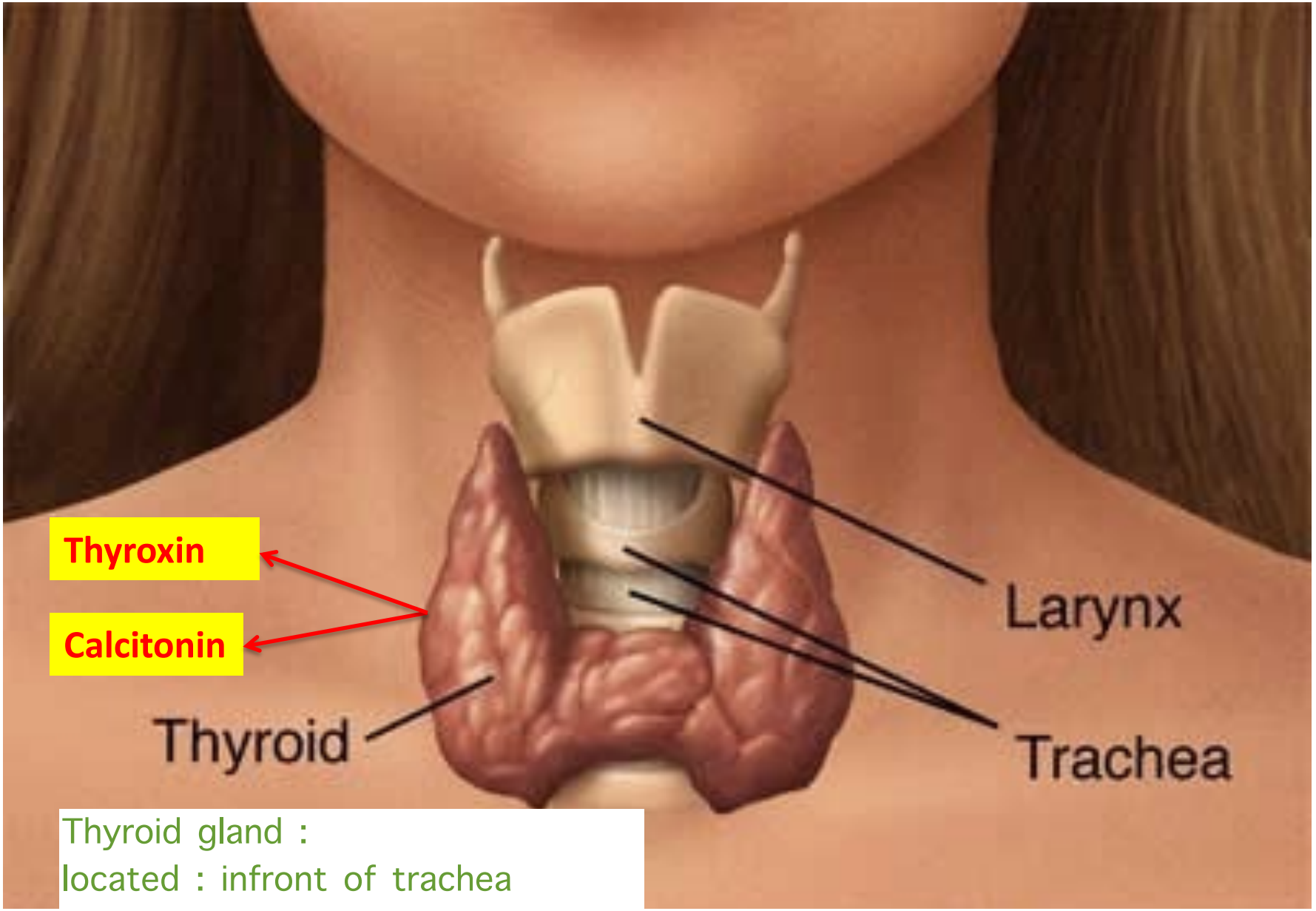
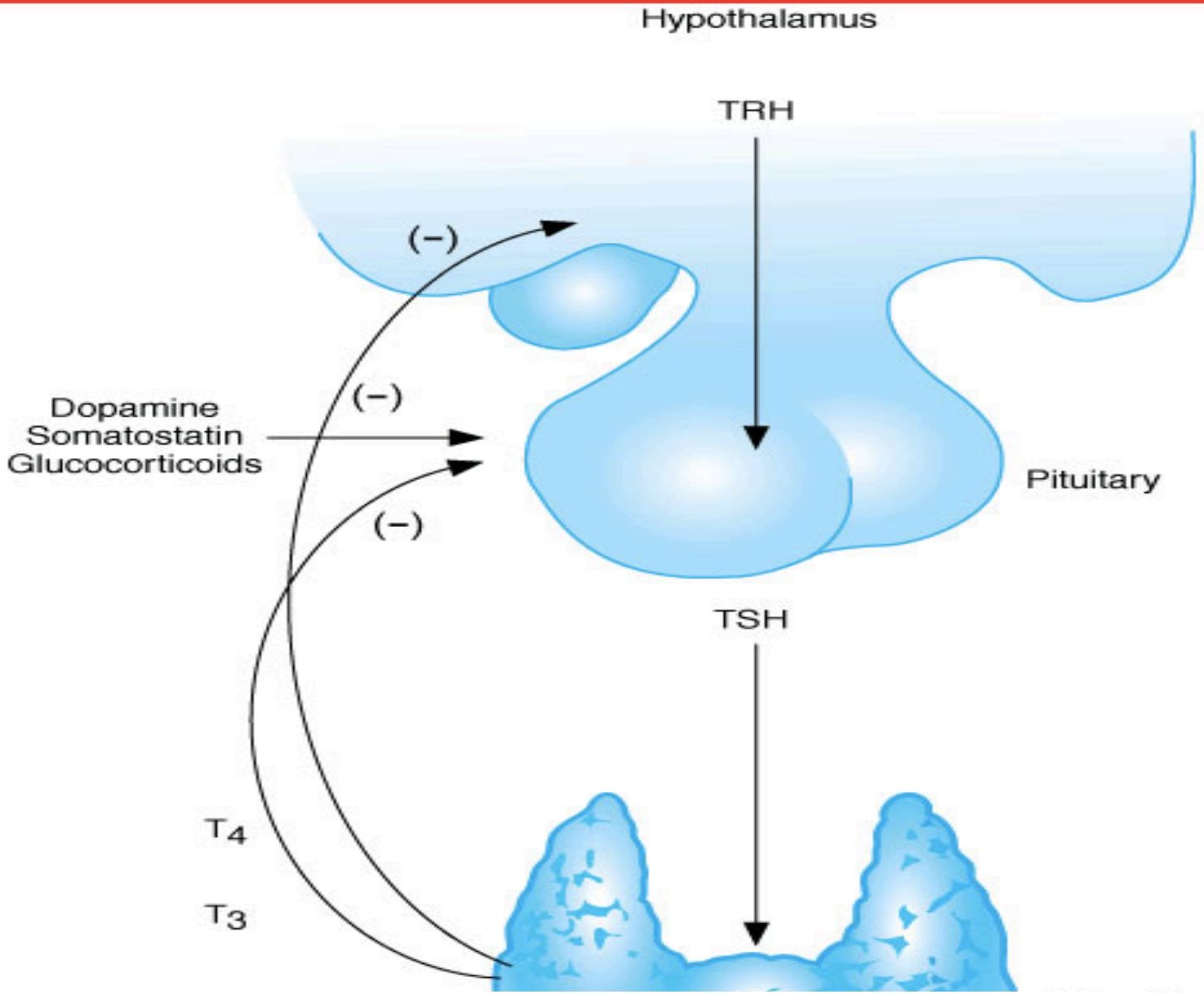
Objectives

- Thyroid Anatomy and physiology
- Hypothyroidism
- Hyperthyroidism
- Rickets

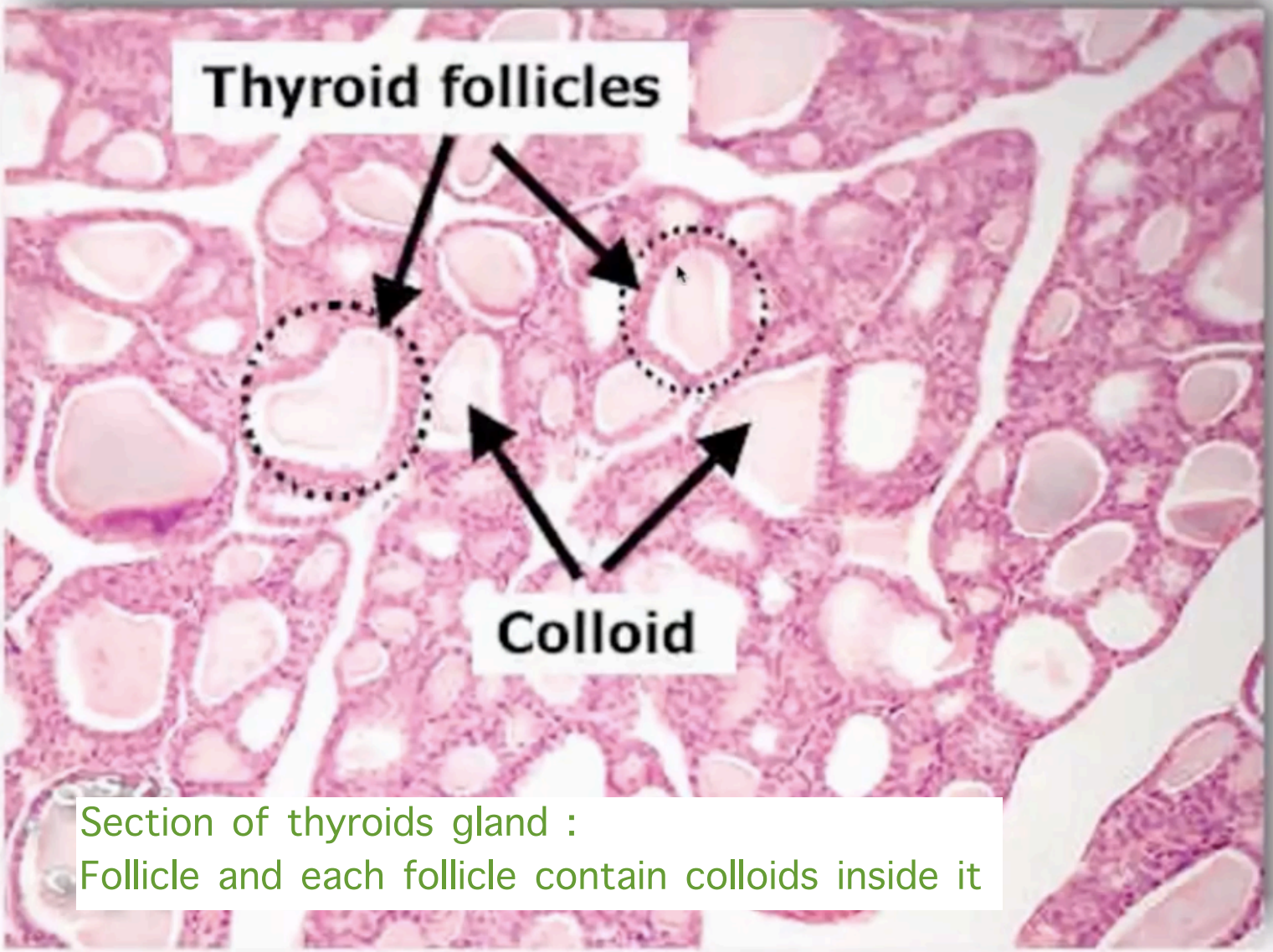


Thyroid gland :
located : infront of trachea
Secrete : thyroxin, calcitonin

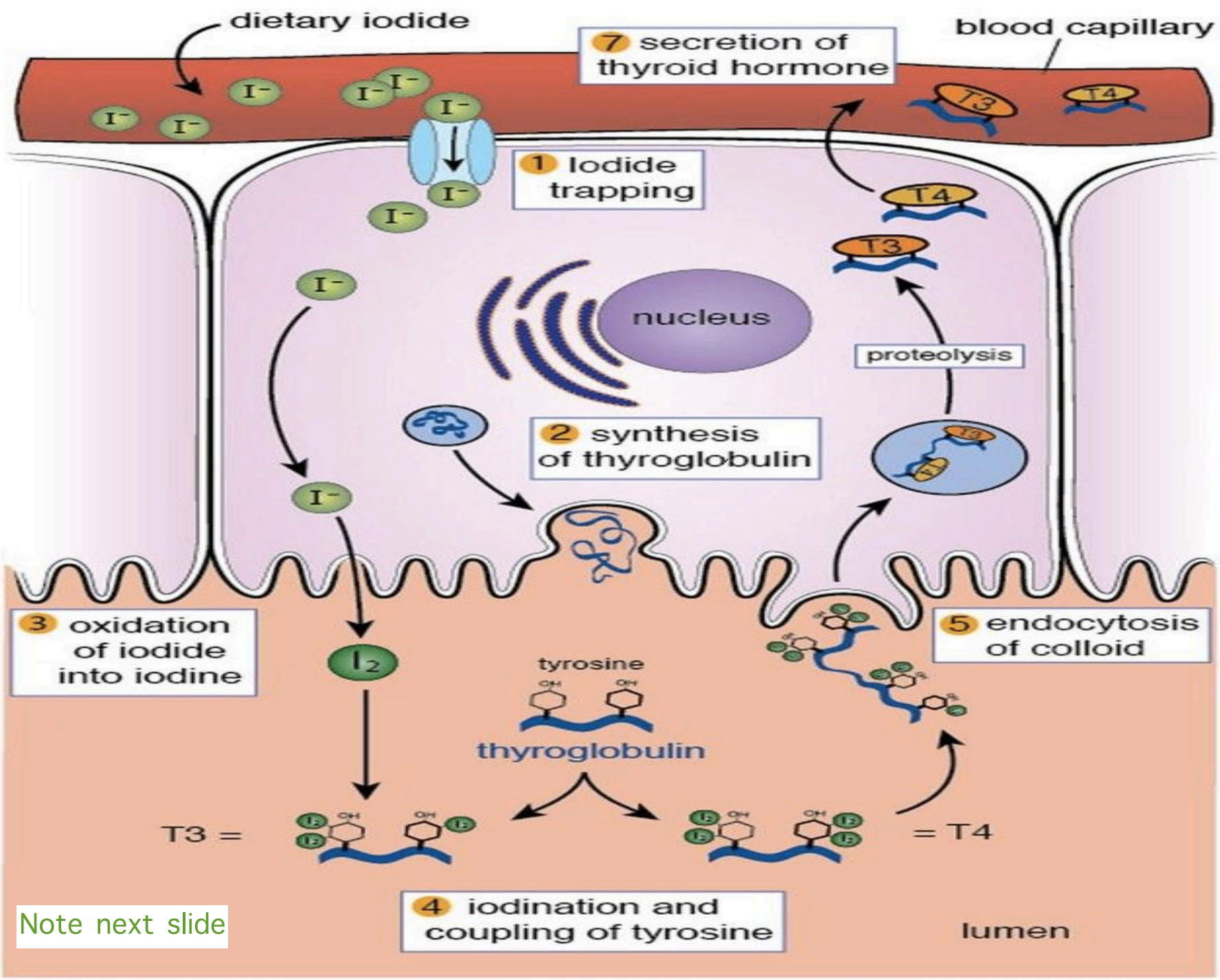


this secretion is regulated through secretion of hypothalamus (TRH) —> pituitary (TSH) —> thyroids (T4/3)—> -ve feedback on TRH

Also TRH is inhibited by : Dopamine, Somatostatin, glucocorticoids



Section of thyroids gland :
Follicle and each follicle contain colloids inside it



Note next slide

you don't have to memorize this pathway but doctor said understanding it will help you when something get wrong to know the abnormality that cause it

1- dietary iodide in blood vessels until it reach thyroid then it get transported through iodide transporter to
2- thyroid cells —>
- lumen : where oxidation to iodine and coupling happen then get endocytosis back to
- cells : where proteolysis happen to get excreted as T3/4 into the blood

QUESTION:
if you have problem at the level of transporter —> no iodine is going inside —> no T3/4 —> hypothyroidism
what is the aetiology of this hypothyroidism is it autoimmune or other process ?
Ans: usually this is congenital hypothyroidism due to Dyshormonogenesis (due to problem in the cycles)

Thyroid Function: blood tests

TSH	0.4 –5.0 mU/L
Free T4 (thyroxine)	9.1 – 23.8 pmol/l
Free T3 (triiodothyronine)	2.23-5.3 pmol/l

these are KKUH normal data which differs from other labs

Most of our production is T4 but it get converted to T3 in periphral circulation

Remember that : we check the T4 level after 6-8w from initiating the treatment (explanation down)

	T4	T3
Potency	1	10
Protein Bound	10-20	1
Half-Life	5-7d	< 24h
Secreted by thyroid	100 ug/d	6 ug/d

Why we need to know the potency - half life .... ?

To know how to monitor the treatment affect ; T4 half life is 5-7D while T3 is <24h so the appropriate time to check thyroid hormone levels after starting the treatment (study state level) is after 5-7 half-lifes which means 6-8w for T4 and after 1w for T3

this also include when we stop the meds we should wait 6-8w

Effects of thyroid hormones

- Linear growth & pubertal development
- Normal brain development & function
- Calcium mobilization from bone
- Increase in basal metabolic rate
- Inotropic & chronotropic effects on heart
- Stimulates gut motility
- Increase in serum glucose, decrease in serum cholesterol
- Play role in thermal regulation

less than 3y

The part of the brain affected by thyroid hormone is myelination of the axons which are completed by 3y so hormone agenesis —> it will impact the IQ level

HYPOTHYROIDISM

Causes of hypothyroidism

Primary

- Congenital
- Autoimmune (Hashimoto)
- Iodine deficiency
- Subacute thyroiditis
- Drugs (amiodarone)
- Irradiation
- Thyroid surgery

Secondary

- TSH deficiency
- TRH deficiency

2ndery caused by : in (I) :
ischemia
iatrogenic (surgery)
idiopathic
infeltration (tumor)
infection

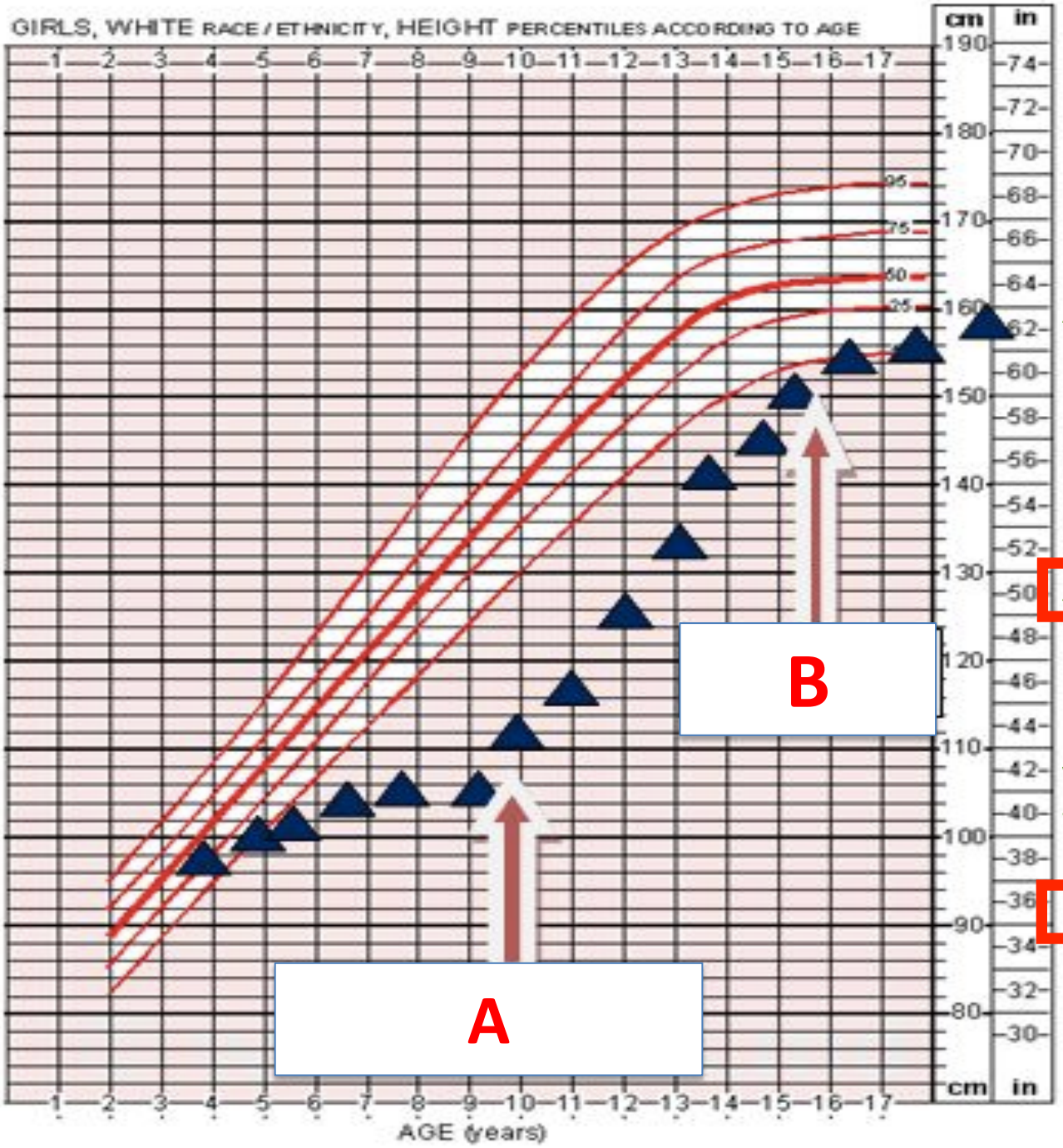
Clinical features

- Poor growth ….. Stop growing (Short stature)
- Delayed bone age
- Poor school performance Low IQ in less than 3y + thinking will be slow
- Delayed puberty
- Weight gain
- Fatigue
- Constipation
- Goiter
- Dry skin
- Cold Intolerance
- Sinus Bradycardia
- Delayed reflexes

Highlight :

pediatric not replacing thyroxine they wont grow.

if u replace they will grow



Girls growth chart
Hight :
platue until point A then start increase until B

A: Thyroxine
pt was hypothyroidism until point A where we give her thyroxine

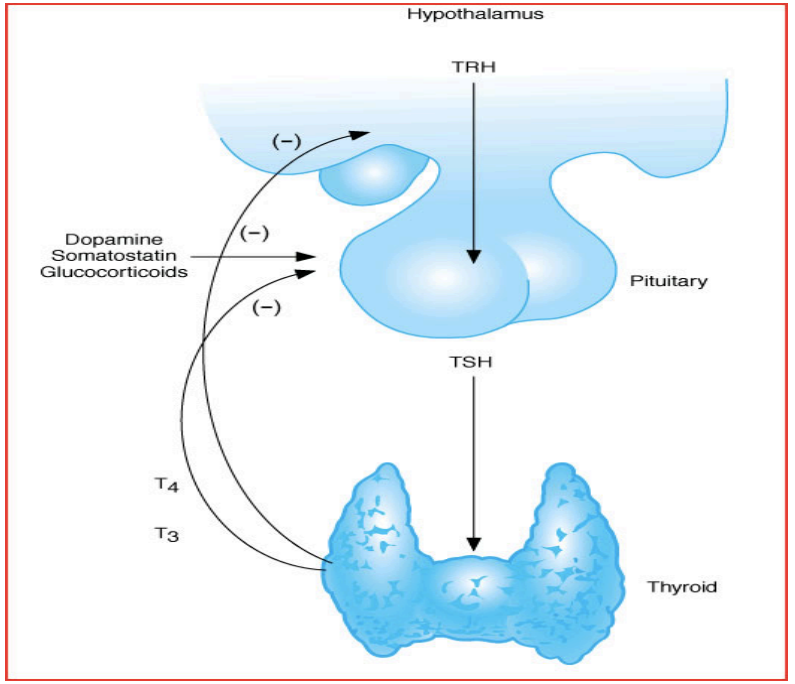
B: Menarche
pt stop growing due to menarche (final adult hight)

Primary Hypothyroidism

Way to diagnose it :

- Decreased thyroid hormone levels
  - ↓↓T4
  - Possibly ↓ T3
  - ↑TSH

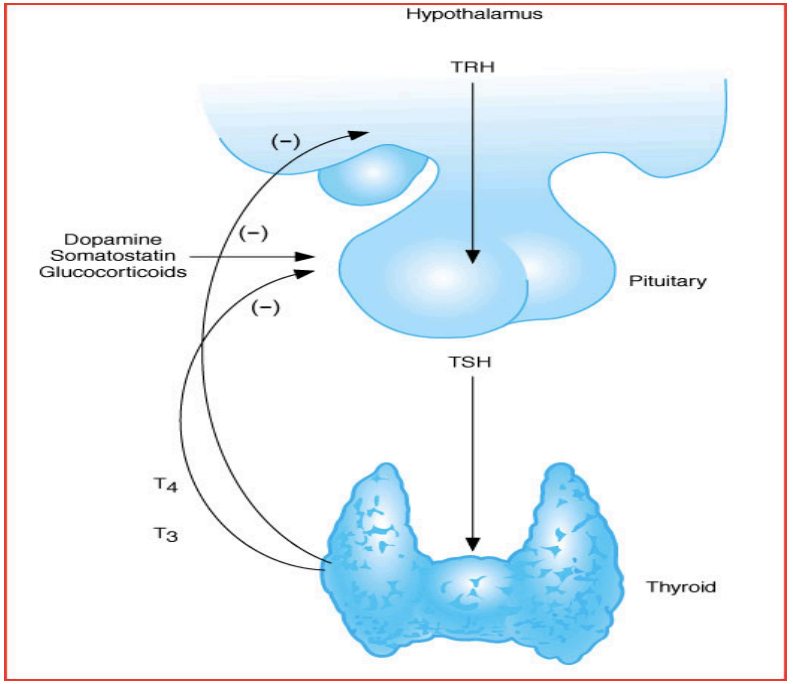
Issue in thyroids



Secondary Hypothyroidism

- Decreased thyroid hormone levels
  - ↓↓T4
  - ↓ T3
  - ↓ TSH

Issue in Hypothalamus or pituitary
TSH is the difference



Hashimoto's thyroiditis

- Most common cause of hypothyroidism
- Autoimmune lymphocytic thyroiditis
- Antithyroid antibodies:
  - Thyroglobulin Ab
  - Microsomal Ab
  - TSH-R Ab (block)
- Females > Males
- Runs in Families!

Congenital Hypothyroidism

- 1 in 3000-4000 neonate
- The most common cause of treatable and preventable mental retardation….. The earlier dx the better IQ by replacing the thyroxin early
- Congenital Anomalies increased by 10%(cardiac)
- In more than 90% of the cases it is permanent

we will continuoe the thyroxin for life even if menarche start and growing was stopped

Impact on IQ when diagnosis is delayed

Age of Diagnosis	% with IQ > 85
3 months	78%
6 months	19%
> 7 months	0%

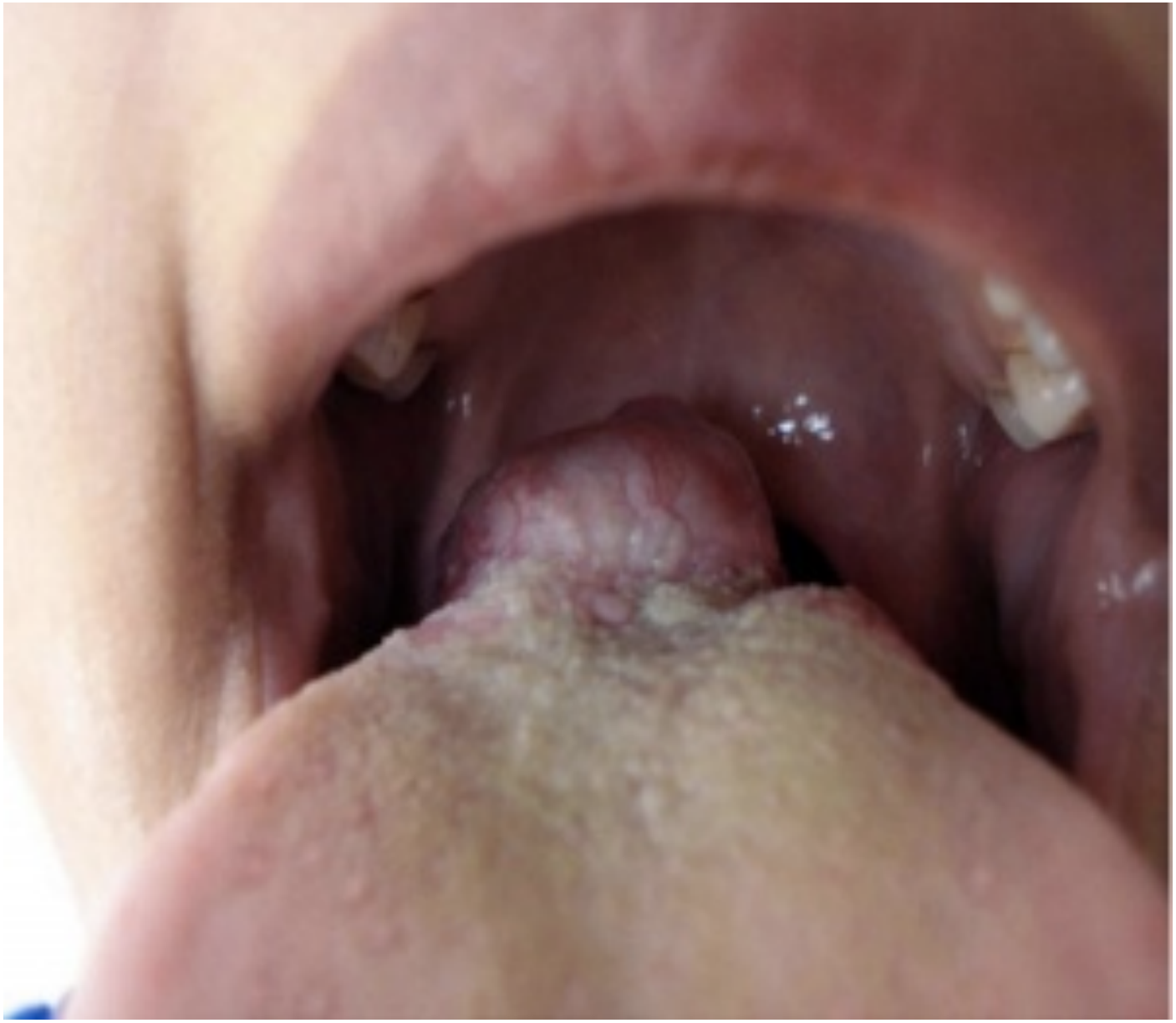
for exp : if u dx after 7m almost all baby will have IQ less than 85% which is equivalent to = mental retardation

Congenital Hypothyroidism: Causes

- Agenesis — Glands are not formed
- Dysgenesis — Glands are formed abnormally
- Dyshormonogenesis — Thyroids is formed normally but there is problem in the cycle
- Ectopic gland
- Iodine deficiency
- Maternal anti-thyroid medication

Clinical Features of Congenital Hypothyroidism in babies

Finding	%
Lethargy	**96%**
Constipation	**92%**
Feeding problems	**83%**
Respiratory problems	76%
Dry skin	76%
Thick tongue	67%
Hoarse cry	67%
Umbilical hernia	67%
Prolonged jaundice	12%
Goiter	8%

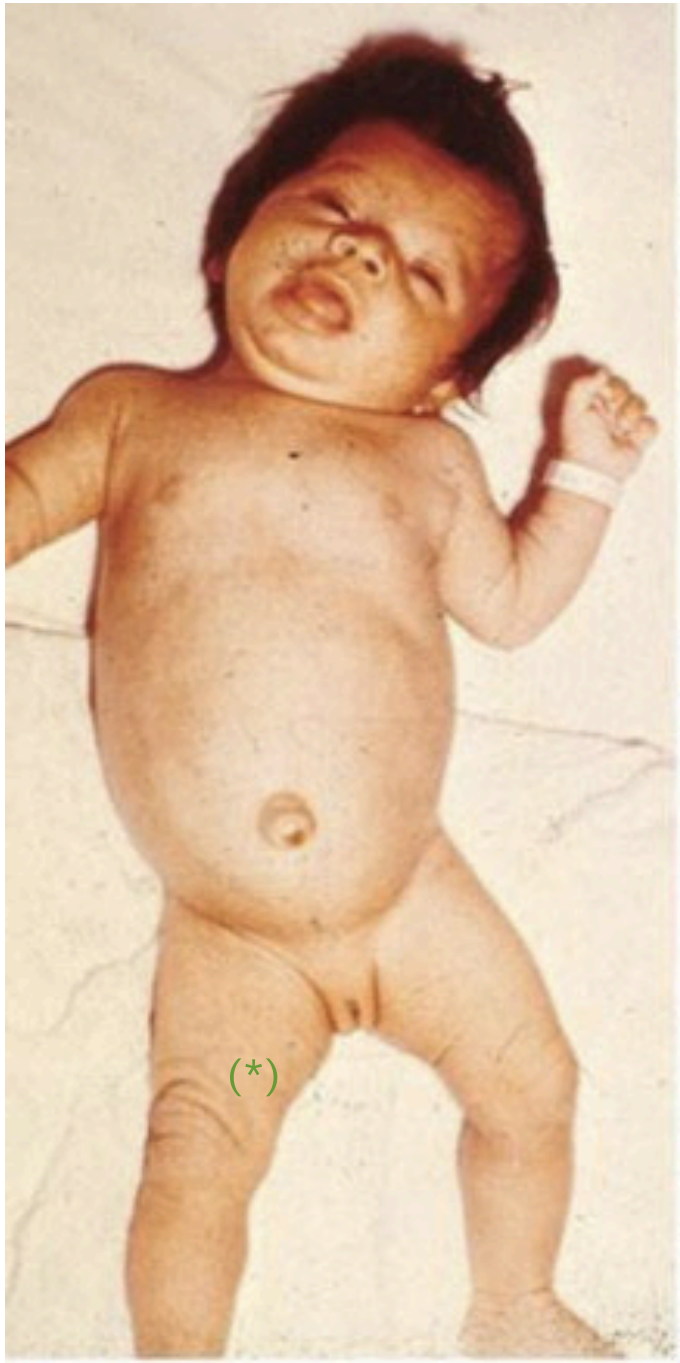


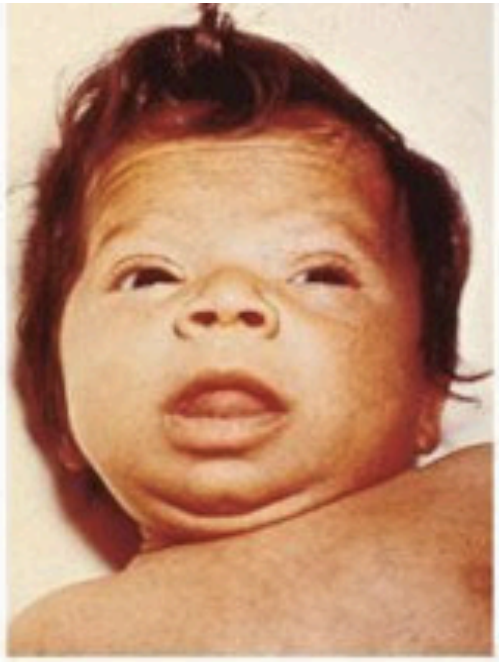
Lingual thyroid = ectopic gland = not working

- large protruding tongue

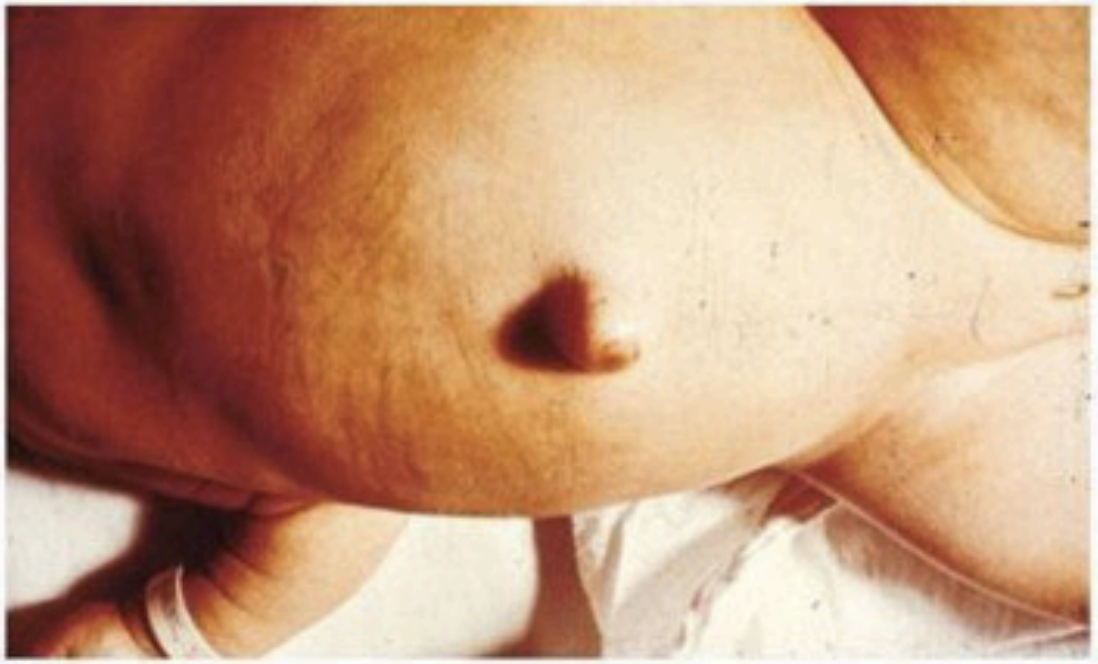
- baby looks lethargic

- Baby face look older

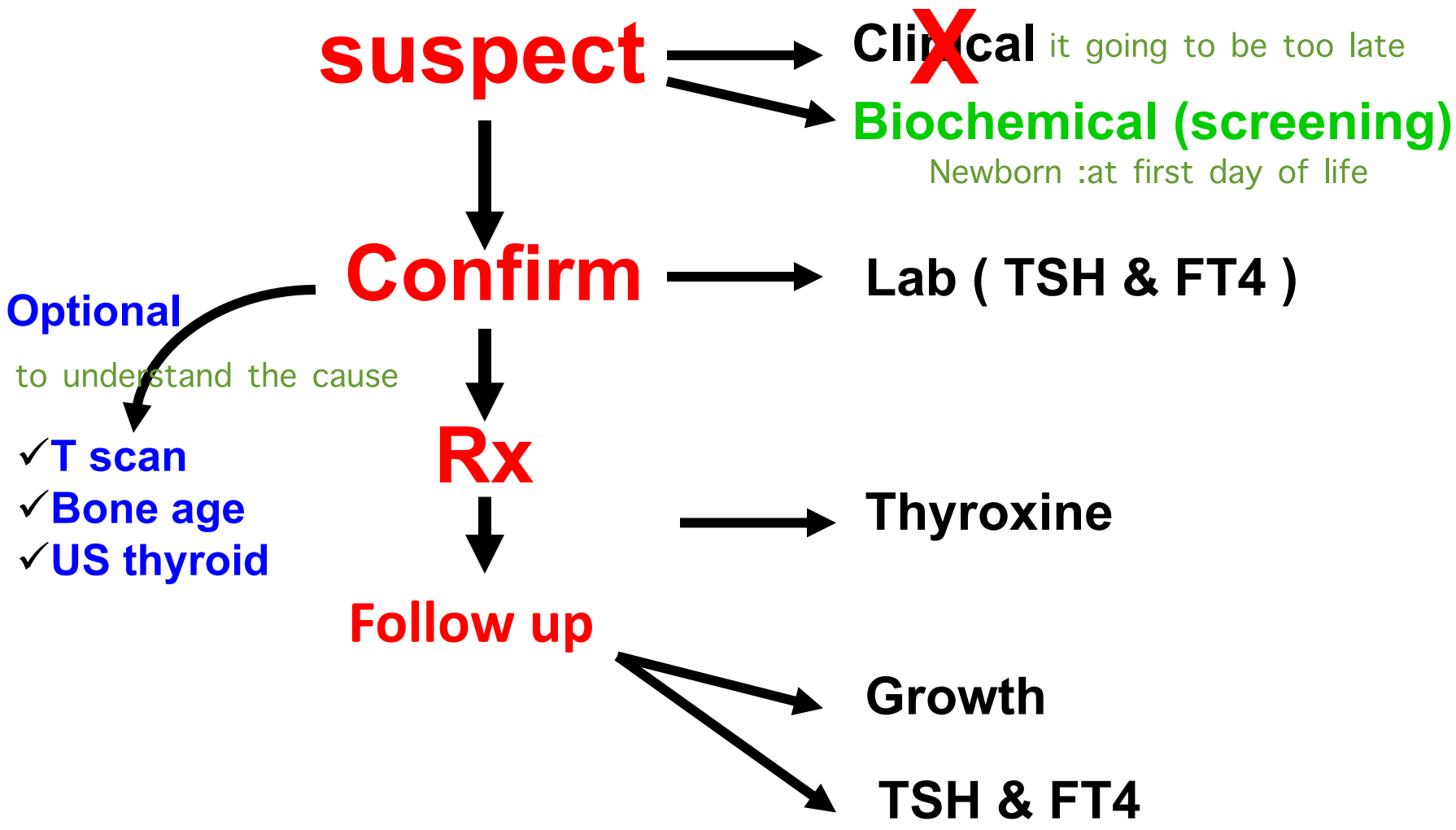




lethargic baby
protruding tongue
Umbilical hernia
(*)Folds —> issues in wight gain
elderly look (called : wizened look)



Congenital Hypothyroidism



Management

High TSH & Low T4

Levothyroxine (T4)

we said Normal T4 needs 6-8 w
but we start observe the rising from the 2nd w to reach the normalization on 6-8w

Dose

10 -15 ug/kg/day
12 -17 ug/kg/day
37.5 – 50 ug/day

Higher dose in
Severe cases
T4< 5ug/dl

Form

Tablets
25-50-75 ug
Crush it, add to
5-10 cc water
Or milk

Goals

Normal T4
In 2 wks
(upper ½ of N)

Normal TSH
In one month
(lower ½ of N)

- Never give syrup
- give it on empty stomach and wait 30m to feed
- give it at the same time every day

Newborn Screening Criteria

test done on the 1st to 3d of baby life

- Aim is to identify affected infants before development of clinical signs
- High incidence 1/3,000 to 1/4,000
- Mental retardation if not treated
- Levothyroxine $3.00 cost —> cheap

Other screening test :
- Metabolism error : galactosemia , phenylketonuria
- Endocrine : congenital adrenal hyperplasia, congenital hypothyroidism

Screening Technique

- Specimen is a blood spot on a filter paper
  - Obtained by heel brick

  Or

  - cord blood
- TSH or TSH+FT4 or FT4

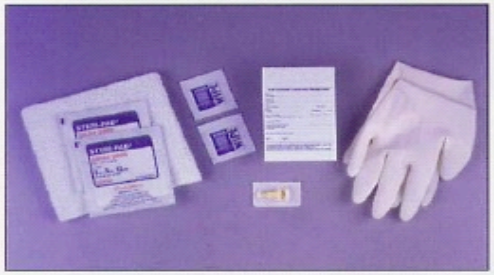
depend on the hospital
KKUH —>we do TSH

What are the cases that you will not diagnose with screenng that depend on TSH only ? Secondary hypothyroidism

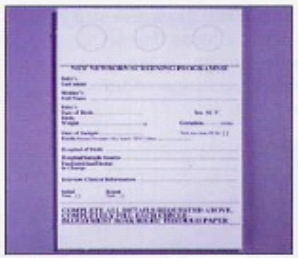
cuz in our hospital test the cut-off point for TSH is 30 if the TSH was
>30 —> congenital hypothyroidism
<30 —> it could normal or 2ndery or even tertiary hypothyroidism

Neonatal Screening

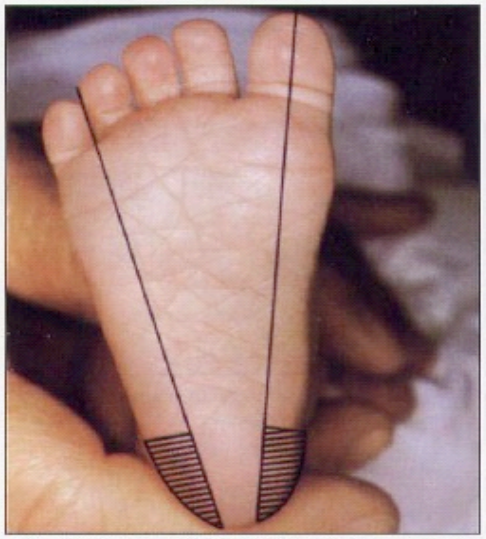
Blood Specimen Collection and Handling Procedure



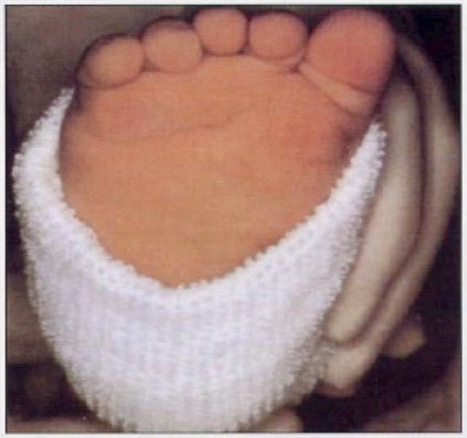
1 Equipment: sterile lancet with tip approximately 2.0 mm, sterile alcohol prep, sterile gauze pads, soft cloth, blood collection form, gloves.



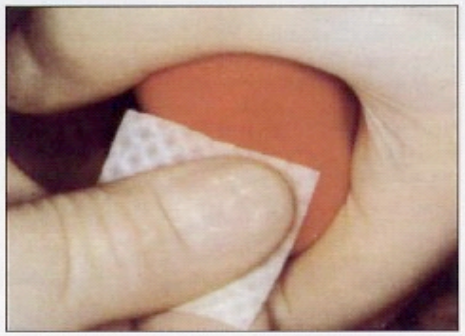
2 Complete ALL information. Do not contaminate filter paper circles by allowing the circles to come in contact with spillage or by touching before or after blood collection. Keep "SUBMITTER COPY" if applicable.



3 Hatched area ( ) indicates safe areas for puncture site.



4 Warm site with soft cloth, moistened with warm water up to 41°C, for three to five minutes.



5 Cleanse site with alcohol prep. Wipe DRY with sterile gauze pad.

Over

how we draw blood :
we prick the lower outer part (the shed part) after wipping with alcohol

COLLECTION AND REPORTING (CARE) FORM - *NEBRASKA NEWBORN SCREENING PROGRAM*

Birth Date ___/___/___ Time ___:___ (Military)
Collection Date ___/___/___ Time ___:___ (Military)
Collector's initials _____ Initial ☐ Repeat ☐
☐ Specimen collected prior to 24 hours
☐ Transfused prior to specimen collected
If ✓'d specify type _____ date _____ time _____
☐ TPN ☐ Meconium Ileus ☐ Baby on antibiotics
Gestational age _____ (wks) Birth Weight _____

NEWBORN'S INFORMATION:

Name _____
Last
_____
First Middle
_____
Patient Record Number
Place of Birth _____
Home Birth Yes ☐ No ☐ Sex M ☐ F ☐

MOTHER'S INFORMATION:

Name _____
Last
_____
First Middle
Address _____
Telephone (___)___-____ Birthdate ___/___/___

SUBMITTER'S INFORMATION: SN XXXXXXX

Name _____
Address _____
_____
Telephone (_____)_____-_____

NEWBORN'S PHYSICIAN INFORMATION:

Name _____
Last First
Telephone (_____)_____-_____

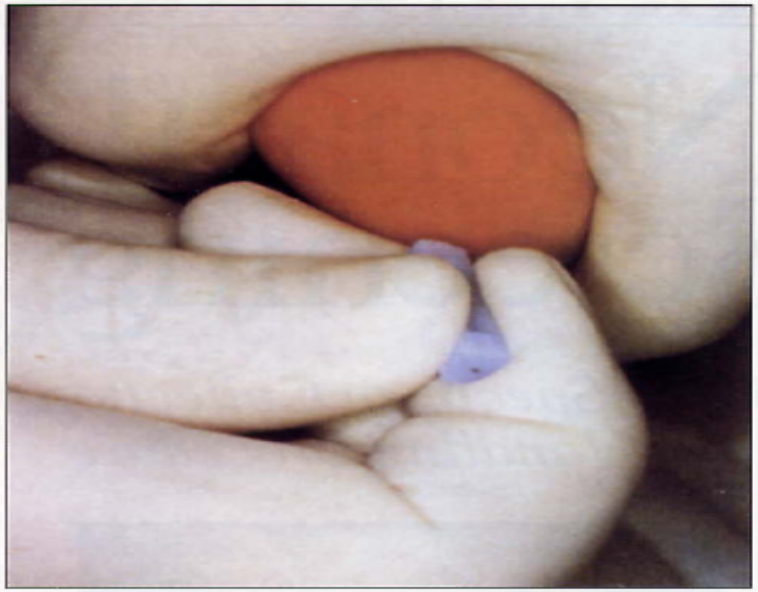
- Allow to air dry in a horizontal position for at least 3 hours.
- Do not allow the blood spots to touch anything before they are dry.
- Ship within 24 hours (when transport available) to:

PerkinElmer
PerkinElmer Genetics
90 Emerson Lane, Suite 1403
P.O. Box 219
Bridgeville, PA 15017
Phone: 412-220-2300

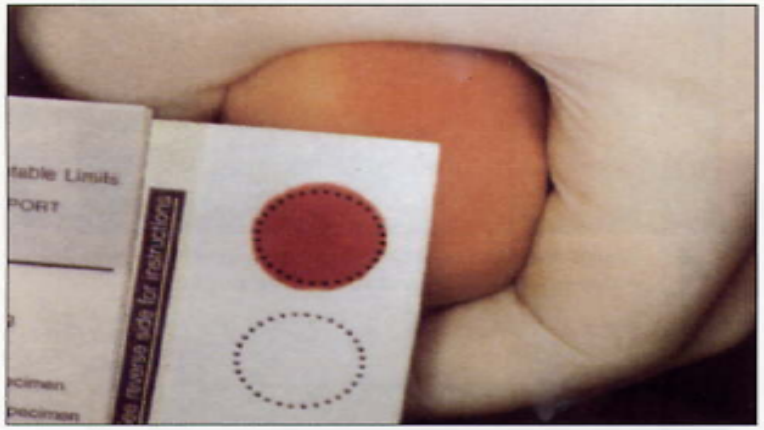
RECEIVED XXXXXXX REPORTED

Whatman 903® W071 XXXXXXXX XXXXXXX

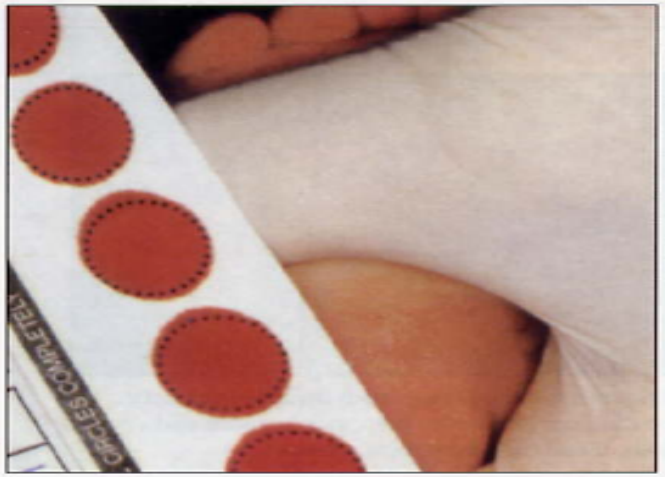
then we fill these circles with blood



6 Puncture heel. Wipe away first blood drop with sterile gauze pad. Allow another LARGE blood drop to form.



7 Lightly touch filter paper to LARGE blood drop. Allow blood to soak through and completely fill circle with SINGLE application to LARGE blood drop. (To enhance blood flow, VERY GENTLE intermittent pressure may be applied to area surrounding puncture site). Apply blood to one side of filter paper only.

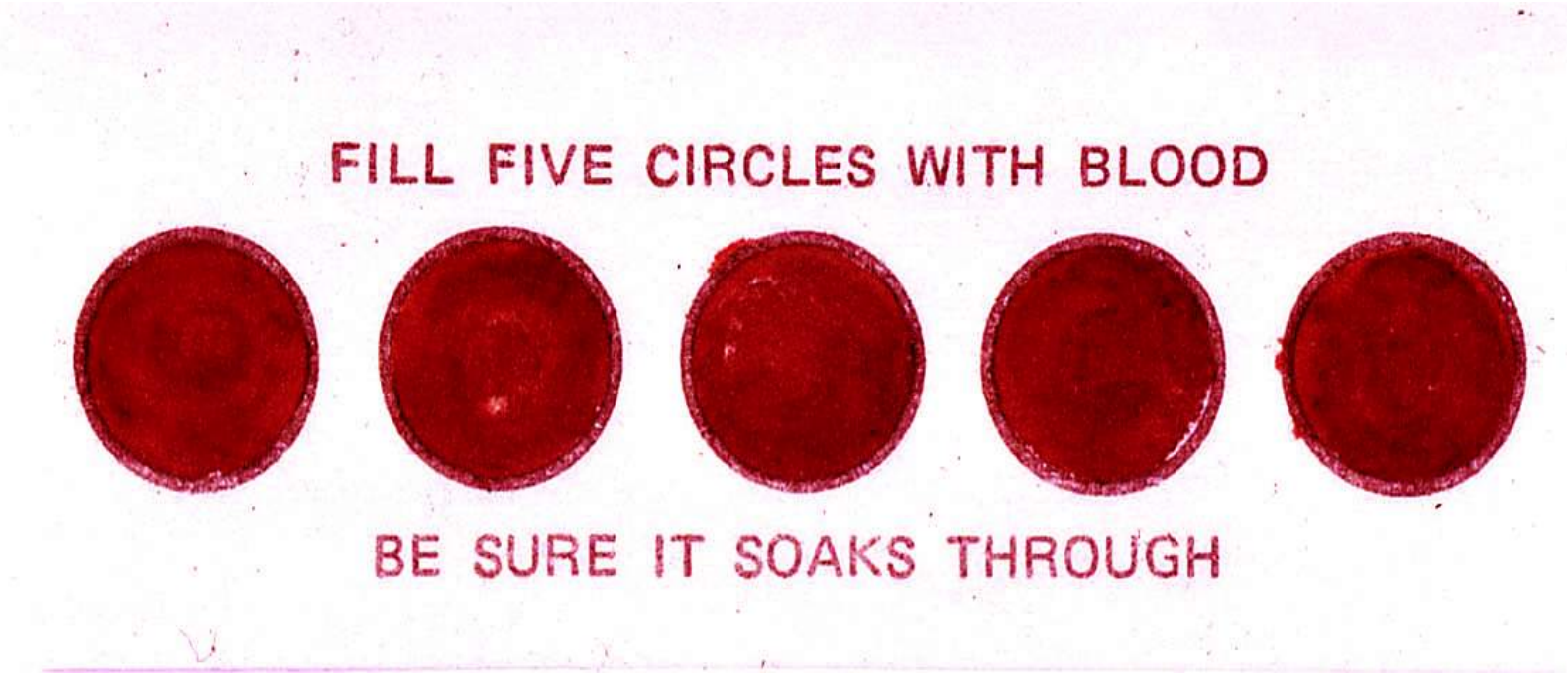


8 Fill remaining circles in the same manner as step 7, with successive blood drops. If blood flow is diminished, repeat steps 5 through 7. Care of skin puncture site should be consistent with your institution's procedures.

9 Dry blood spots on a dry, clean, flat non-absorbent surface for a minimum of four hours.

10 Mail completed form to testing laboratory within 24 hours of collection.

Good Specimen



IQ Outcome

for hypothyrodism baby

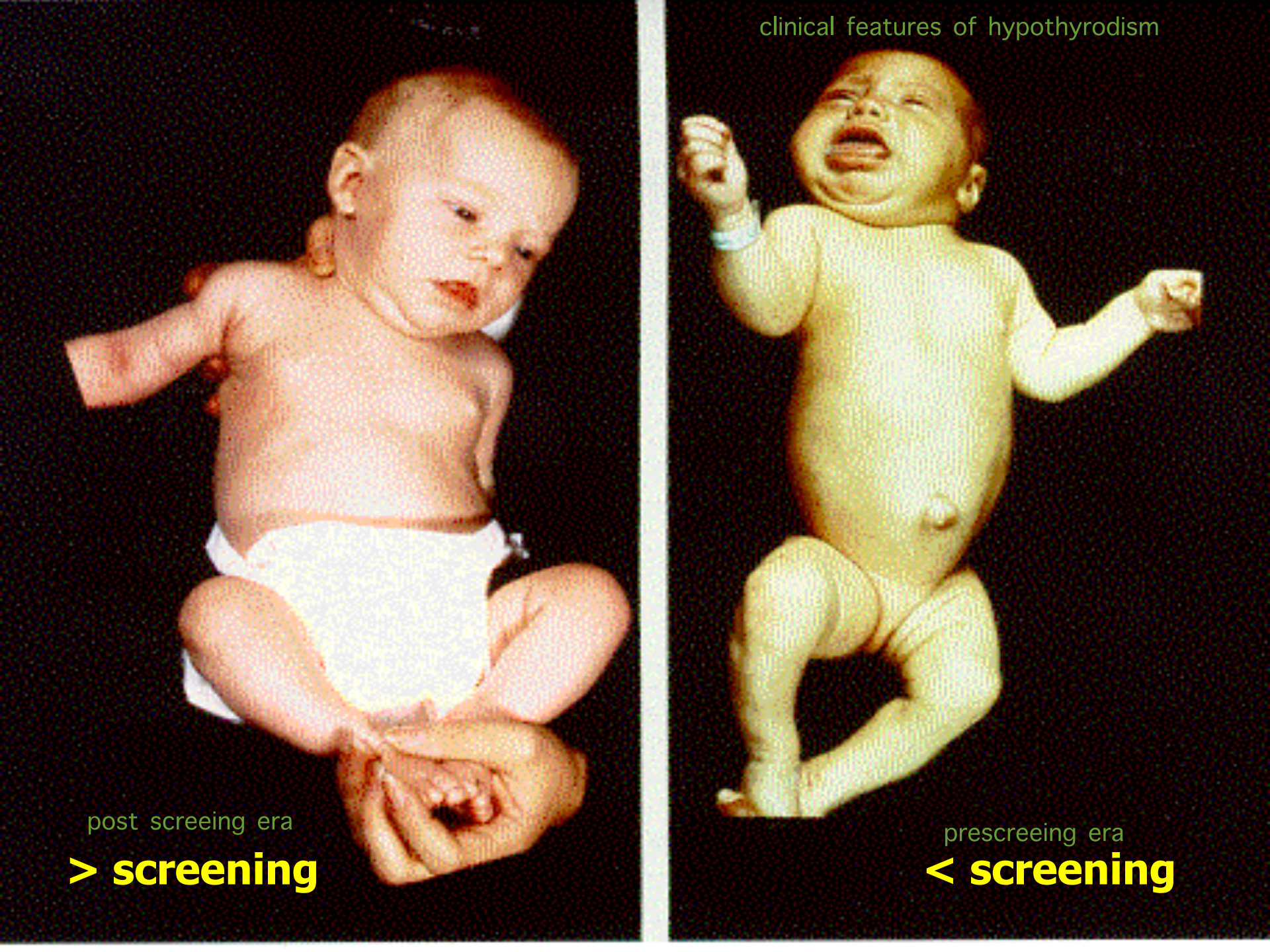
Pre-screening

average IQ in pre-screeing era

- **76**

Post-screening

- **104** which is normal


clinical features of hypothyrodism
post screeing era
> screening
prescreeing era
< screening

wheel chair pt with with low IQ face look abnormal

A man and 3 females (age range, 17-20 y) with myxedematous cretinism from the Republic of the Congo in Africa, a region with severe iodine deficiency.

Treatment of Hypothyroidism

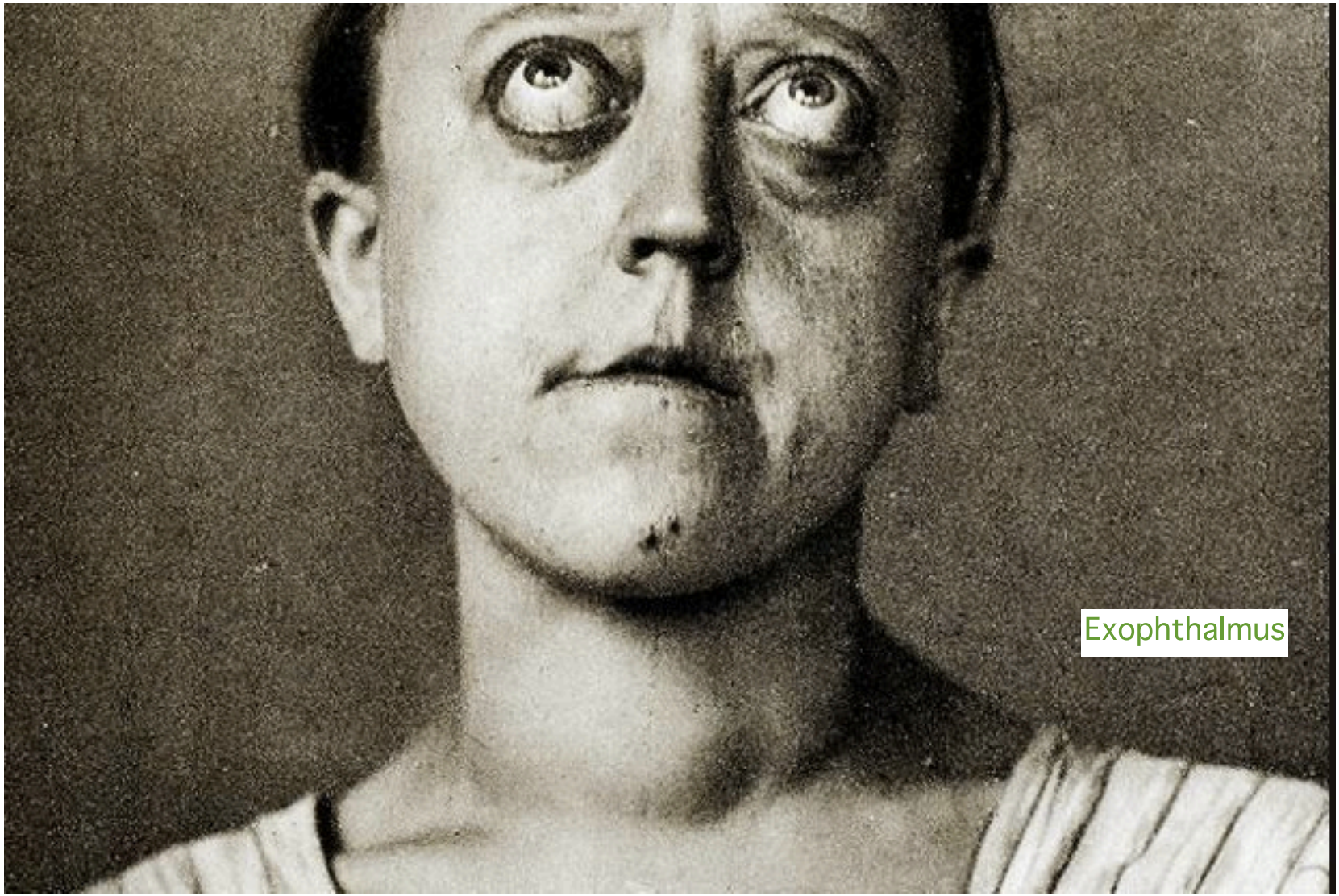
- Replacement thyroid hormone medication: Thyroxine

Your turn

- 2 days old baby has a TSH= 150, FT4= 5 on newborn screening. what is your next best step:

A. Repeat TSH, FT4, follow up in 1 week
B. Do US thyroid after 1 week
C. Start levothyroxin 50mcg
D. repeat TSH, FT4 and start treatment

Ans : D
if I can't do test then I will start treatment (due to age) never delay



HYPERTHYROIDISM

Causes of hyperthroidism

- Graves Disease
- Overtreatment with thyroxine
- Thyroid adenoma (rare)
- Transient neonatal thyrotoxicosis

Hyperthyroidism

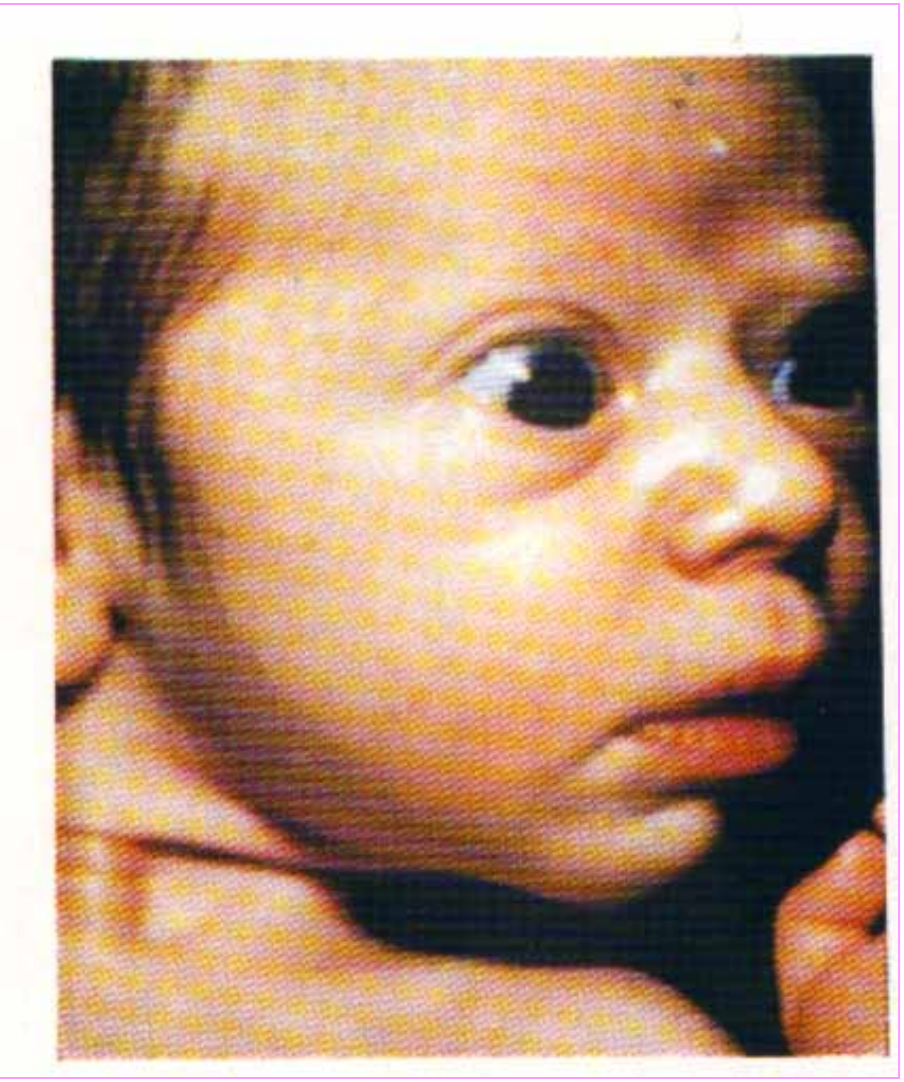
- Increased thyroid hormone levels
  - ↑ T4 +/- High T3
  - ↓ TSH (suppressed) due to -ve feedback

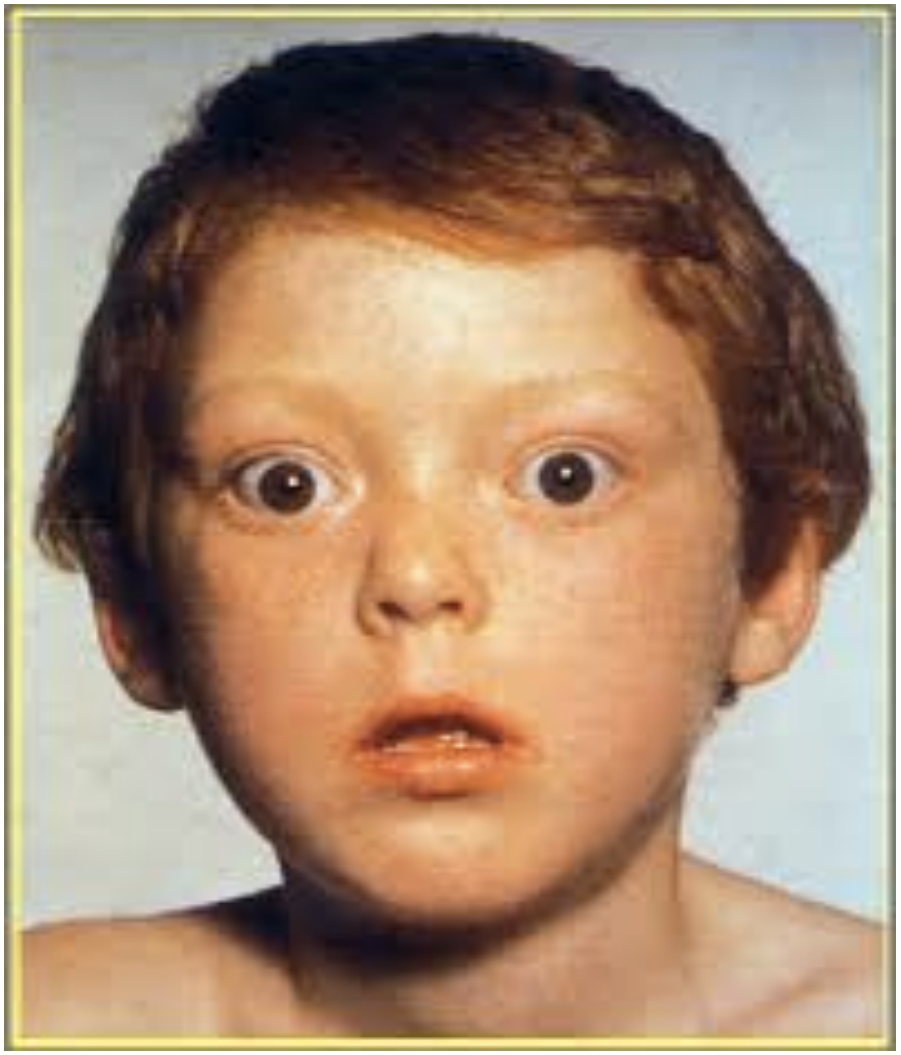
Graves' Disease

- Most common cause of hyperthyroidism
- Autoimmune process
- TSH-R stimulating antibody
- 40-70% relapse after 2 years of treatment

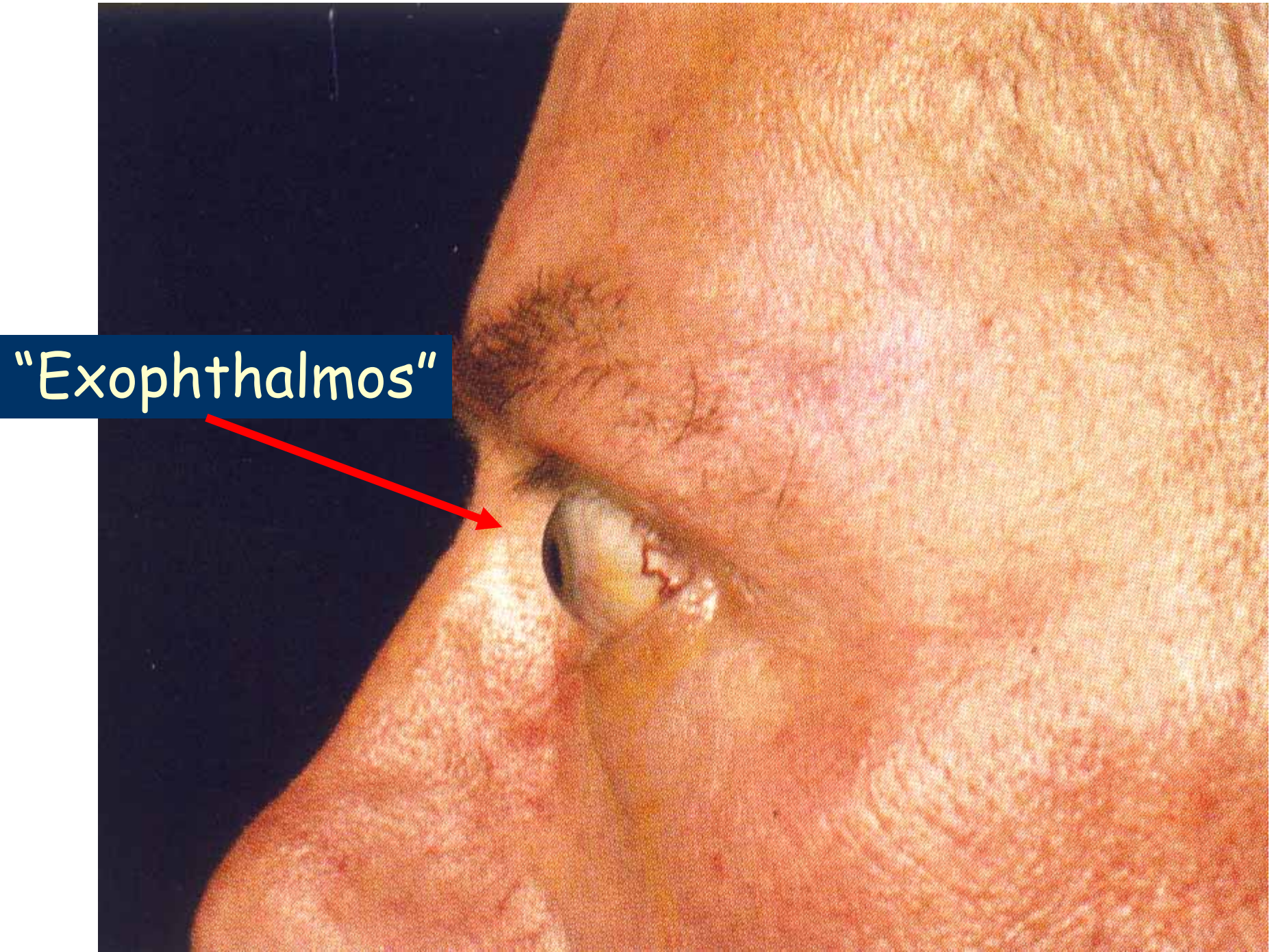
Clinical manifestations

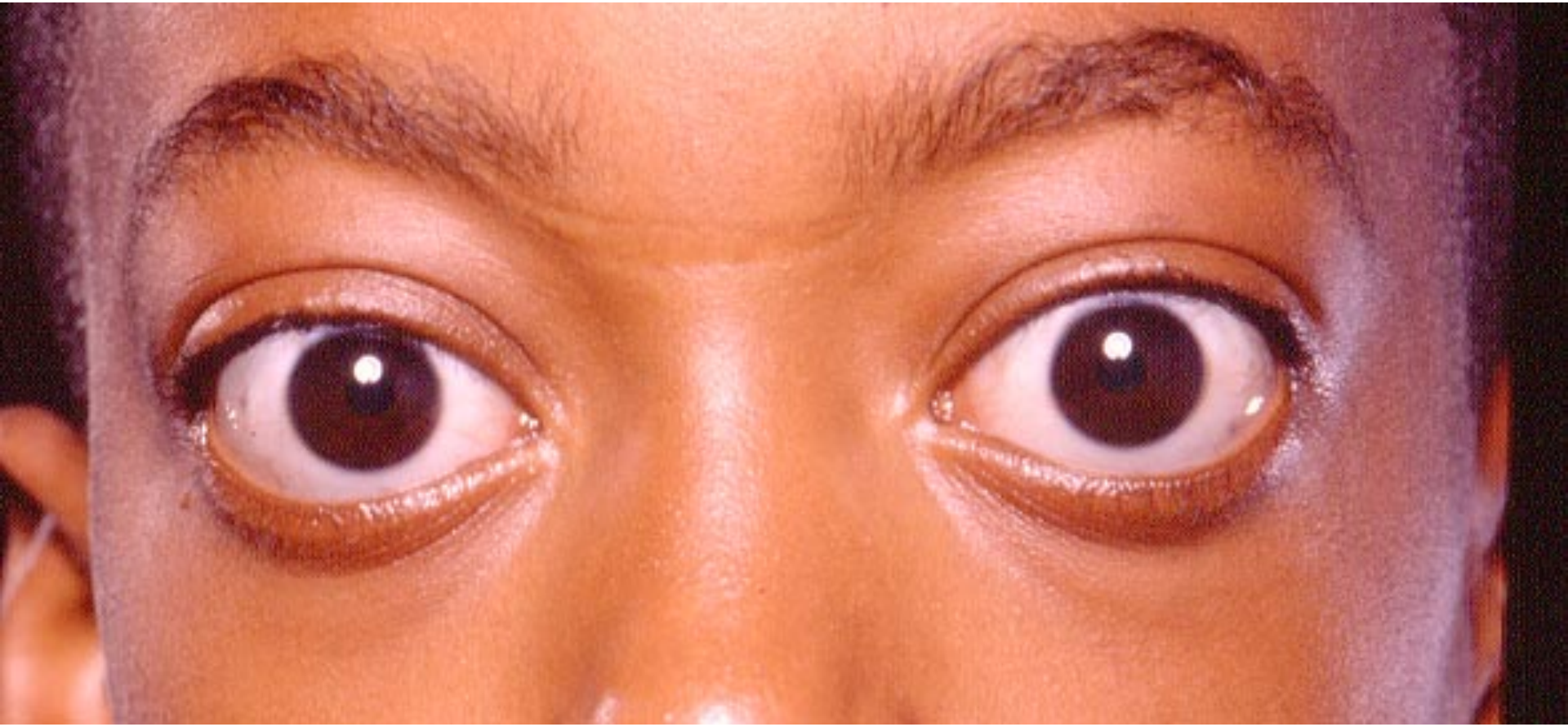
- Heat intolerance
- Hyperactivity, irritability
- Weight loss
- normal to increased appetite
- diarrhea
- Tremor, Palpitations
- sweating
- Lid retraction & Lid Lag (thyroid stare)
- Proptosis
- menstrual irregularity
- Goitre





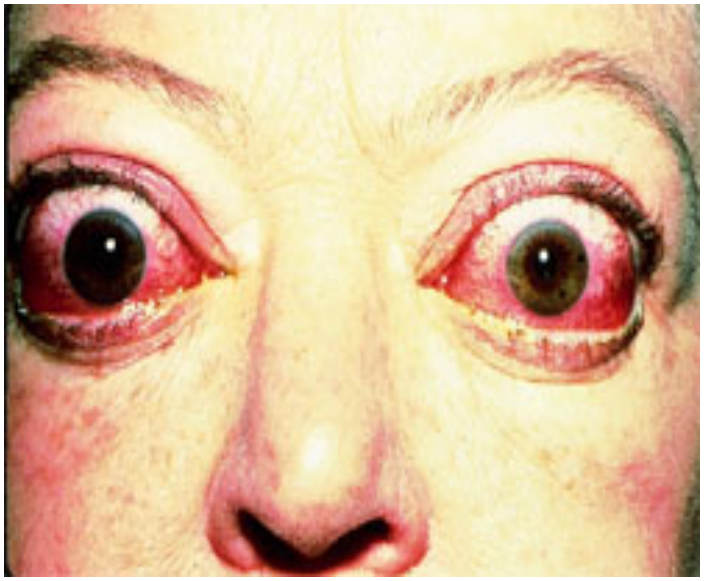
staring look : lid retraction = upper part of the iris is not covered with lid


"Exophthalmos"



Grave’s
ophthalmopathy

Hyperthyroid Eye Disease

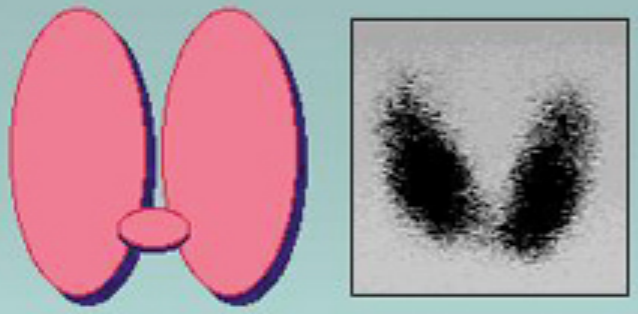


lid lag sign

Investigations

- TSH, free T3&T4
- Thyroid antibodies (TSH receptors antibodies)
- Radionucleotide thyroid scan (incease uptake)

Thyroid Scan in Thyrotoxicosis

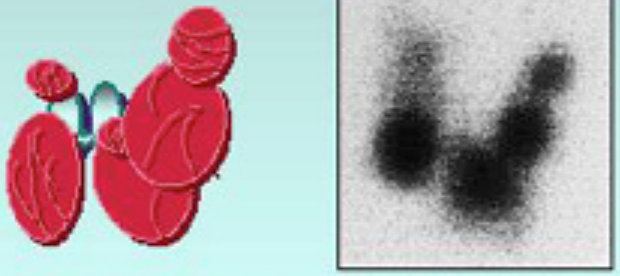


Graves' Disease

increase uptake bilateral homogenous

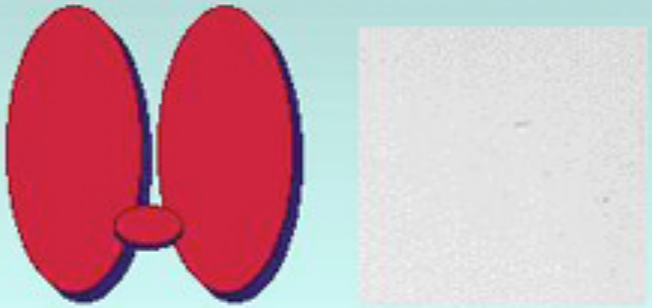
single nodule uptake

Follicular Adenoma



Multinodular Goiter

increase uptake irregulary



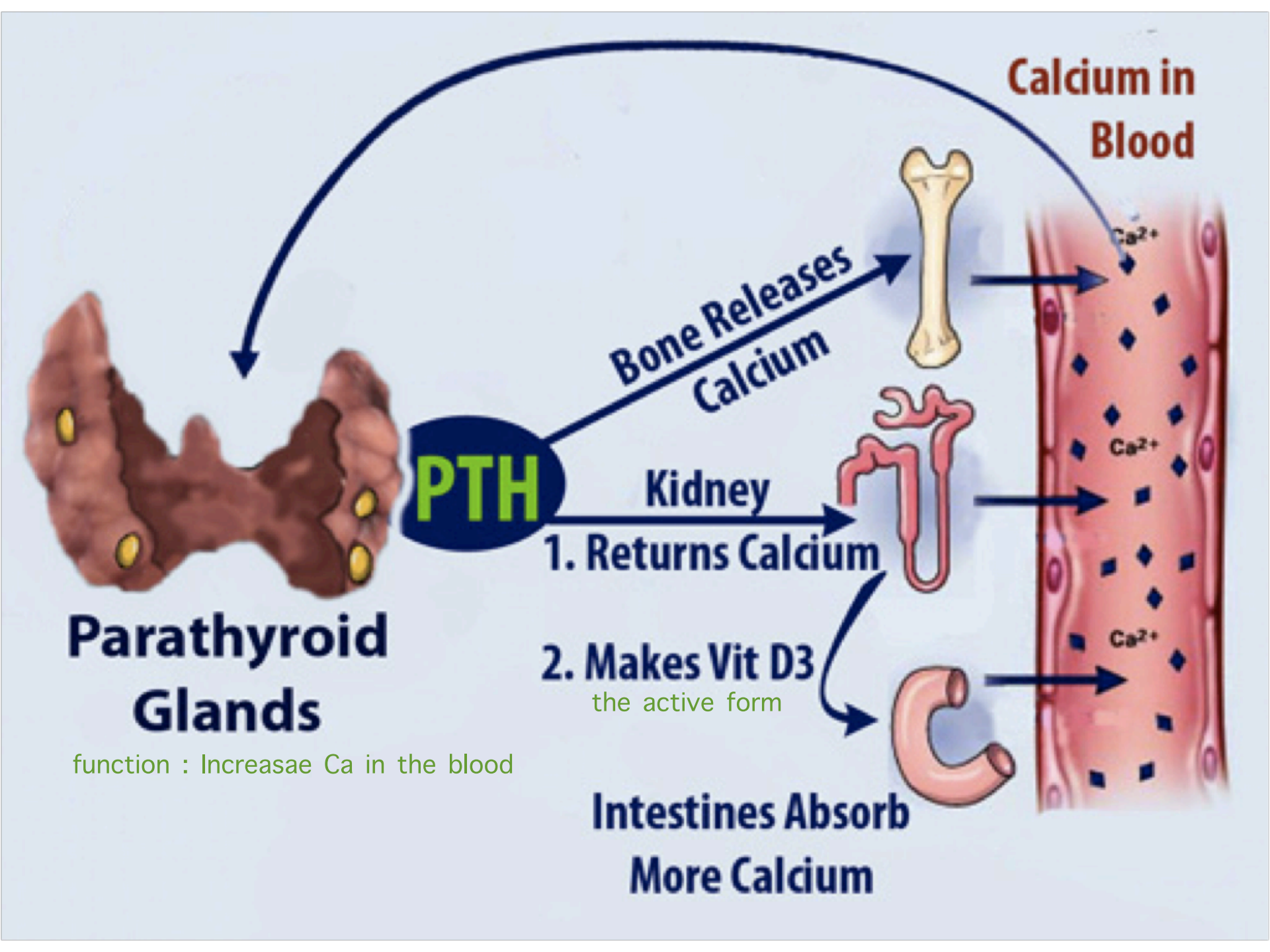
Subacute Thyroiditis

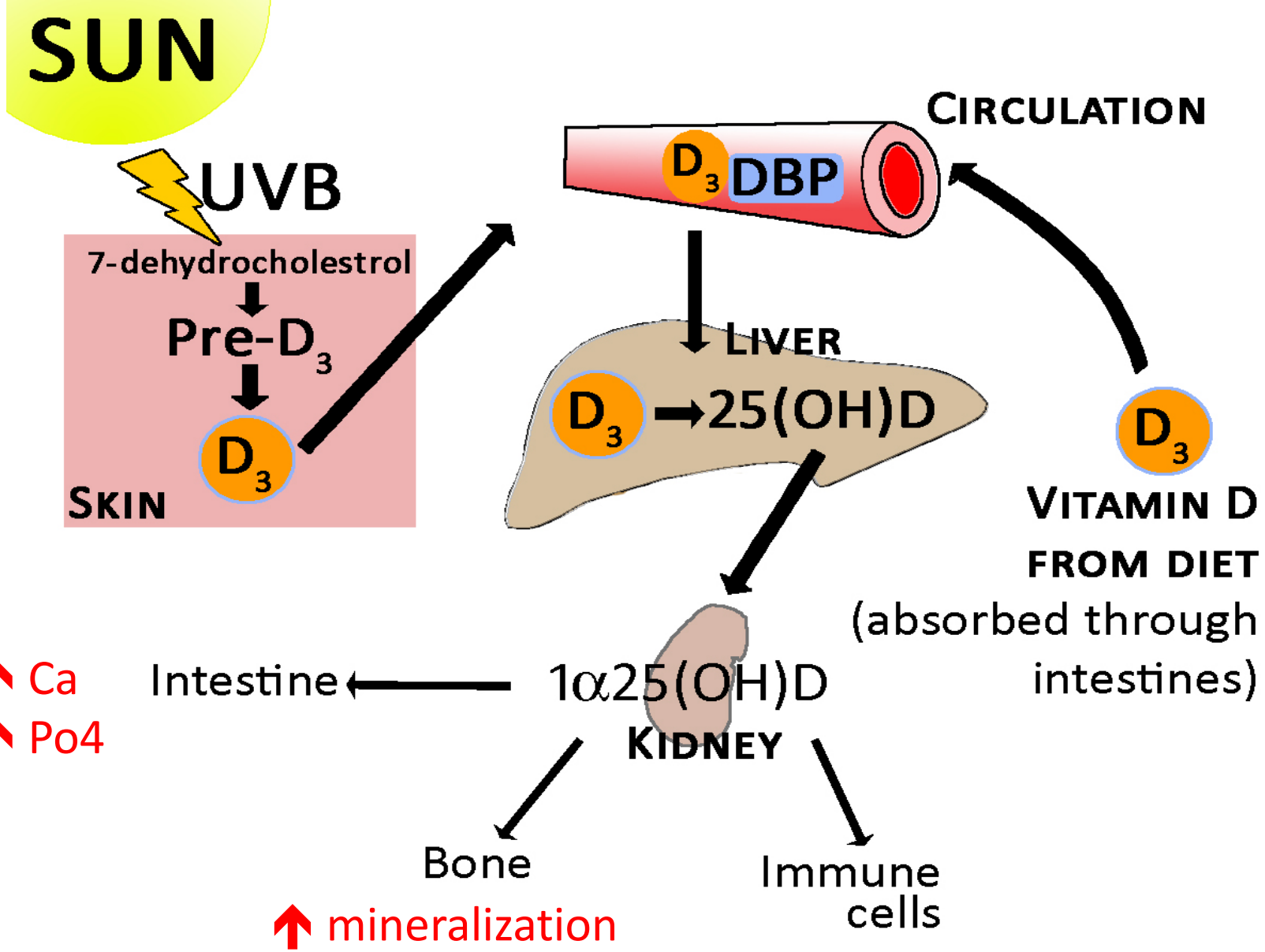
No uptake

Treatment

- *Beta*-blockers — stop the affect of hormone on heart
- Carbimazole
- PTU (propylthiouracil)
- Radioactive iodine (in adults) — to destroy most of the gland —> decrease hormones
- surgery

RICKETS


Calcium in Blood
Bone Releases Calcium
PTH
Kidney
1. Returns Calcium
2. Makes Vit D3
the active form
Parathyroid Glands
function : Increasae Ca in the blood
Intestines Absorb More Calcium
Ca2+
Ca2+
Ca2+



Major Vit D come from the sun through our skin OR minor from intestine (diet) —> to the liver get hydroxylation to 25(OH) —> Go to kidney get hydroxylation to 1-a25(OH) —> go to :

- Intestine —> increase absorption of Ca
- Bone —> mineralization

Calcitonin

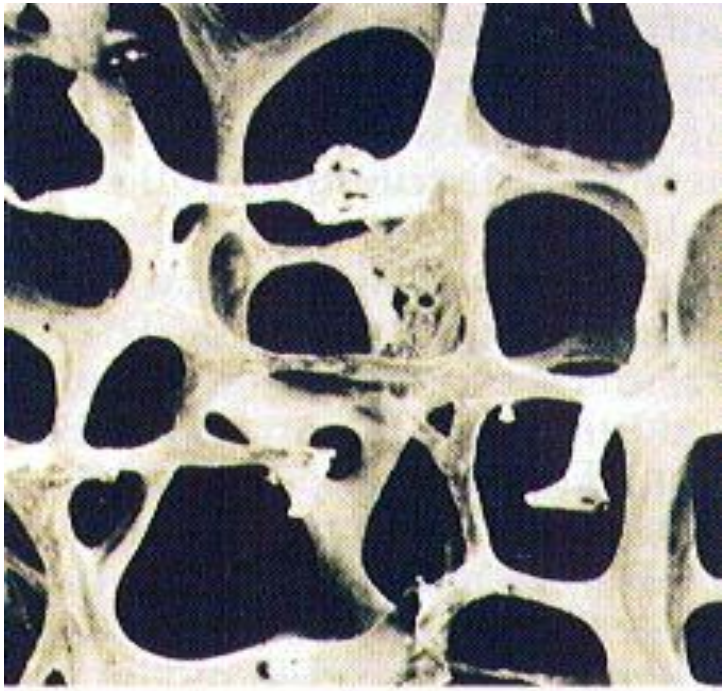
- It is a calcium lowering hormone
- Secreted by Thyroid C cells

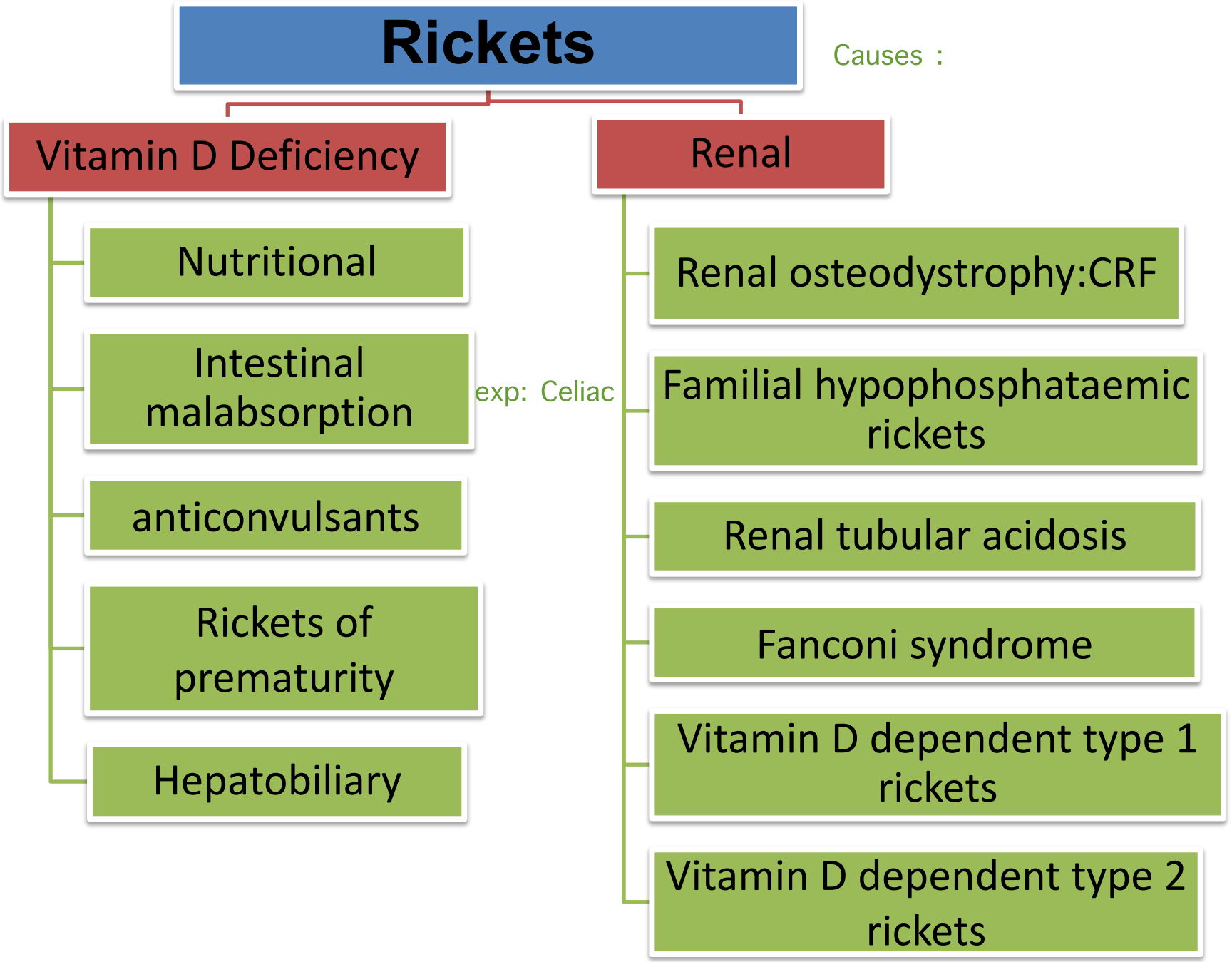
Anti - PTH

Rickets

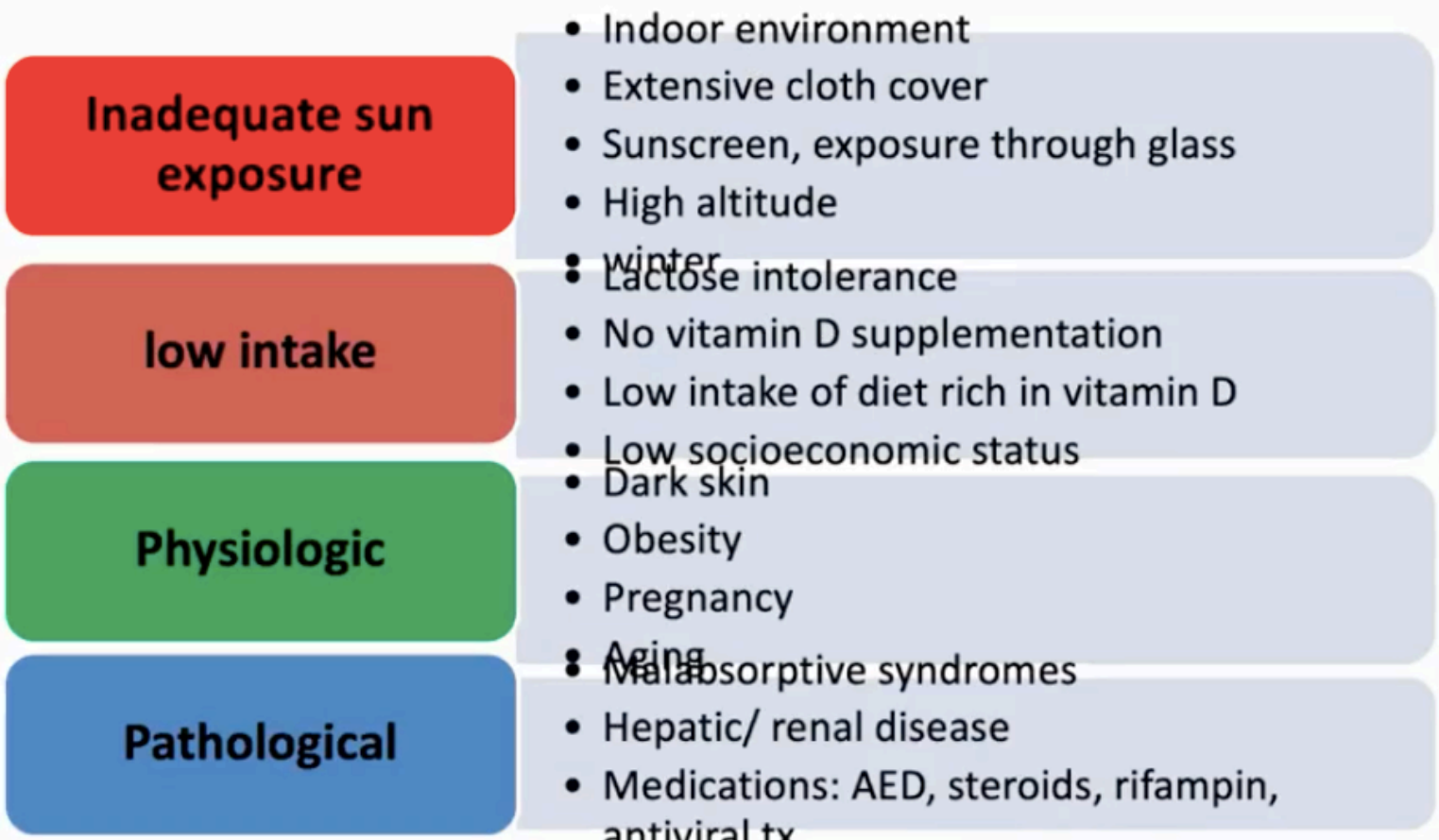
- Reduced **mineralization**

  of bone matrix due to calcium deficiency.




Rickets
Causes :
Vitamin D Deficiency
Renal
Nutritional
Intestinal malabsorption
exp: Celiac
anticonvulsants
Rickets of prematurity
Hepatobiliary
Renal osteodystrophy:CRF
Familial hypophosphataemic rickets
Renal tubular acidosis
Fanconi syndrome
Vitamin D dependent type 1 rickets
Vitamin D dependent type 2 rickets

Risk factor for Rickets caused by nutrition



Who to screen ?

pt with sign of :

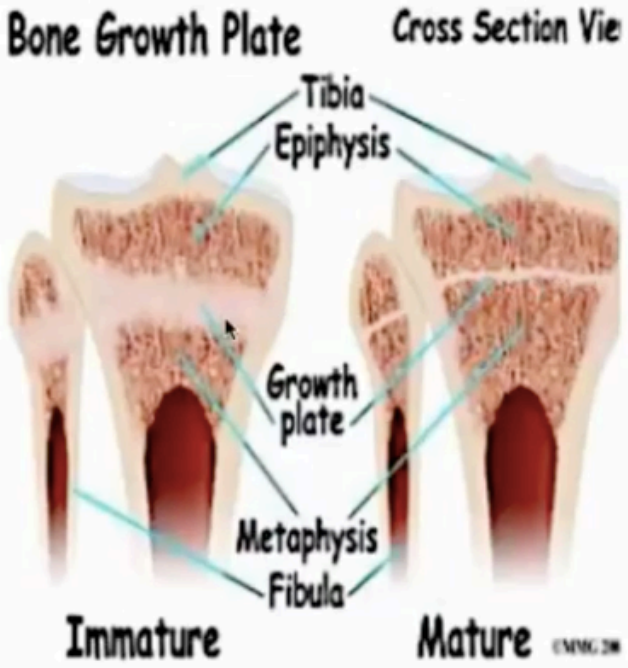
- Rickets
- Osteomalacia
- Osteoporosis
- Dark skin
- living in areas with reduced sun exposure
- institutionalized children
- Obesity
- long-term parenteral nutrition
- Chronic kidney disease
- Hepatic failure
- Malabsorption syndromes
- Bariatric surgery
- Radiation enteritis
- Hyperparathyroidism
- Medications: Antiseizure medications, Glucocorticoids, AIDS medications, Antifungals, Cholestyramine
- Pregnant and lactating women
- Older adults with history of falls, or nontraumatic fractures
- Granuloma-forming disorders

Rickets Effect at growth end plate

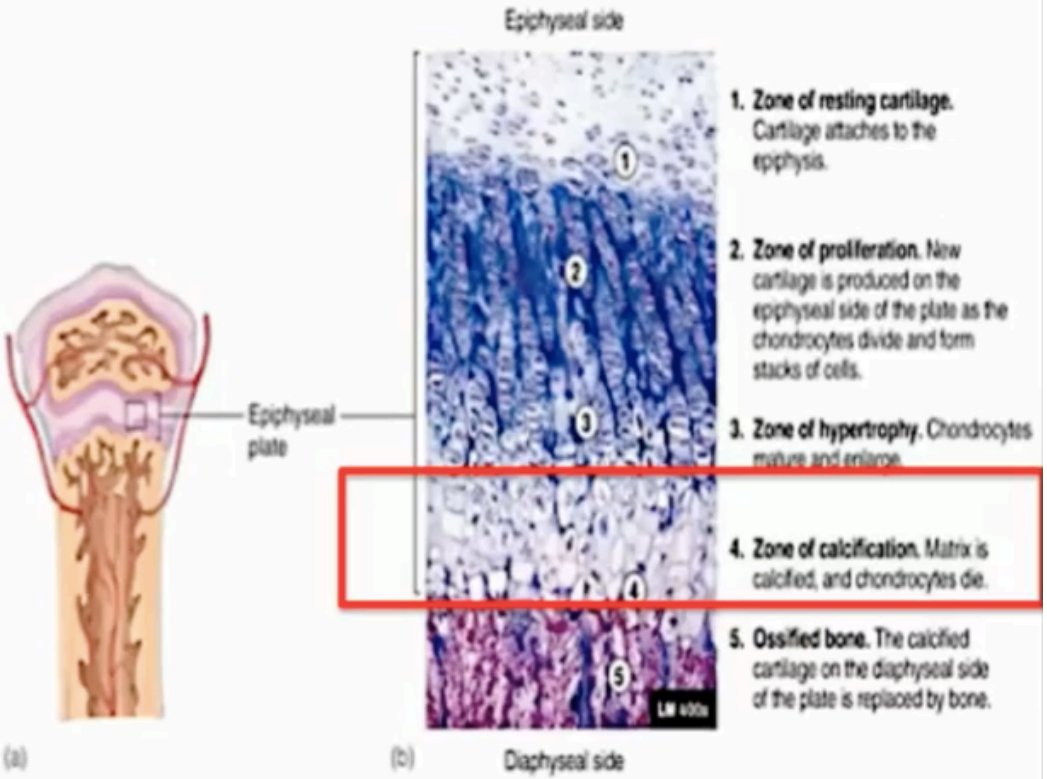
Inadequate growth plate mineralization.

The growth plate increases in thickness.

The columns of cartilage cells are disorganized.

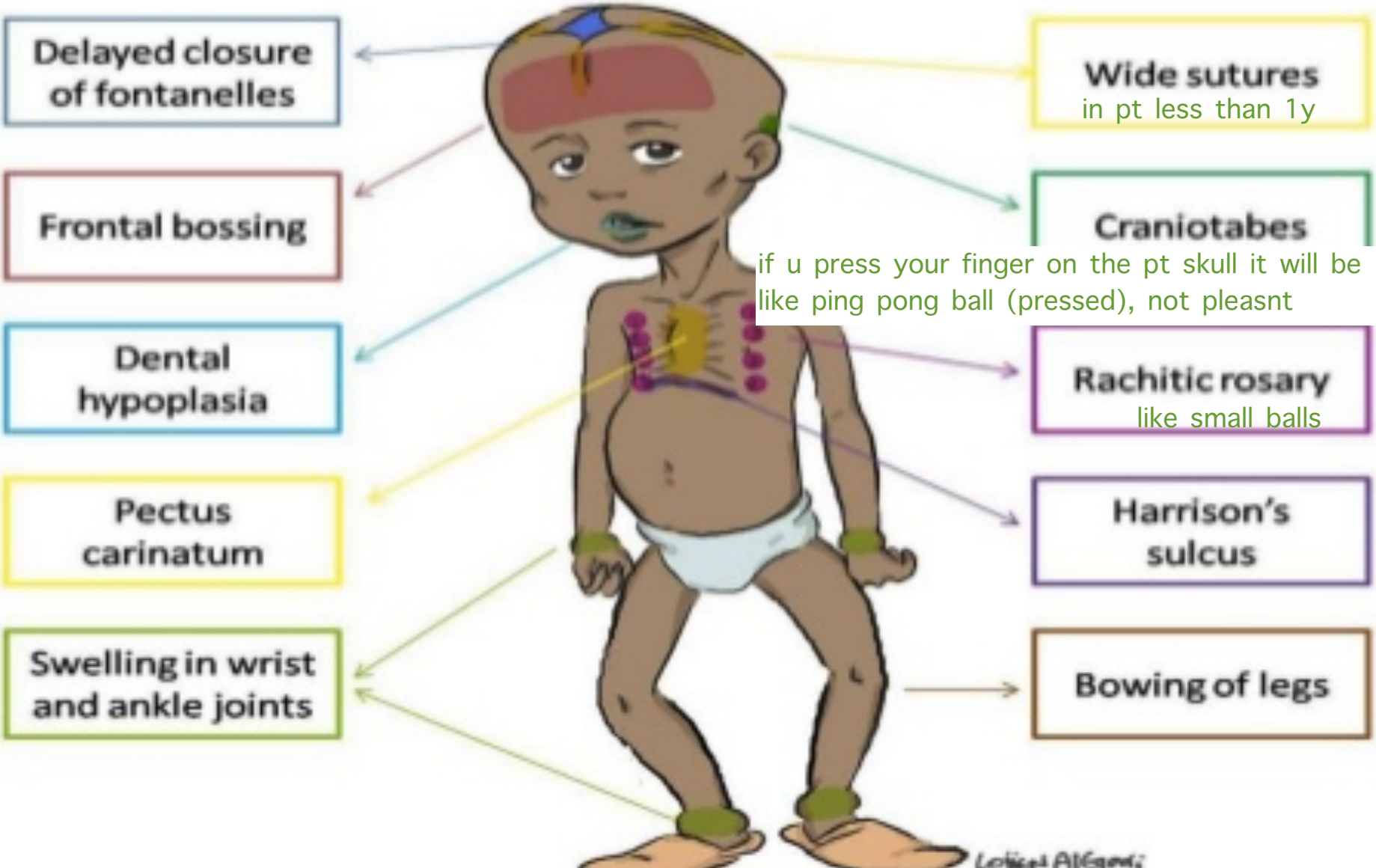


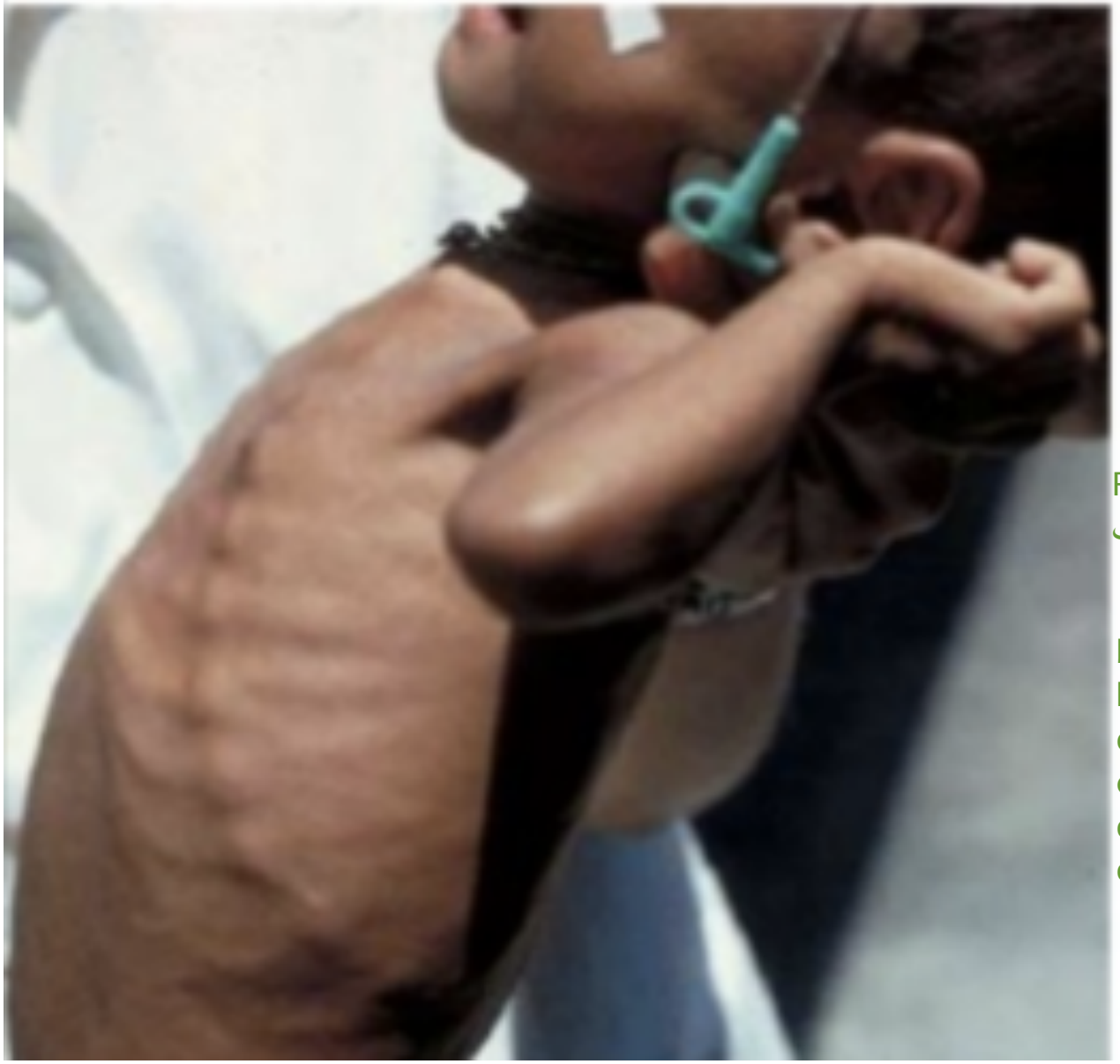
thick growth plate



main part that is affected :
Zone of calcification —> end up with large hypertrophied cartilages that are not ossified

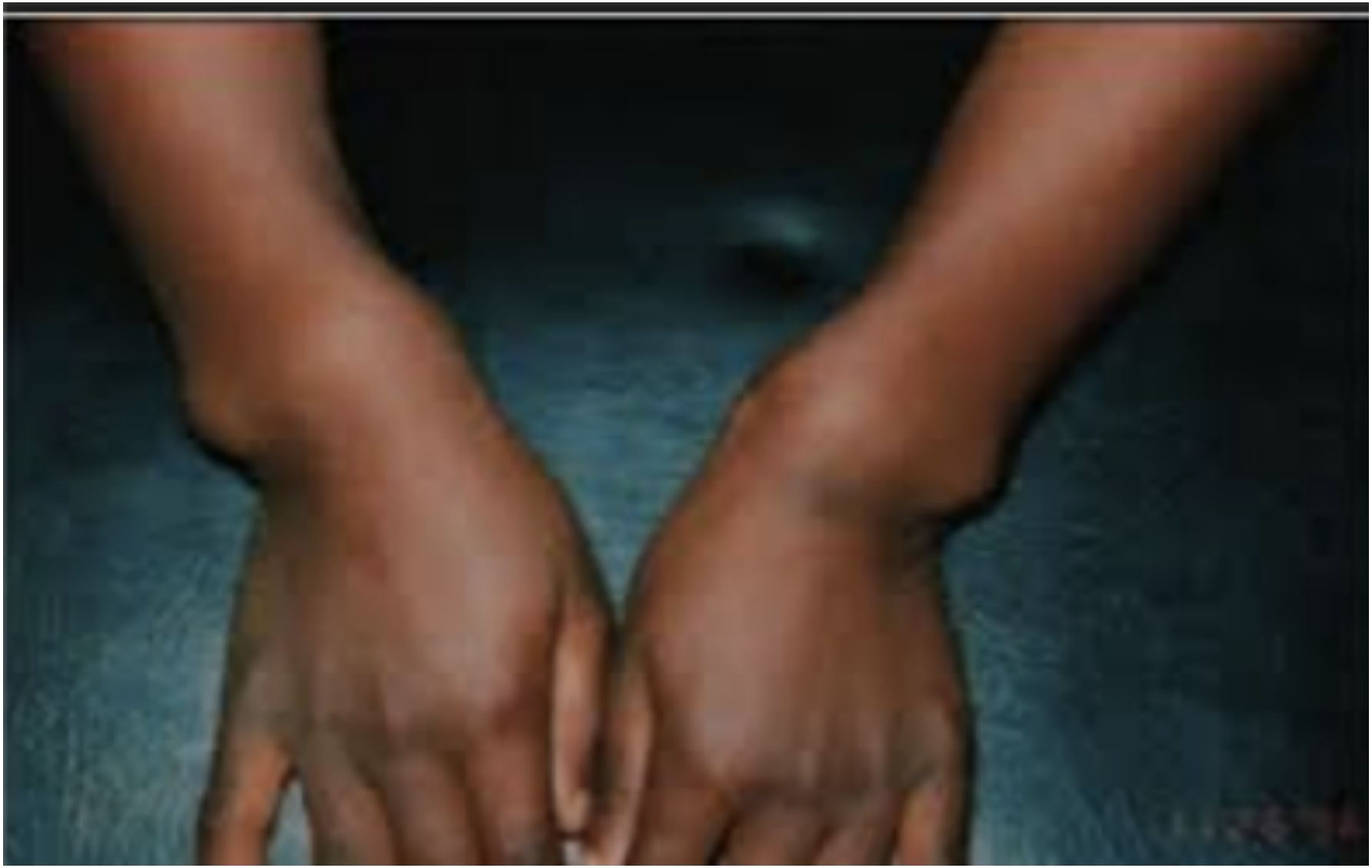
10 important clinical features in Rickets



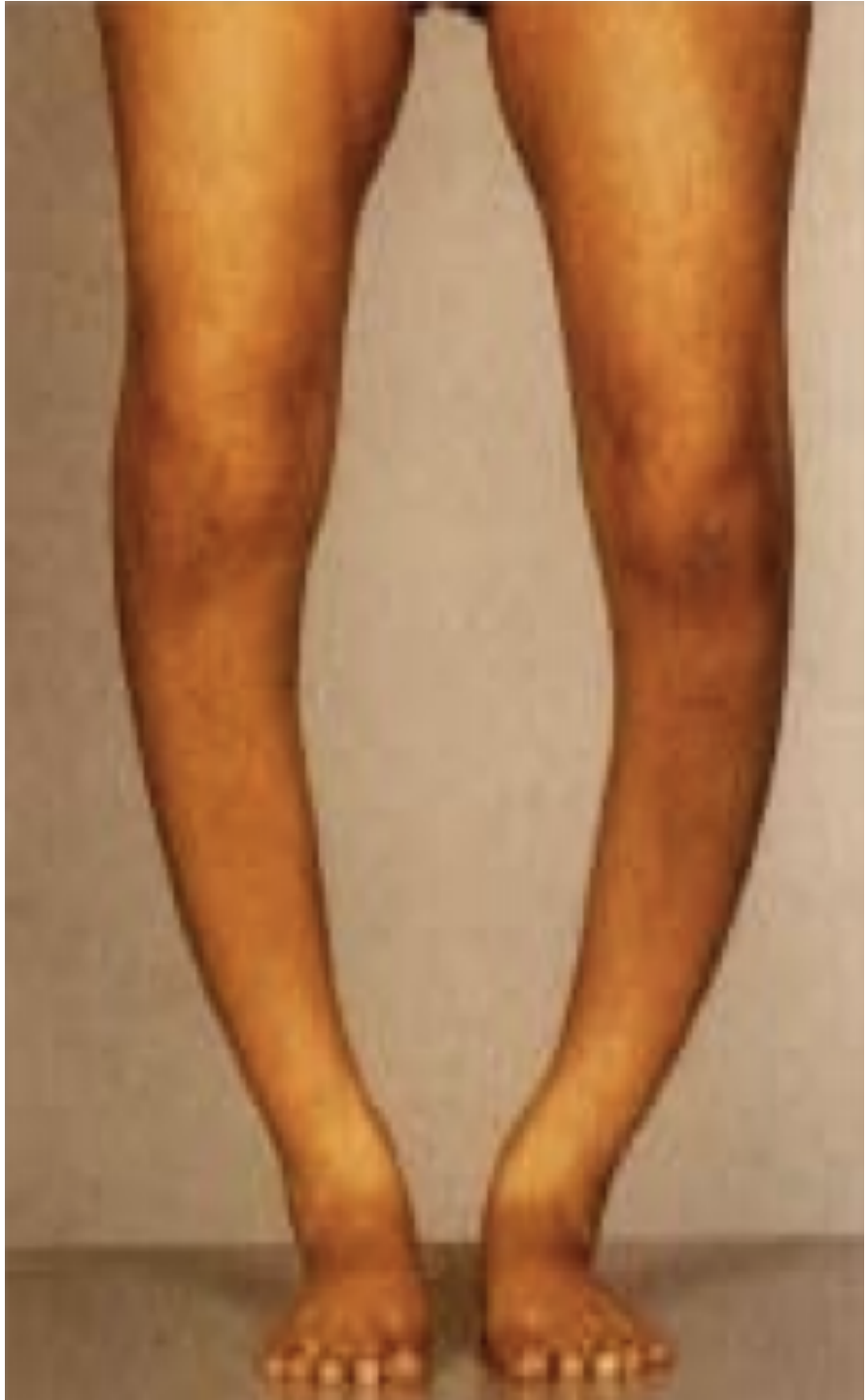


Rachitic rosary :
كأنها خرزات

because of hypertrophied cartilage in every costrochondral cartilage



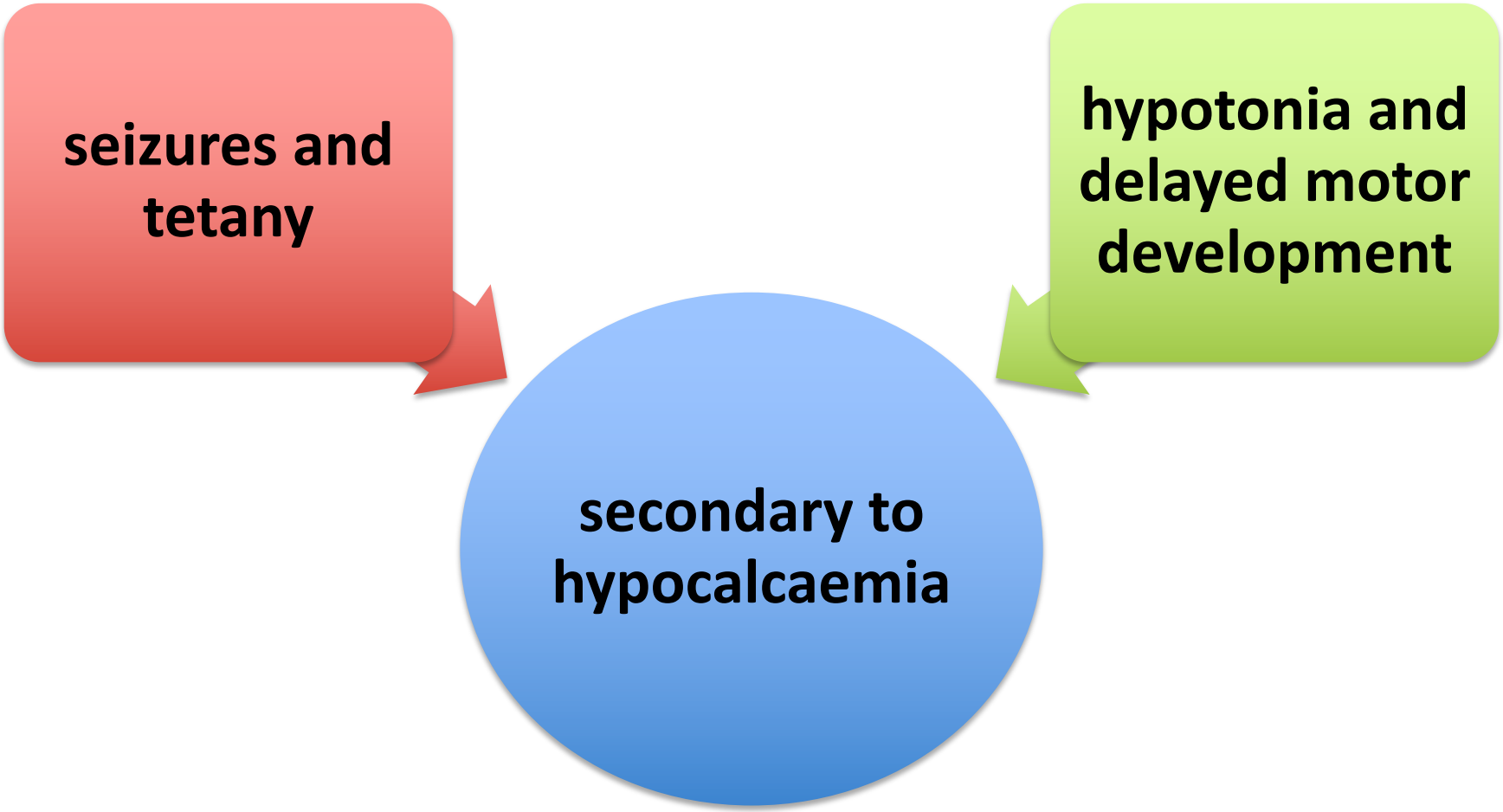
wide wrist joint



Bowing of the leg

various degree of bowing

Extra – skeletal manifestations



Vitamin D Status

nmol/l

Deficiency	50
Insufficiency	51-72.5
Sufficiency	75- 250
Excess	-

TABLE 1 Biochemical Manifestations of Different Stages of Vitamin D Deficiency

	Plasma Ca^{++}	Plasma PO_4	ALP	PTH	25(OH)-D	Radiograph Changes
Early	N/↓	N/↓	↑	↑	↓	Osteopenia
Moderate	N/↓	↓	↑↑	↑↑	↓↓	Rachitic changes +
Severe	↓↓	↓↓	↑↑↑	↑↑↑	↓↓↓	Rachitic changes ++

we observe early : minor low Vit D - Ca - PO4 level
as the vit D get lower the severe disease will be and severe changes will happen

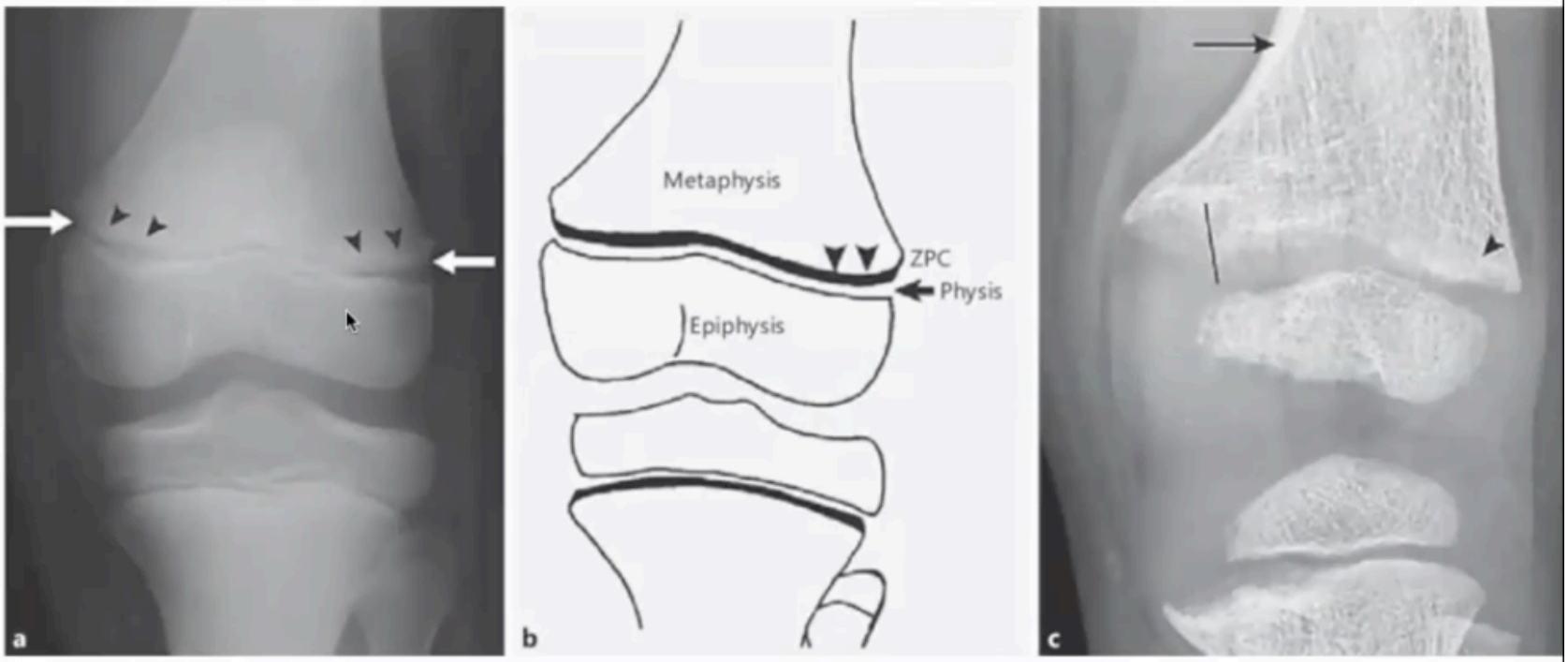
HOW CAN YOU DIFFERENTIAE BETWEEN LOW PTH VS. LOW VITAMIN D ?

Investigations

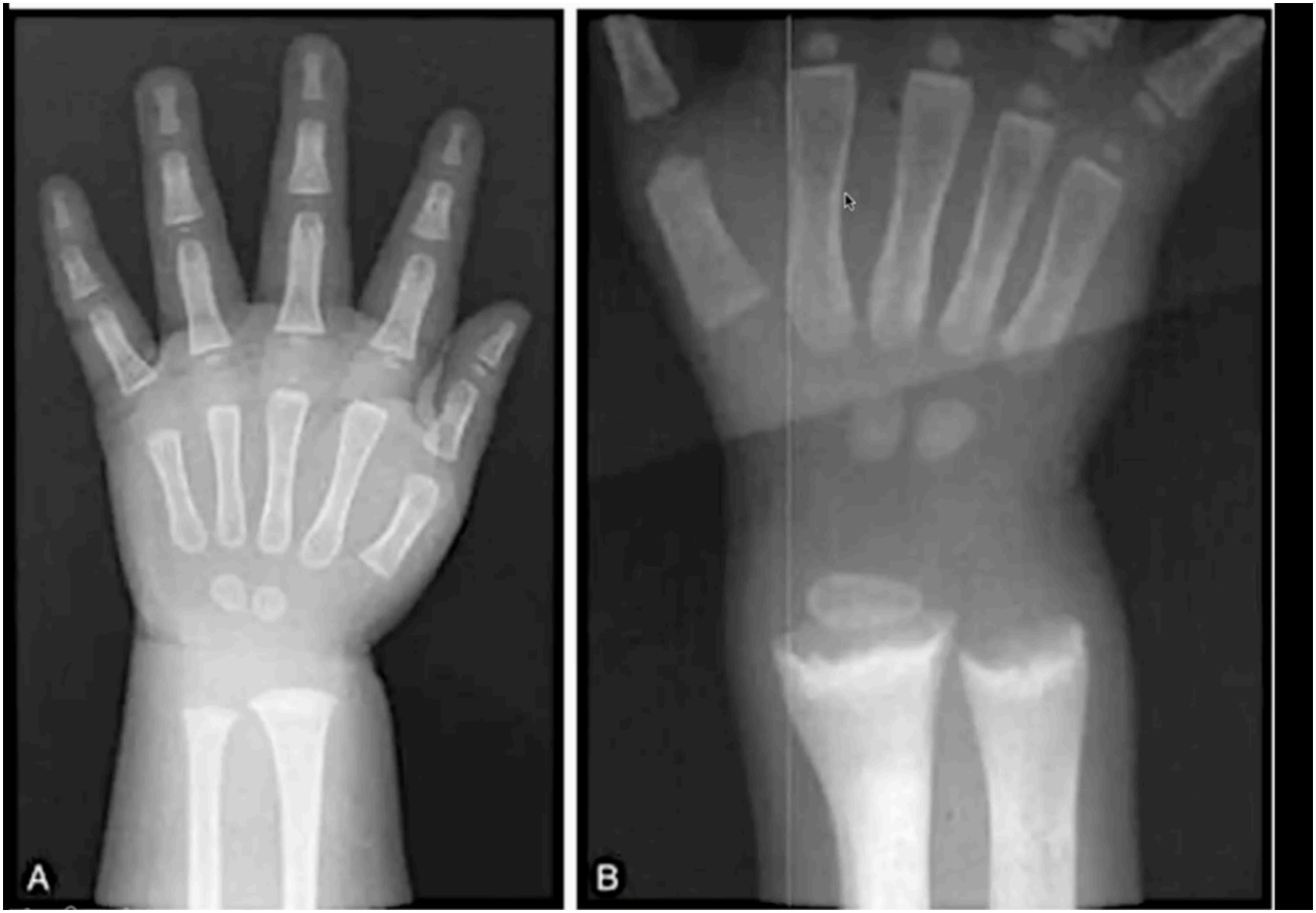
	Vitamin D def	Low PTH
Calcium	↓	↓
Phosphorus	↓	↑
Vit D level	↓	N
PTH	↑	↓

Vit D and PTH take long time in the labs so
How can I know if there is deficiency without knowing Vit D and PTH results?
from the Phosphorus

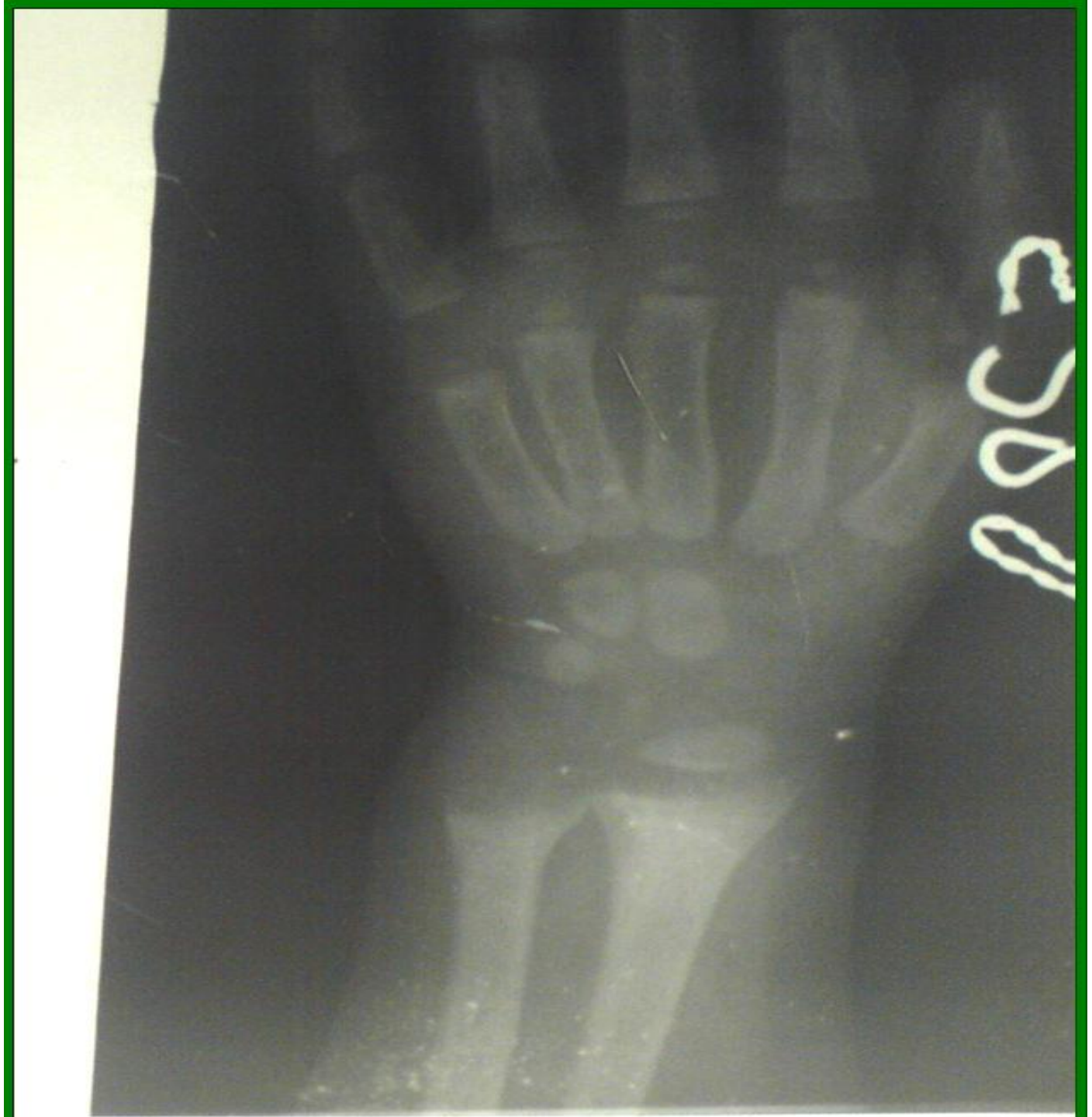
joints affected by rickets



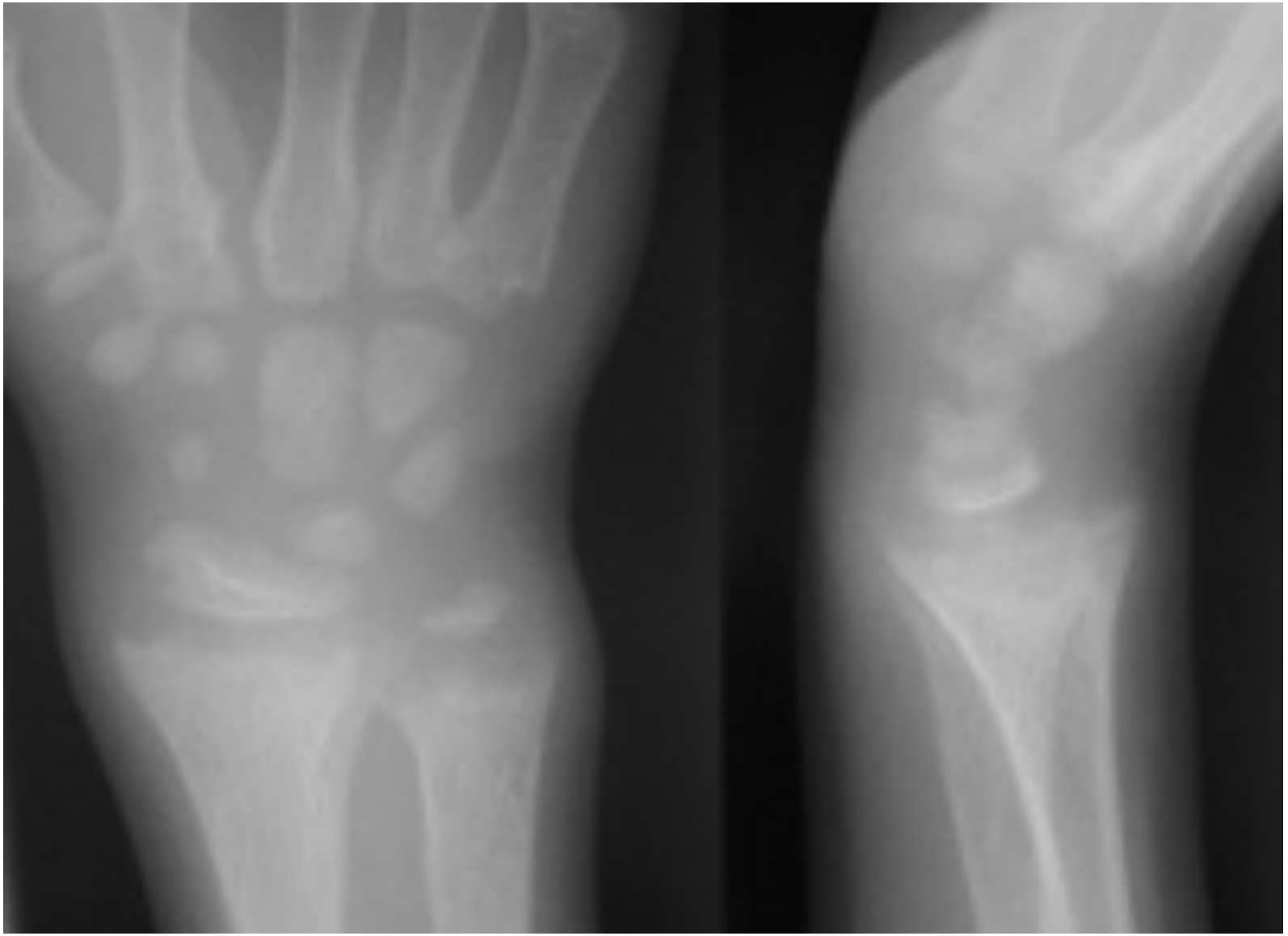
wide space between Meta and EPiphysis



Cupping and osteopenia

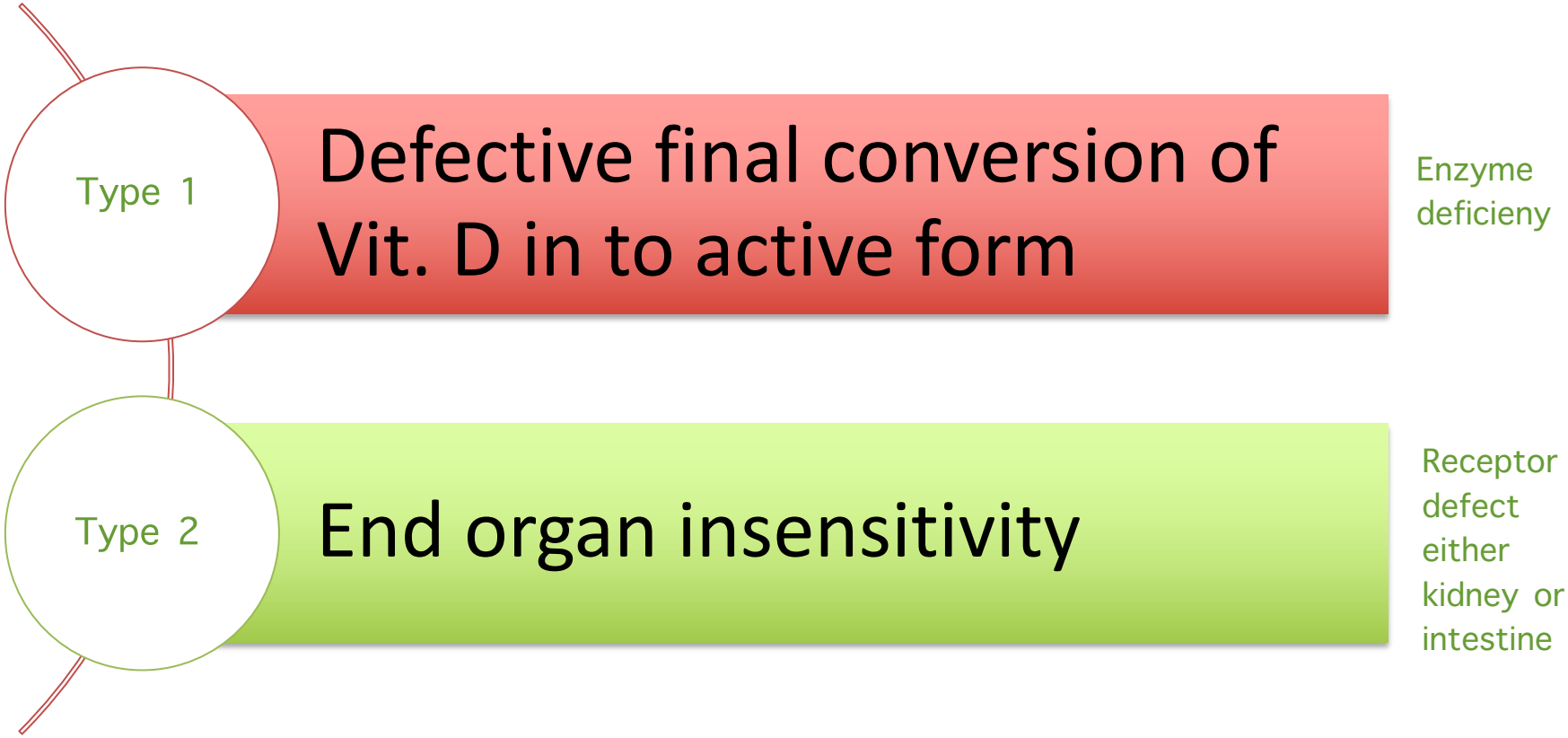


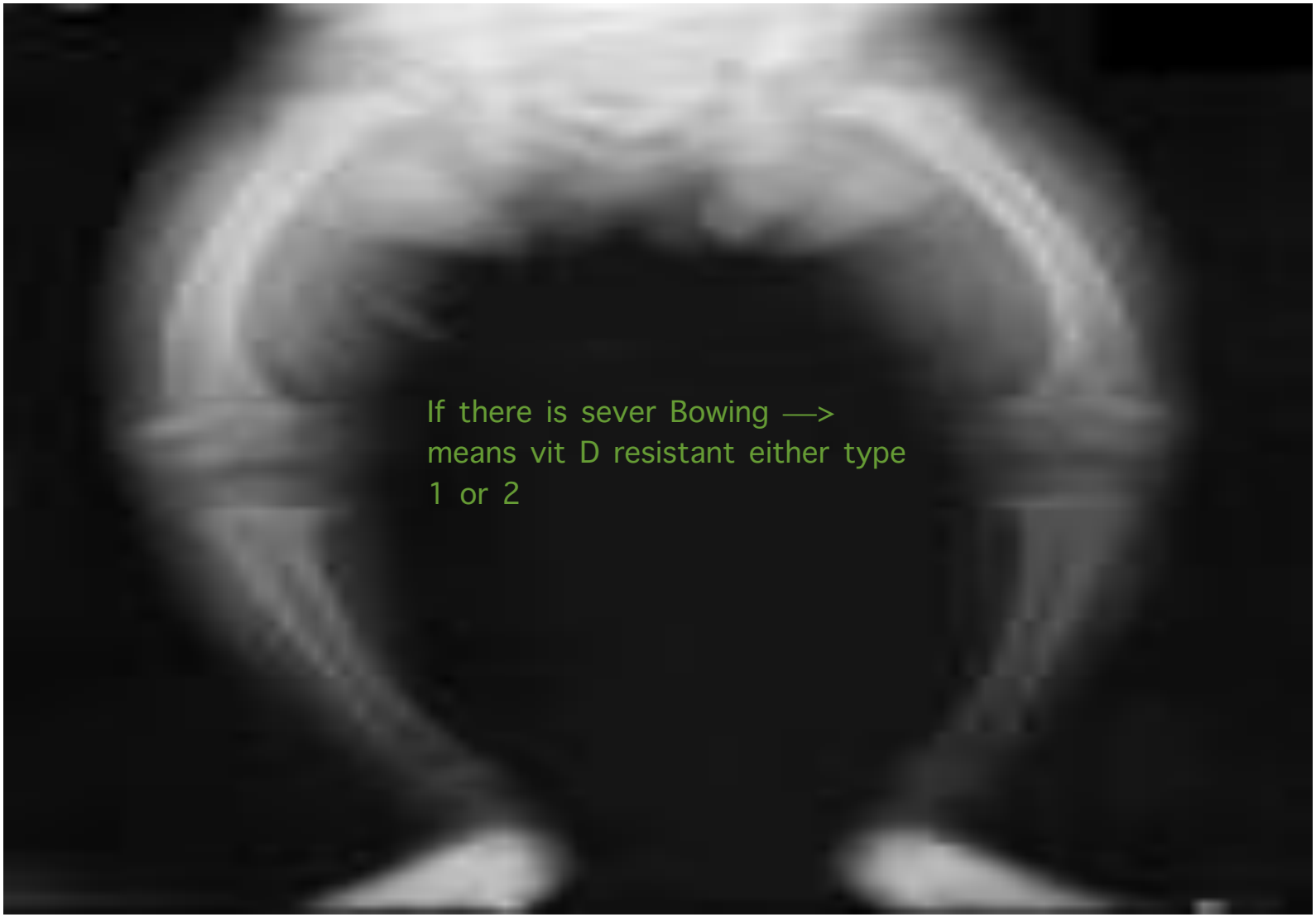
Cupping and osteopenia



Cupping and osteopenia

Vitamin D Resistant Rickets




If there is sever Bowing —>
means vit D resistant either type
1 or 2

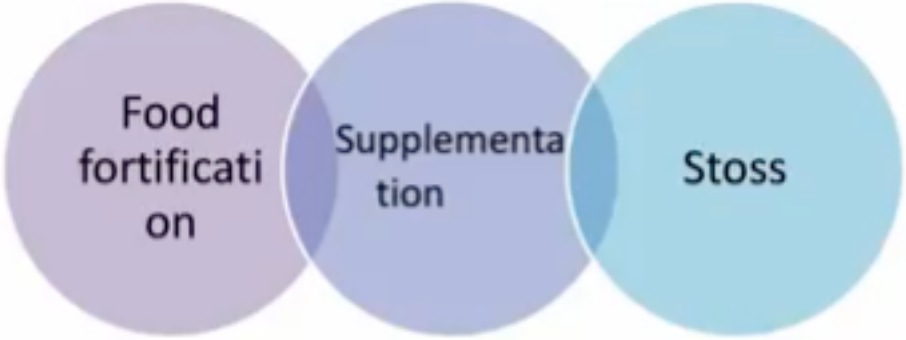
Treatment of nutritional vitamin D deficiency rickets

- Vitamin D supplement:
- 2000-5000 IU daily or 50,000IU weekly for 8 weeks as adult
- And calcium supplementation 50-70mg/kg/day to avoid hungry bone syndrome

huge dose of Vit D —> mineralization of the bone —> deposit alot of Ca in the bone —> hypocalcemia = Hungry bone syndrome

How to take vitamin D?

- Empty stomach or with a meal
- given three times a year, once a week, or once a day



Source of Vit D

- Full-body exposure for 10 -15 min in an adult with lighter pigmentation = 10,000 - 20,000 IU

- Fortified food
  only seafood and egg

Full term 1 year old girl who presented with afebrile tonic clonic convulsions. she has no chronic illnesses or medication. On examination he has no apparent dysmorphic features and his vital signs were normal.

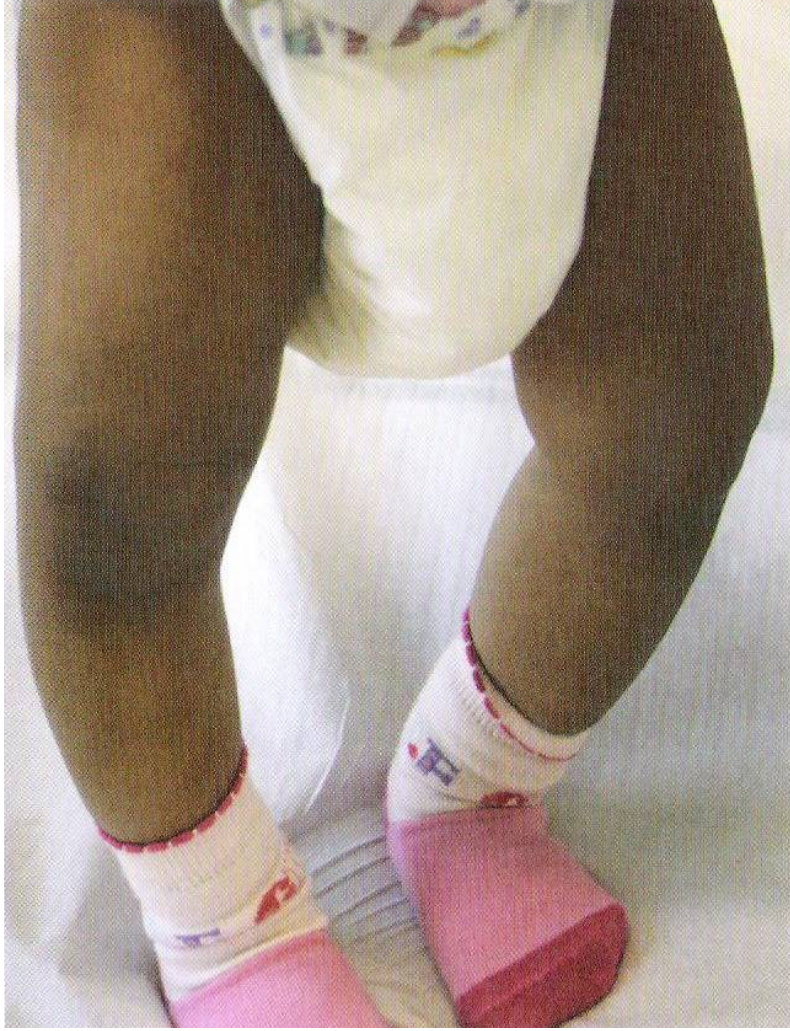
Labs are most likely to show:

A ↓ Ca, ↓ Phosphorus, ↑ ALP

B ↓ Parathyroid hormone

C ↓ Ca, ↑ Phosphorus, ↑ ALP

d ↓ Ca, ↑ Phosphorus, ↓ ALP



Ans : A

Rickets with hypocalcimic seizures