THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

39yo F With Low Phosphate

Isabel Casimiro, MD PhD

Endorama 6-16-18

To earn credit for today's activity text code:

GELYAH to 773-245-0068

Dr. Casimiro does not have any relevant financial relationships with any commercial interests.

Objectives

- To discuss the etiology, signs and symptoms of hypophosphatemia
- To review the clinical and laboratory findings of primary hyperparathyroidism
- To review cases reporting unusual causes for severe hypophosphatemia

HPI

- 38F with Hx of Crohn's disease (15 yrs) presented to her GI doctor for f/u & having some fatigue
- Currently Crohn's ileocolitis is in remission on treatment
- Previous Hx of intermittent hypercalcemia with normal PTH checked in 2012
- Prior Hx of anemia treated with IV iron infusions (did not tolerate PO iron)
- Prior Hx of vit D deficiency on MVI, switched to 2000 U 1 month ago
- Labs were drawn: BMP, phos, TFTs, CBC

ROS

- Constitutional: **Positive for appetite change, fatigue and unexpected weight change.**
- HENT: **Positive for mouth sores.**
- Eyes: Negative.
- Respiratory: Negative.
- Cardiovascular: Negative.
- Gastrointestinal: **Positive for abdominal distention, abdominal pain, constipation and nausea**. Negative for blood in stool.
- Genitourinary: Positive for frequency.
- Musculoskeletal: Negative.
- Allergic/Immunologic: Negative.
- Neurological: Negative.
- Hematological: Negative.
- Psychiatric/Behavioral: Negative.

PMH:
Crohn's dz
Psoriasis
HTN
Iron Deficiency Anemia
Hx of Nephrolithiasis
Hx of Gallstone Pancreatitis
Ovarian cyst

PSH:
Lap cholecystectomy
Abd hysterectomy
C section

Meds:
Azathioprine/Imuran 100mg Qd
Losartan-HCTZ 50mg-12.5mg Qd
MVI
Omeprazole 20mg Qd
Ustekinumab/Stelara 90mg Q8 wks

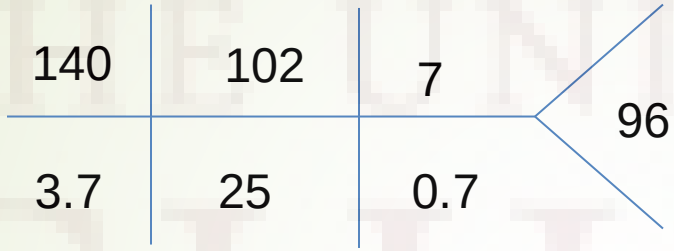
SH:
Married with 2 kids. She is an elementary school teacher. Non smoker

FH:
Mat GM Colon cancer
Father HTN
Mother DM
Paternal GM Wegener's

Physical Exam

- Blood pressure 130/87, pulse 73, temperature 37 °C (98.6 °F), temperature source NCIT, height 175.3 cm (5' 9"), weight 103.8 kg (228 lb 12.8 oz).
- The patient is alert and oriented x 3, in no acute distress.
- HEENT: Extraocular motion intact. Pupils equal, round and reactive to light. Oropharynx is clear. Sclerae are nonicteric. Neck: There is no lymphadenopathy; the thyroid is not palpable.
- CARDIAC: RRR, normal S1, S2. No murmurs, rubs or gallops.
- PULMONARY: Clear bilaterally to auscultation and percussion.
- BACK: No CVA tenderness.
- ABDOMEN: **Obese.** Soft, **well-healed low transverse scar; healing lap chole scars. Epigastric discomfort to palpation.** Bowel sounds are present. No obvious hepatomegaly, splenomegaly, or masses. No hernias or ascites.
- LYMPHATICS: No palpable nodes in the neck.
- MUSCULOSKELETAL: Normal gait and station, digits and nails. Extremities are all normal without edema.
- SKIN: No evidence of psoriasis lesions.
- NEUROLOGICAL: Cranial nerves intact, deep tendon reflexes normal.
- PSYCHIATRIC: Appropriate judgement and insight, oriented to time, place and person, has normal recent and remote memory, and appropriate mood and affect.

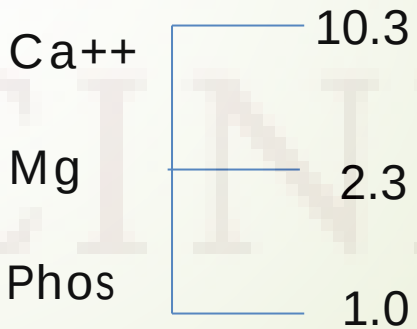
Labs



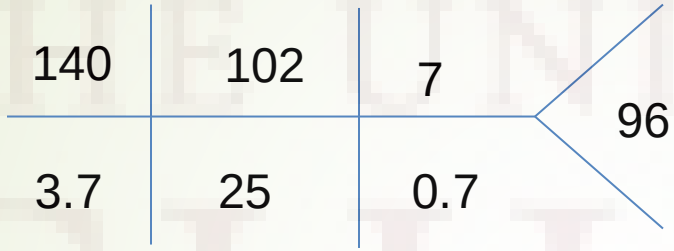
% sat 8.9% (14-50%)
Iron: 30 (40-160)
Ferritin 11 (10-220)
TIBC: 337 (230-430)

25-OH vit D: 23 (17, 1ya)

Albumin: 4.5
TSH: 1.59
FT4: 1.13



Labs



% sat **8.9%** (14-50%)
Iron: **30** (40-160)
Ferritin 11 (10-220)
TIBC: 337 (230-430)

25-OH vit D: 23 (17, 1ya)

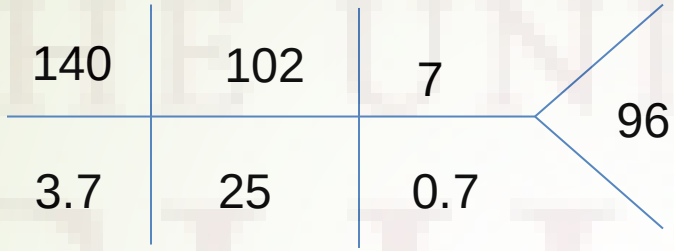
Albumin: 4.5
TSH: 1.59
FT4: 1.13

Ca++ **10.3** (8.4-10.2)

Mg 2.3

Phos **1.0**

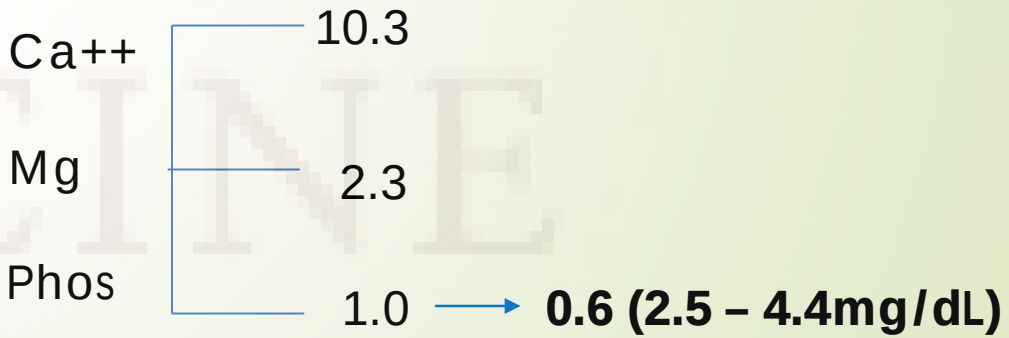
Labs



% sat 8.9% (14-50%)
Iron: 30 (40-160)
Ferritin 11 (10-220)
TIBC: 337 (230-430)

25-OH vit D: 23 (17, 1ya)

Albumin: 4.5
TSH: 1.59
FT4: 1.13



PTH 130 (15-75)

Continued Course

- Pt was directly admitted due to low phosphate (0.6mg/dL)
- She was started on IV phosphate
- Endocrinology was consulted

Hypophosphatemia

- Phosphorus is a major component of bone mineral (cortical and trabecular bone), membrane phospholipids, energy storing nucleotides, and nucleic acids
- Symptoms usually arise when phosphate drops <1.0 mg/dL (0.32 mmol/L)
- Conditions associated with hypophosphatemia: chronic alcoholism, TPN without phosphate supplementation, urinary phosphate wasting syndromes, chronic ingestion of antacids or phosphate binders, HD, severe PHPT
  - Severe hypophosphatemia can also be seen in DKA during prolonged hyperventilation (very rare)
- Reduction of 2,3-diphosphoglycerate (DPG) reduces the affinity of Hg for oxygen & reduces oxygen release at the tissue level
- Intracellular fall of ATP -> failure of cellular function

Effects of Severe Hypophosphatemia

- Bone:
  - Acute: Induction of 1,25 vit D -> bone calcium release -> hypercalciuria
  - Chronic: rickets and osteomalacia due to decreased bone mineralization
- CNS: neurologic symptoms irritability, paresthesias, seizures, coma; metabolic encephalopathy from ATP depletion
- CPS: Impaired myocardial contractility, ventricular arrhythmia, impaired diaphragmatic contractility
- Muscle: proximal myopathy, dysphagia, ileus, rhabdomyolysis
- Hematologic: erythrocyte rigidity, hemolysis (<0.5mg/dl/0.16 mmol/L), reduction in phagocytosis, chemotaxis, thrombocytopenia

Evaluation of Hypophosphatemia: Etiology

- 1. Acute movement of extracellular phosphate into the cells
- 2. Decreased net intestinal absorption
- 3. Increased urinary phosphate excretion

Major causes of hypophosphatemia

Graphic 71616 Version 9.0

Major causes of hypophosphatemia

Graphic 71616 Version 9.0

Major causes of hypophosphatemia

Internal redistribution
Increased insulin secretion, particularly during refeeding
Acute respiratory alkalosis
Hungry bone syndrome

Major causes of hypophosphatemia

Internal redistribution
Increased insulin secretion, particularly during refeeding
Acute respiratory alkalosis
Hungry bone syndrome
Decreased intestinal absorption
Inadequate intake
Inhibition of phosphate absorption (eg, antacids, phosphate binders, niacin)
Steatorrhea and chronic diarrhea
Vitamin D deficiency or resistance

Major causes of hypophosphatemia

Internal redistribution
Increased insulin secretion, particularly during refeeding
Acute respiratory alkalosis
Hungry bone syndrome
Decreased intestinal absorption
Inadequate intake
Inhibition of phosphate absorption (eg, antacids, phosphate binders, niacin)
Steatorrhea and chronic diarrhea
Vitamin D deficiency or resistance
Increased urinary excretion
Primary and secondary hyperparathyroidism
Vitamin D deficiency or resistance
Hereditary hypophosphatemic rickets
Oncogenic osteomalacia
Fanconi syndrome
Other - acetazolamide, tenofovir, IV iron, chemotherapeutic agents

Differential Diagnosis?

25-OH vit D: 23-> 33

Albumin: 4.5
TSH: 1.59
FT4: 1.13

PTH 130

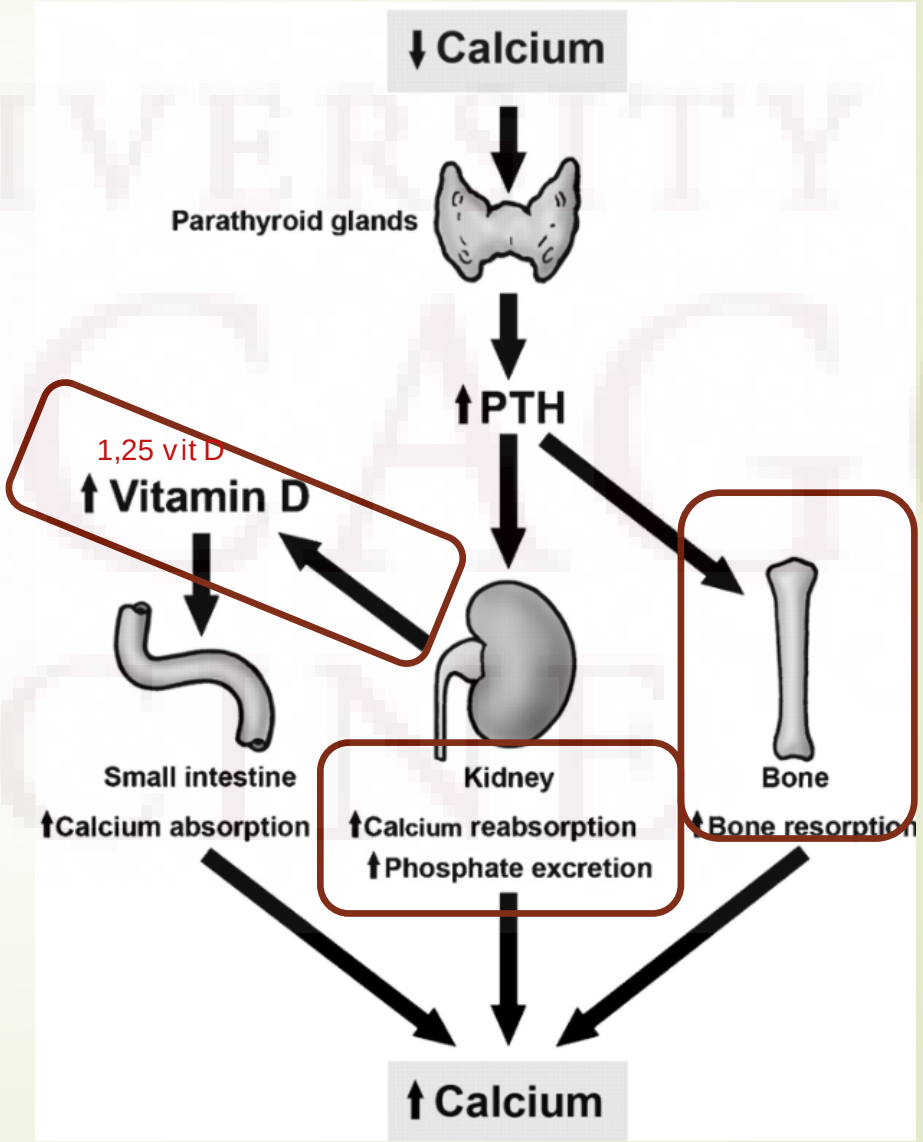
Ca++ 10.3

Mg 2.3

Phos 1.0 → 0.6

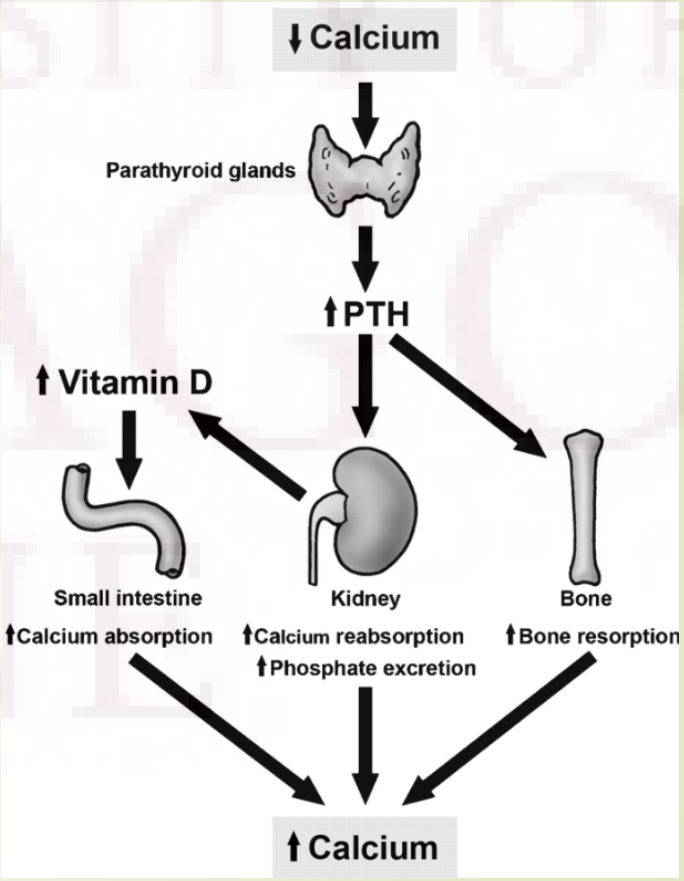
PTH Regulation of Calcium & Phosphate

- Increased intestinal calcium absorption mediated by increased renal production of 1,25-vit D (calcitriol)
- Decreased urinary calcium excretion due to stimulation of calcium reabsorption in the distal tubule
- Increased bone resorption by PTH

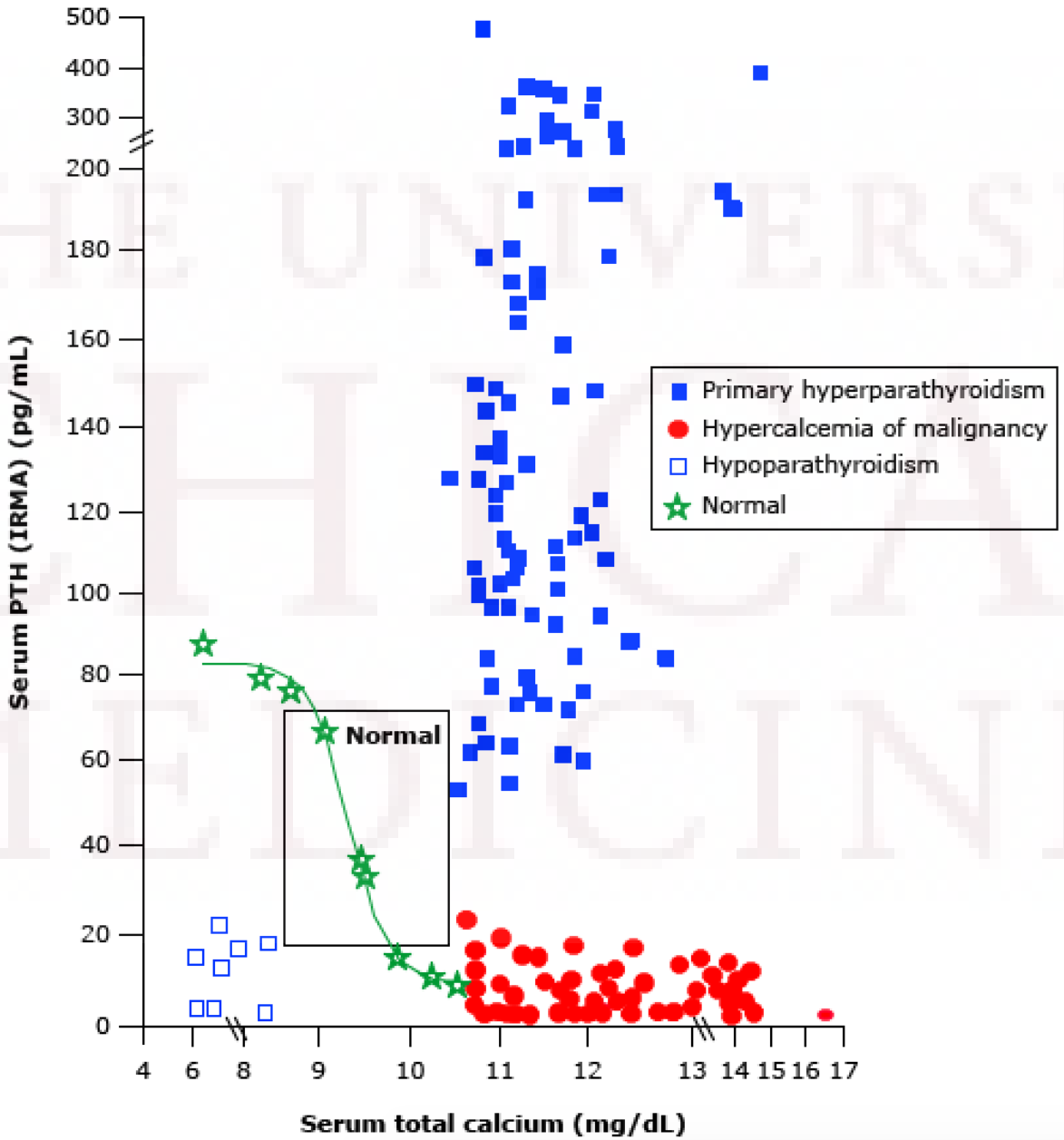


Primary Hyperparthyroidism (PHPT)

- Most common clinical presentation is asymptomatic hypercalcemia
- PHPT is diagnosed by the finding of a high PTH in a patient with hypercalcemia
  - 80-90% of patients with PHPT have serum PTH concentrations above the normal range for the assay
- The triad of hypercalcemia, hypophosphatemia, and urinary phosphate wasting is often present in primary hyperparathyroidism



Serum parathyroid hormone (PTH) concentrations in hypercalcemia and hypocalcemia

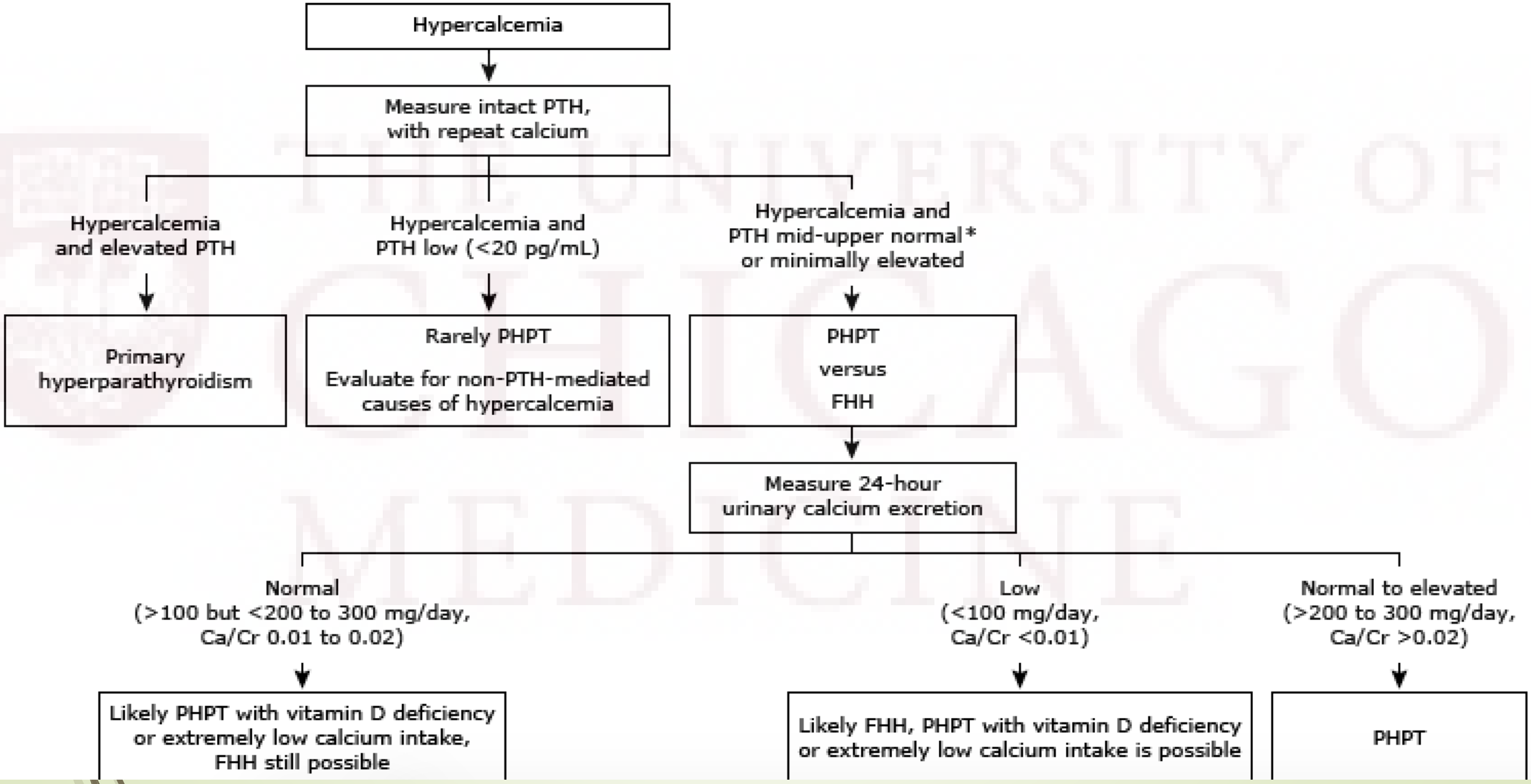


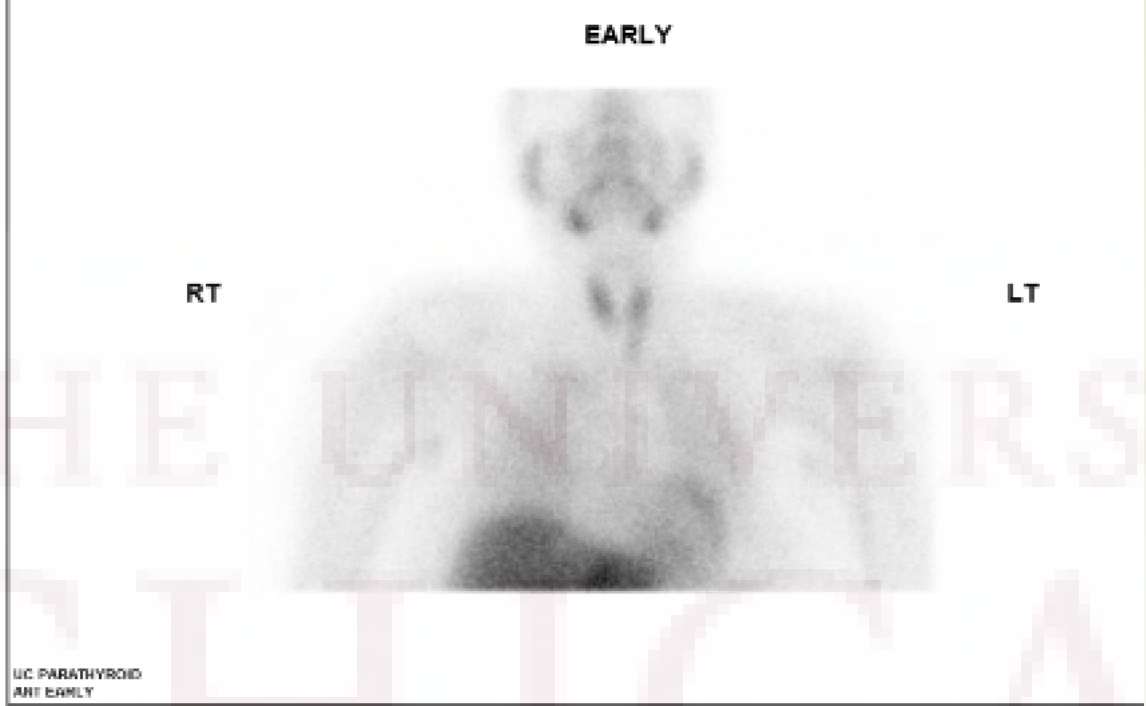
	22 10/15/2014 1002	21 4/6/2015 1548	20 8/5/2015 1140	19 3/21/2016 1534	18 7/13/2016 1204	17 3/8/2017 0839	16 7/10/2017 1629	15 4/2/2018 1603
BASIC & COMPREHENSIVE								
Glucose, Ser/Plasma	91 *		92	95		100 * ▲	95	96 *
Sodium	137 *		140	138		138	140	140
Potassium, Ser/Plasma	4.0 *		4.0	4.2		4.0	4.2	3.7
Chloride	104 *		106	102		104	101	102
Carbon Dioxide	22 * ▼		21 ▼	26		20 ▼	25	25
Anion Gap	11 *		13	10		14	14	13
BUN	8 *		6 ▼	8		8	8	7
Creatinine	0.8 *		0.7	0.7		0.7	0.6	0.7
GFR Estimate (Calc)	81 *		95 *	94 *		94 *	112 *	93 *
Calcium	10.1 *		10.3 ▲	10.2		10.6 ▲	10.7 ▲	10.8 ▲
Calcium Interface ...								
Inorganic Phosphate								
Inorganic Phosphat...								
Magnesium								
Total Protein	7.5 *	7.5	7.2	7.6	7.5	7.4	7.9	8.0
Albumin	4.3 *	4.4	4.2	4.3	4.1	4.4	4.4	4.5
					0.3	0.8	0.4	0.3

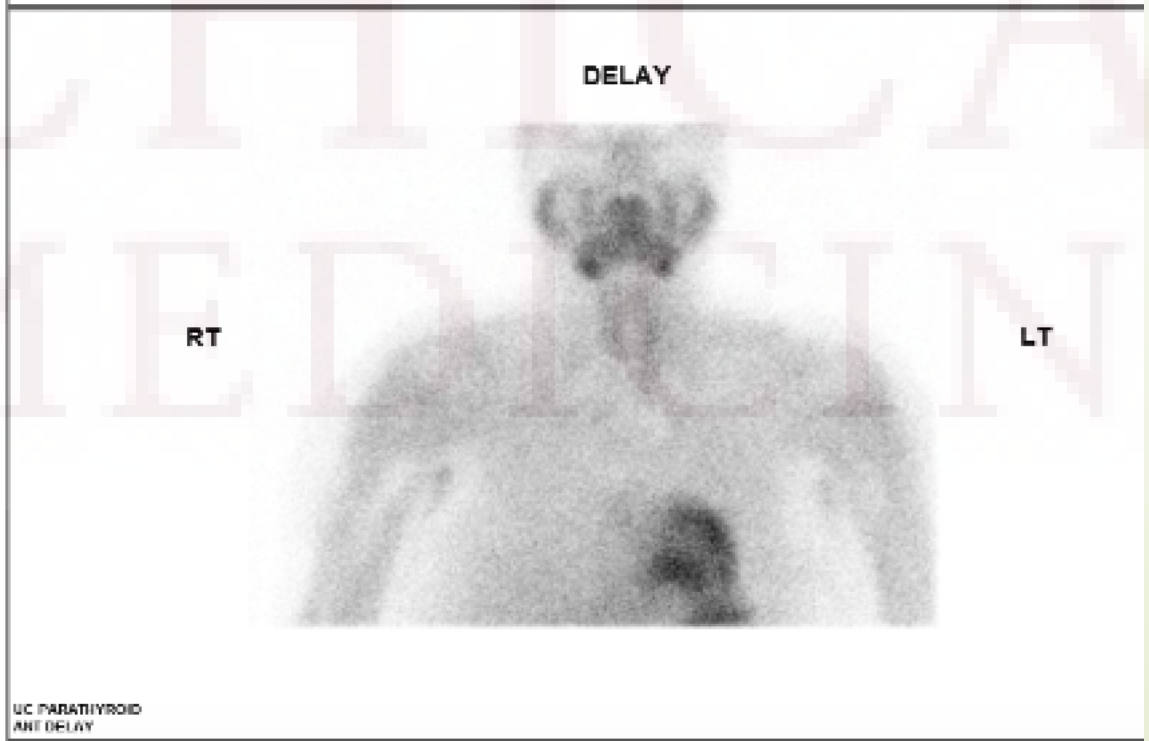
	3/5/2012 1500	3/8/2017 0839	4/2/2018 1603	5/17/2018 0845	5/21/2018 1823
METABOLIC BONE DIS...					
Actual Ca++					
PTH, Intact	64			130 ▲	103 ▲

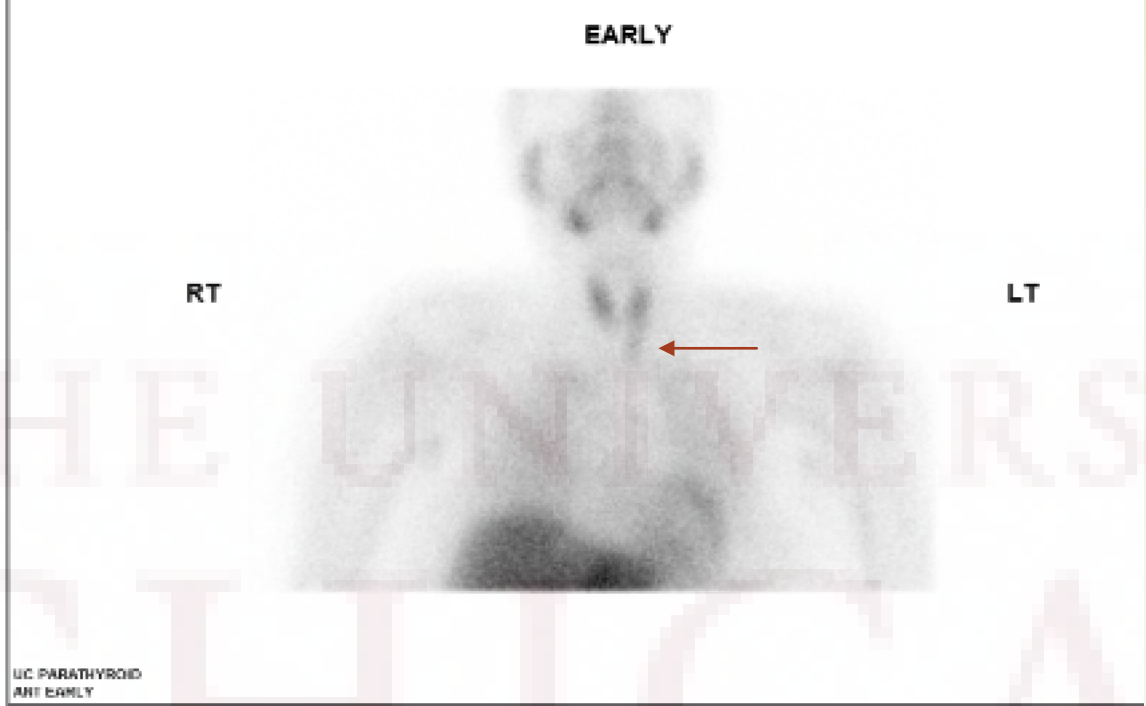
Pt reported Hx of kidney stones for the last 7 yrs, last was 3 ya

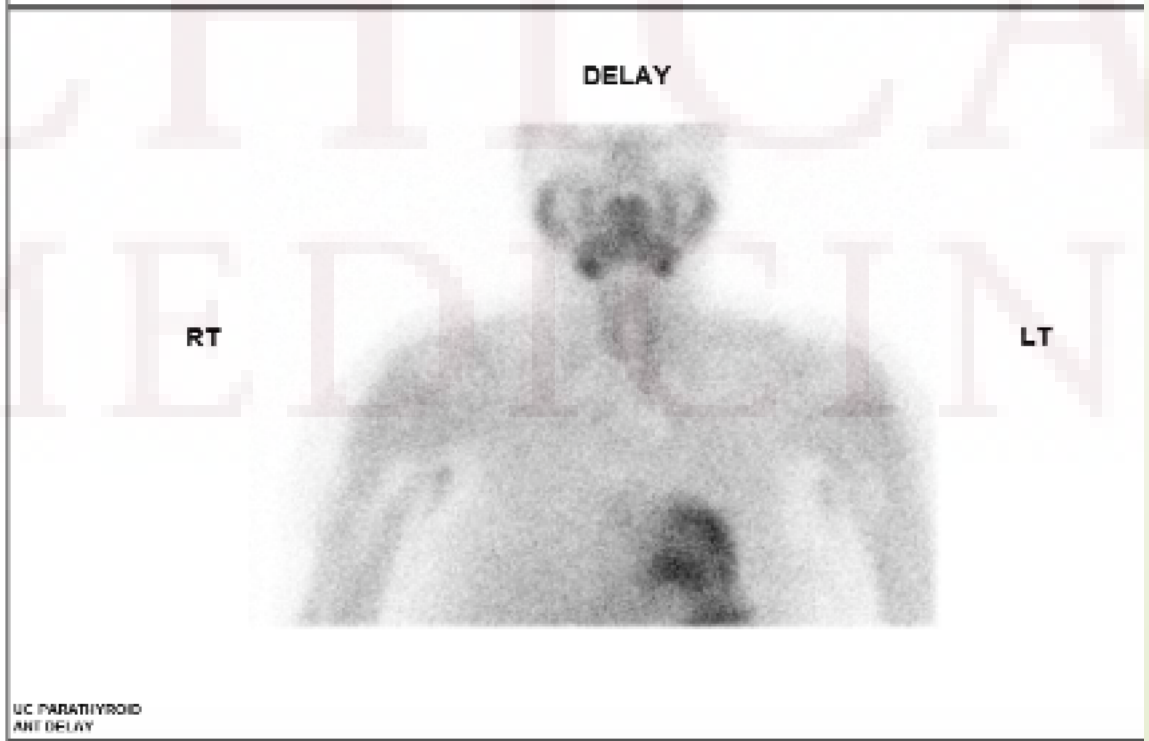
Diagnosis of primary hyperparathyroidism




EARLY
RT
LT
UC PARATHYROID
ANT EARLY

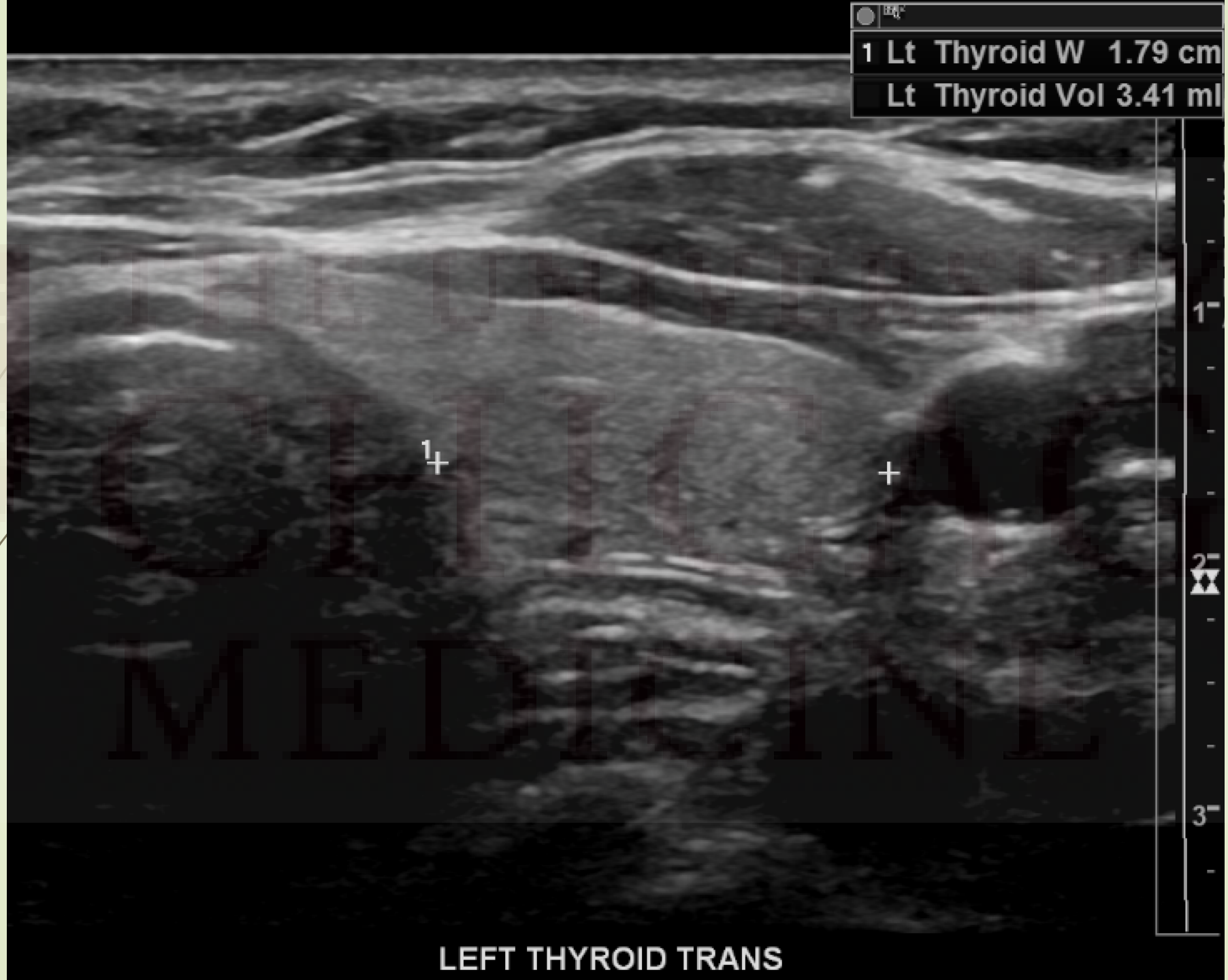

DELAY
RT
LT
UC PARATHYROID
ANT DELAY

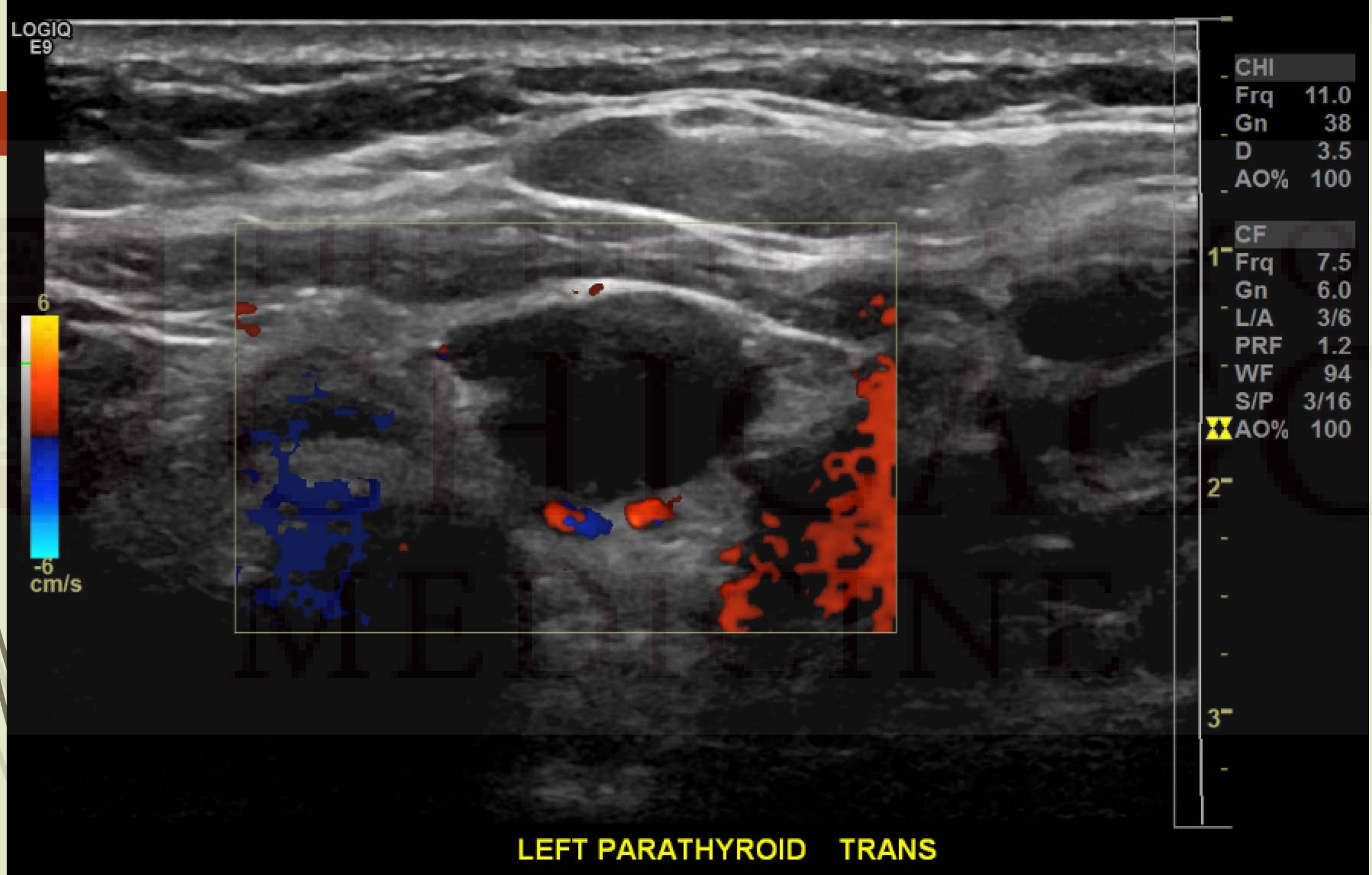

EARLY
RT
LT
UC PARATHYROID
ANT EARLY

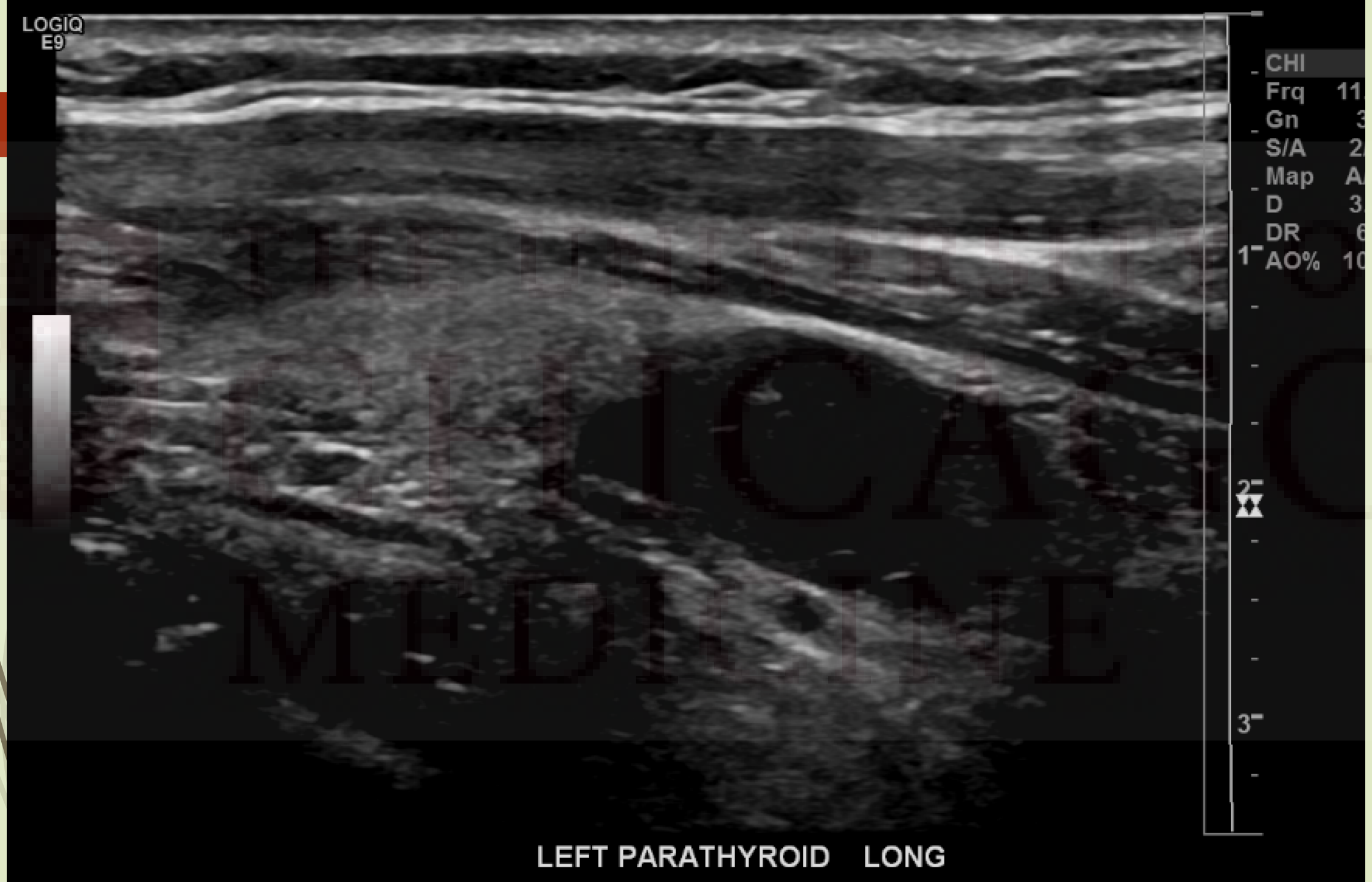

DELAY
RT
LT
UC PARATHYROID
ANT DELAY

US Thyroid US

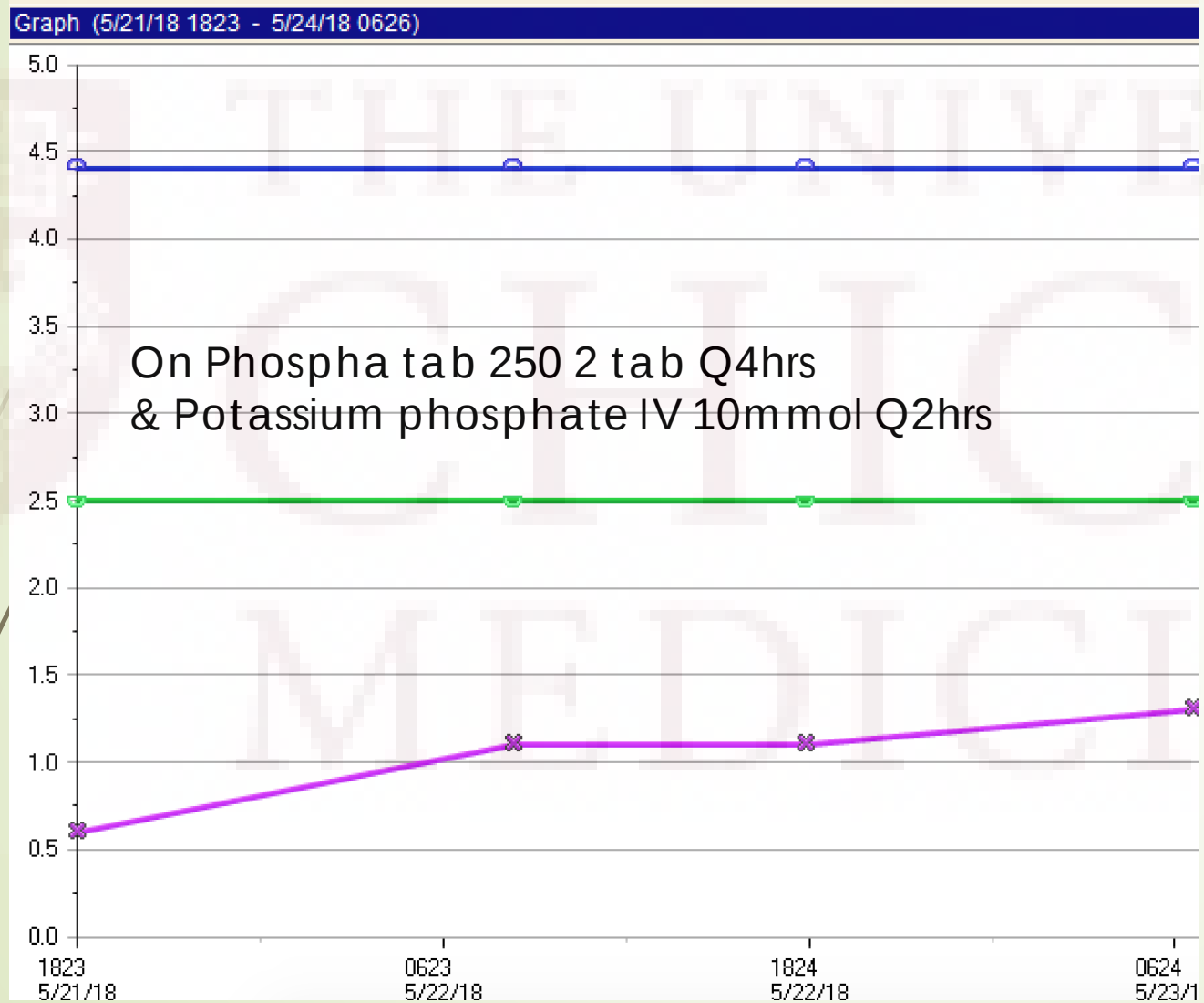
- RIGHT LOBE MEASUREMENTS: 4.6 x 1.4 x 1.6 cm
- LEFT LOBE MEASUREMENTS: 4.5 x 0.9 x 1.8 cm
- ISTHMUS MEASUREMENTS: 0.3 cm RIGHT LOBE: No significant abnormality noted.
- LEFT LOBE: No significant abnormality noted.
- ISTHMUS: No significant abnormality noted.
- PARATHYROID GLANDS: There is a predominantly hypoechoic extrathyroidal lesion with
- low-level internal echoes inferior to the left thyroid lobe measuring approximately 2.1 x
- 0.9 x 1.4 cm, compatible with the suspected parathyroid adenoma seen on recent sestamibi scan.
- LYMPH NODES: No significant abnormality noted.
- OTHER: No significant abnormality noted.
- **IMPRESSION: Predominantly hypoechoic lesion inferior to the left thyroid lobe compatible**
- **with the suspected parathyroid adenoma on the recent sestamibi scan.**

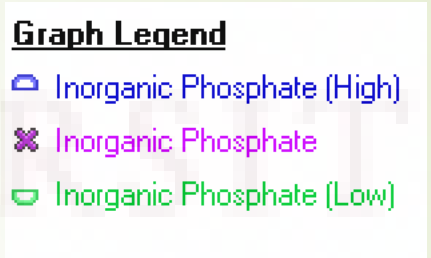

1 Lt Thyroid W 1.79 cm
Lt Thyroid Vol 3.41 ml
1
LEFT THYROID TRANS


LOGIQ
E9
6
-6
cm/s
CHI
Frq 11.0
Gn 38
D 3.5
AO% 100
CF
Frq 7.5
Gn 6.0
L/A 3/6
PRF 1.2
WF 94
S/P 3/16
AO% 100
1
2
3
LEFT PARATHYROID TRANS


LOGIQ
E9
CHI
Frq
Gn
S/A
Map
D
DR
AO%
1
2
3
LEFT PARATHYROID LONG

Patient Course





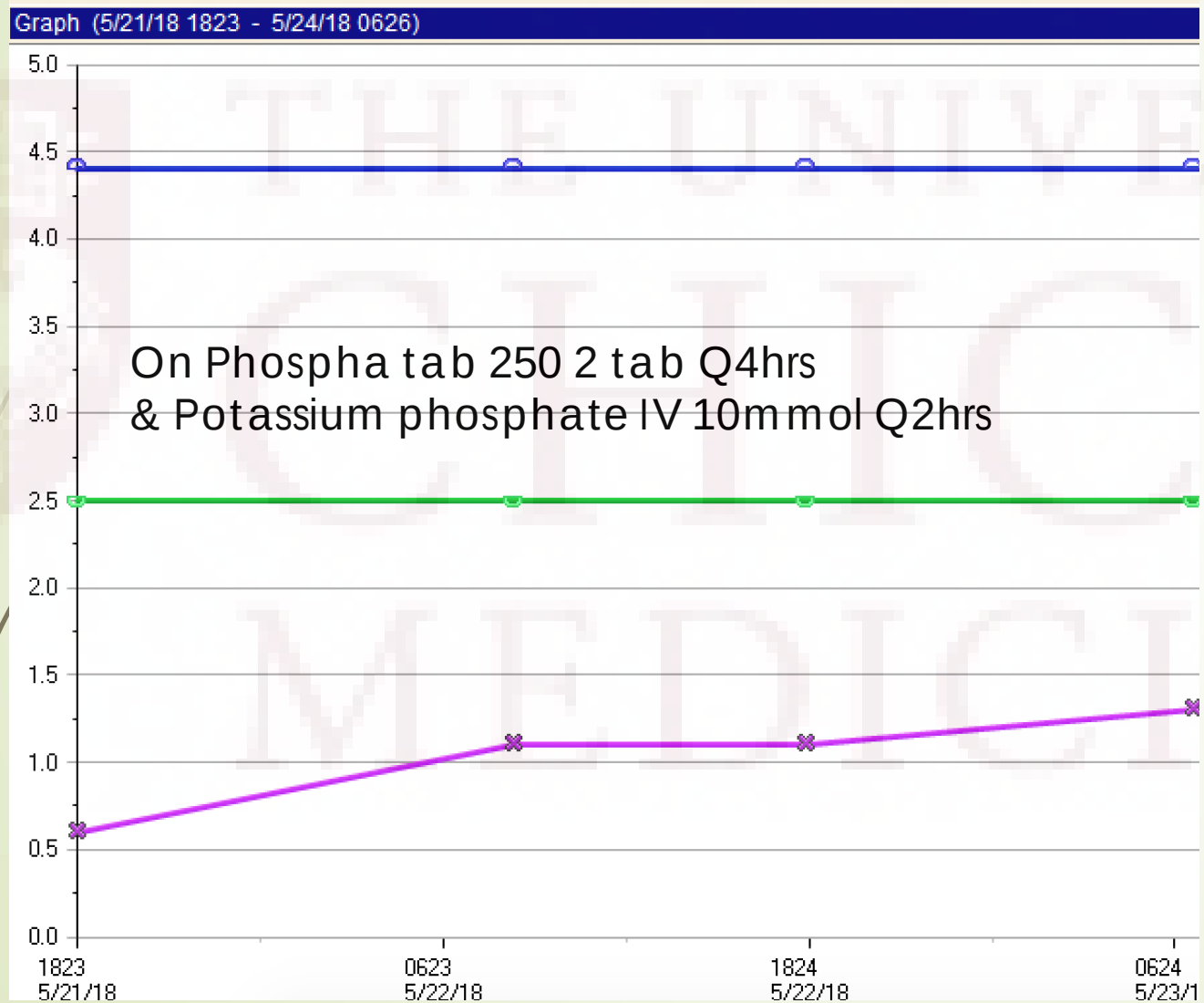
PO:
Phospha tab: 250mg elemental phosphorus, 298mg Na, 45mg K

IV:
10 mmol phosphate=310mg phosphorus

**Each 3mmol IV phosphate provides 4.4 mEq potassium

Getting 5220mg el iP/d

Patient Course



5/23: Started her on 0.25mcg BID calcitriol, asked for 1, 25 vit D level

Major causes of hypophosphatemia

Internal redistribution
Increased insulin secretion, particularly during refeeding
Acute respiratory alkalosis
Hungry bone syndrome
Decreased intestinal absorption
Inadequate intake
Inhibition of phosphate absorption (eg, antacids, phosphate binders, niacin)
Steatorrhea and chronic diarrhea
Vitamin D deficiency or resistance
Increased urinary excretion
Primary and secondary hyperparathyroidism
Vitamin D deficiency or resistance
Hereditary hypophosphatemic rickets
Oncogenic osteomalacia
Fanconi syndrome
Other - acetazolamide, tenofovir, IV iron, chemotherapeutic agents
Removal by renal replacement therapies

Graphic 71616 Version 9.0

Major causes of hypophosphatemia

Internal redist
Increased ins etion, ticularly during refeeding
Acute respira y alka
Hungry bone sy
Decreased intestinal absorption
Inadequate intake
Inhibition of phosphate absorption (eg, antacids, phosphate binders, niacin)
Steatorrhea and chronic diarrhea
Vitamin D deficiency or resistance
Increased urinary excretion
Primary and secondary hyperparathyroidism
Vitamin D deficiency or resistance
Hereditary hypophosphatemic rickets
Oncogenic osteomalacia
Fanconi syndrome
Other - acetazolamide, tenofovir, IV iron, chemotherapeutic agents
Removal by rep replacement therapies

Graphic 71616 Versio

Major causes of hypophosphatemia

Internal redist
Increased ins etion, ticularly during refeeding
Acute respira y alka
Hungry bone sy
Decreased intestinal absorption
Inadequate intake
Inhibition of phosphate absorption (eg, antacids, phosphate binders, niacin)
Steatorrhea and chronic diarrhea
Vitamin D deficiency or resistance
Increased urinary excretion
Primary and secondary hyperparathyroidism
Vitamin D deficiency or resistance
Hereditary hypophosphatemic rickets
Oncogenic osteomalacia
Fanconi syndrome
Other - acetazolamide, tenofovir, IV iron, chemotherapeutic agents
Removal by rena replacement therapies

Graphic 71616 Version

Hereditary hypophosphatemic rickets: hypophosphatemia, rickets or osteomalacia at an early age

Fanconi syndrome: defect in proximal phosphate resorption but also with:

- -glucosuria
- -hypouricemia
- -aminoaciduria
- -hyperchloremic met acidosis due to bicarb wasting

Major causes of hypophosphatemia

Internal redist
Increased ins etion, ticularly during refeeding
Acute respira y alka
Hungry bone sy
Decreased intestinal absorption
Inadequate intake
Inhibition of phosphate absorption (eg, antacids, phosphate binders, niacin)
Steatorrhea and chronic diarrhea
Vitamin D deficiency or resistance
Increased urinary excretion
Primary and secondary hyperparathyroidism
Vitamin D deficiency or resistance
Hereditary hypophosphatemic rickets
Oncogenic osteomalacia
Fanconi syndrome
Other - acetazolamide, tenofovir, IV iron, chemotherapeutic agents
Removal by rena replacement therapies

Graphic 71616 Version

Hereditary hypophosphatemic rickets: hypophosphatemia, rickets or osteomalacia at an early age

Fanconi syndrome: defect in proximal phosphate resorption but also with:

- -glucosuria
- -hypouricemia
- -aminoaciduria
- -hyperchloremic met acidosis due to bicarb wasting

Major causes of hypophosphatemia

Internal redist
Increased ins etion, ticularly during refeeding
Acute respira y alka
Hungry bone sy
Decreased intestinal absorption
Inadequate intake
Inhibition of phosphate absorption (eg, antacids, phosphate binders, niacin)
Steatorrhea and chronic diarrhea
Vitamin D deficiency or resistance
Increased urinary excretion
Primary and secondary hyperparathyroidism
Vitamin D deficiency or resistance
Hereditary hypophosphatemic rickets
Oncogenic osteomalacia
Fanconi syndrome
Other - acetazolamide, tenofovir, IV iron, chemotherapeutic agents
Removal by renal replacement therapies

Graphic 71616 Version

Hereditary hypophosphatemic rickets: hypophosphatemia, rickets or osteomalacia at an early age

Fanconi syndrome: defect in proximal phosphate resorption but also with:

- -glucosuria
- -hypouricemia
- -aminoaciduria
- -hyperchloremic met acidosis due to bicarb wasting

Oncogenic osteomalacia: Mesenchymal tumors that produce FGF23 and other phosphaturic proteins

injectafer® ferric carboxymaltose injection

Important Safety Information
Prescribing Information
Patient Site

Sign Up for Updates

Search...

UNDERSTANDING IDA | CHOOSING INJECTAFER | EFFICACY & SAFETY | REIMBURSEMENT & PATIENT SAVINGS

FOR THE TREATMENT OF IRON DEFICIENCY ANEMIA (IDA) IN ADULT PATIENTS WHO HAVE INTOLERANCE TO ORAL IRON, HAVE HAD UNSATISFACTORY RESPONSE TO ORAL IRON, OR HAVE NON-DIALYSIS-DEPENDENT CHRONIC KIDNEY DISEASE,

Only **Injectafer®** **(ferric carboxymaltose injection)** provides up to **1500 mg of iron** in just **2 administrations**,* separated by at least 7 days

*Two administrations of up to 750 mg each

Photos depict models, not actual patients or healthcare professionals.

Pt received Injectafer® 2 weeks prior

She had received FCM in the past without incident (Venofer®)

Netherlands
The Journal of Medicine

SPECIAL ARTICLE

Severe hypophosphataemia after intravenous iron administration

A. Blazevic, J. Hunze, J.M.M. Boots*

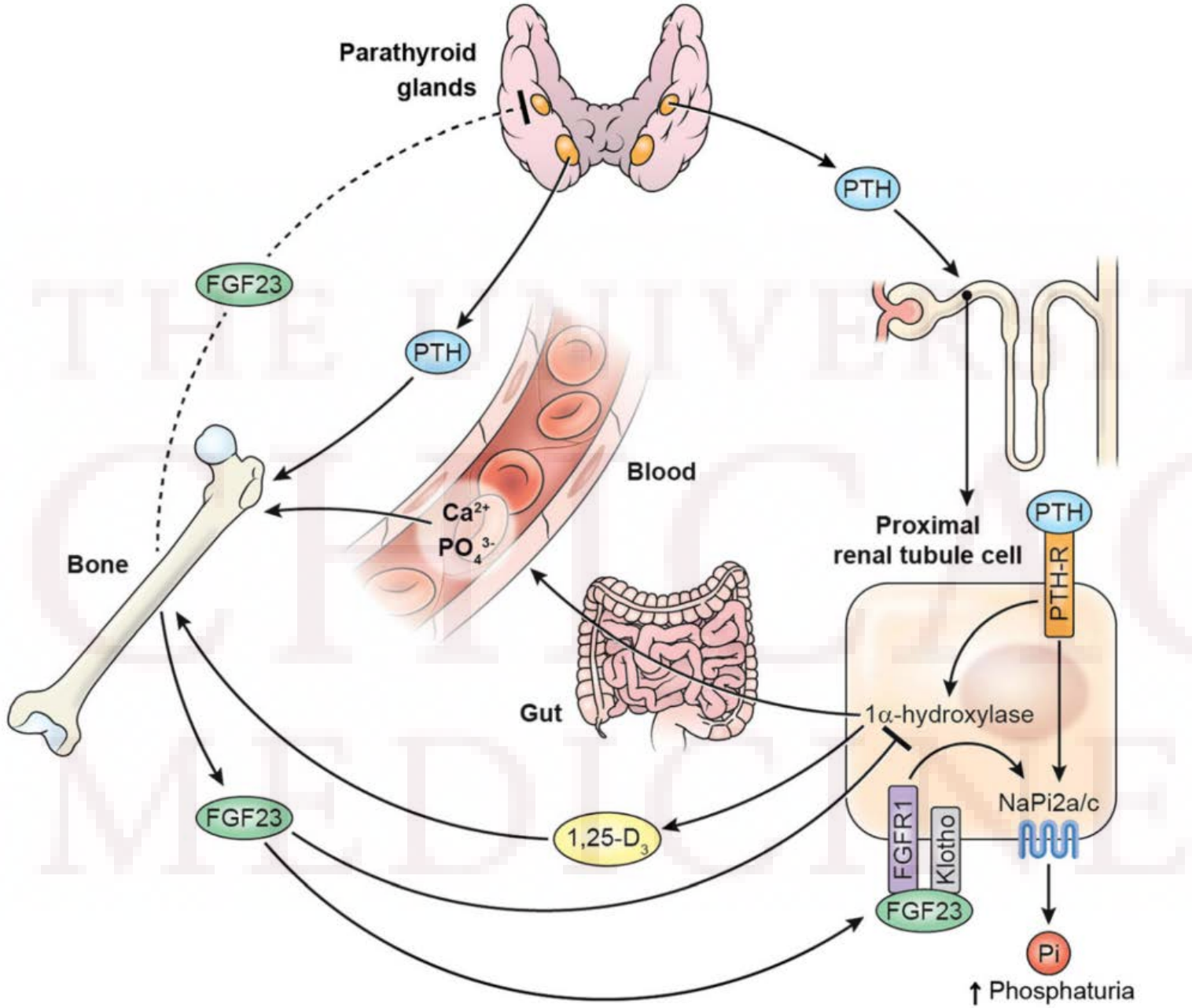
Department of Internal Medicine and Nephrology, Maasstad Hospital, the Netherlands,
*corresponding author: tel.: +31 (0)10-2911833, e-mail: BootsJ@maasstadziekenhuis.nl

IV Iron Has Been Associated with Transient Hypophosphatemia

- 3.8% of chronic kidney patients (not on HD) receiving IV iron showed a transient serum phosphate level decrease (level not "clinically important")
- Four cases were reported of severe and symptomatic hypophosphatemia after IV iron administration (Blazevic & Boots, 2014)
- Findings from case reports:
  - Hypophosphatemia from IV iron infusions can be severe, symptomatic and prolonged
  - 3 out of 4 cases had hyperpara (2 from vit D def); Case 2 did not have hyperpara but all 4 had inadequate phosphate excretion
  - Increased level of FGF23 thought to be mechanism

Fibroblast Growth Factor 23 (FGF23)

- Discovered when a paraneoplastic disease characterized by phosphaturia and hypophosphatemia resolved following the removal of a small mesenchymal tumor that secreted this factor (Meyer et al 1989, Cai et al 1994)
  - "rachitogenic substance"
- Elevated FGF23 found in: Autosomal dominant hypophosphatemic rickets (& in AR, X-linked), McCune-Albright syndrome, Jansen metaphyseal chrondroplasia, osteoglophonic dysplasia, tumor induced osteomalacia (TIO), & renal failure.
  - Search for "phosphatonin" in these diseases lead to discovery of FGF23
  - FGF23 identified in studying 4 families with AD hypophosphatemic rickets (ADHR) (ADHR Consortium, Nature, 2000)
  - FGF23 is confirmed "phosphatonin" that is also elevated in TIO (White, JCEM 2001)
- FGF23 directly down regulates renal 1-α-hydroxylase which decreases production of 1,25-vit D thereby decreasing intestinal phosphate and calcium absorption; FGF23 also directly induces phosphate urinary excretion



FGF23 secretion from bone osteocytes acts on the kidney to induce phosphaturia via NaPi 2a/c transporters similar to PTH

In contrast to PTH to induce 1a hydroxylase, FGF23 suppresses it thereby resulting in less active vit D

Vitamin D & PHPT

- Patients with PHPT convert more 25-vit OH to 1,25 vit D than normal individuals
- Serum concentrations of 1,25 dihydroxyvitamin D may be at upper limits of normal or elevated (measurement not needed for diagnosis however)
- 1,25 vit D did not result in our patient (insufficient material), however, we suspect it was likely very low

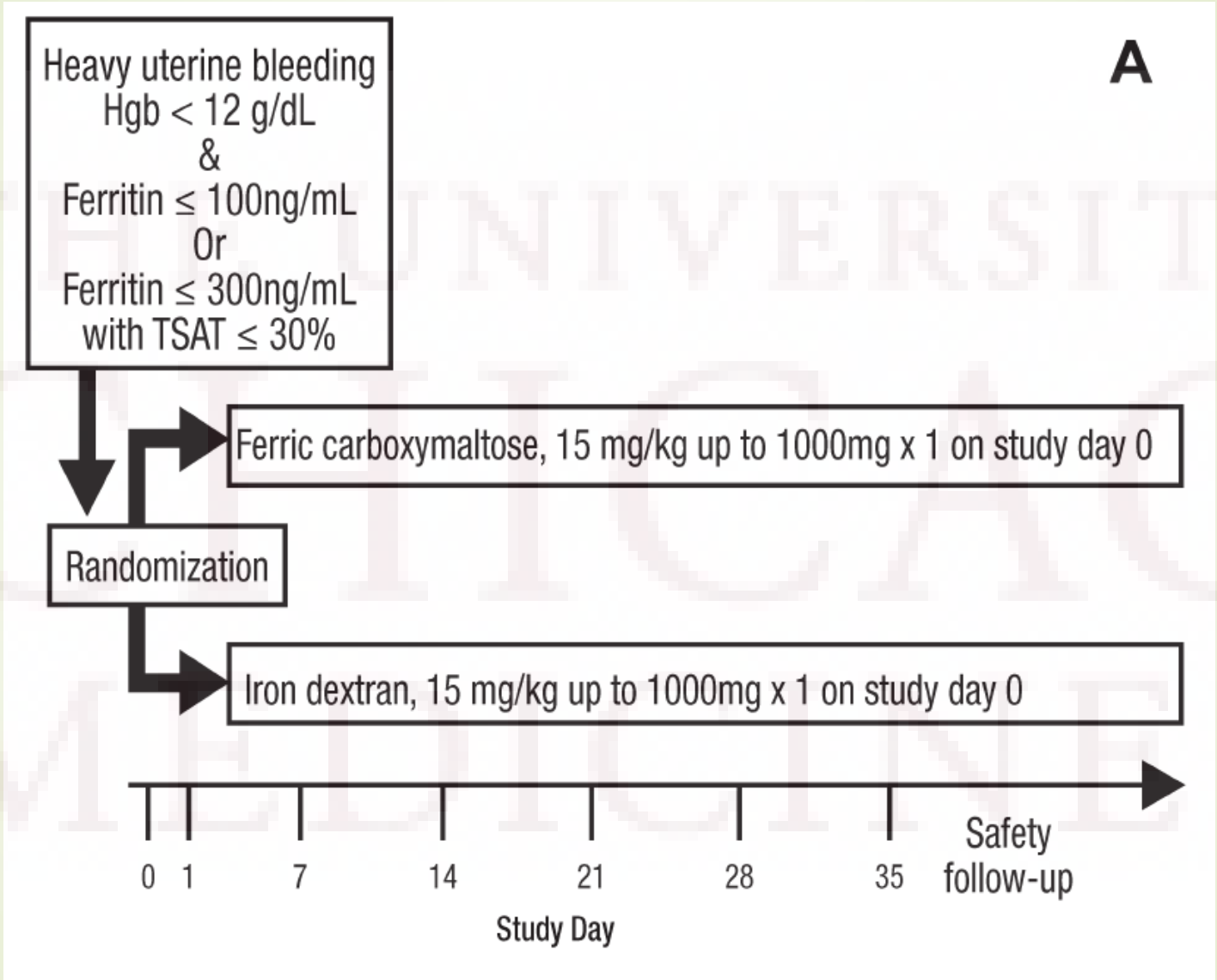
ORIGINAL ARTICLE

JBMR®

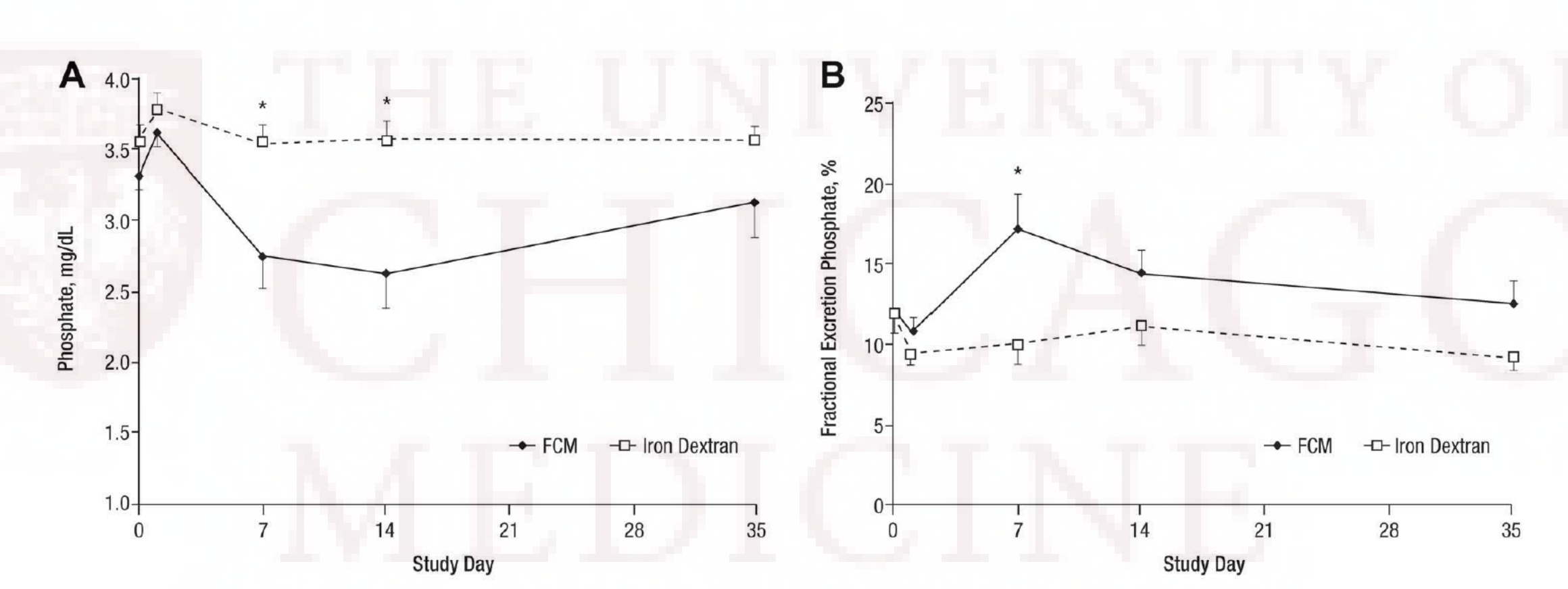
Effects of Iron Deficiency Anemia and Its Treatment on Fibroblast Growth Factor 23 and Phosphate Homeostasis in Women

Myles Wolf,[1] Todd A Koch,[2] and David B Bregman[2,3]

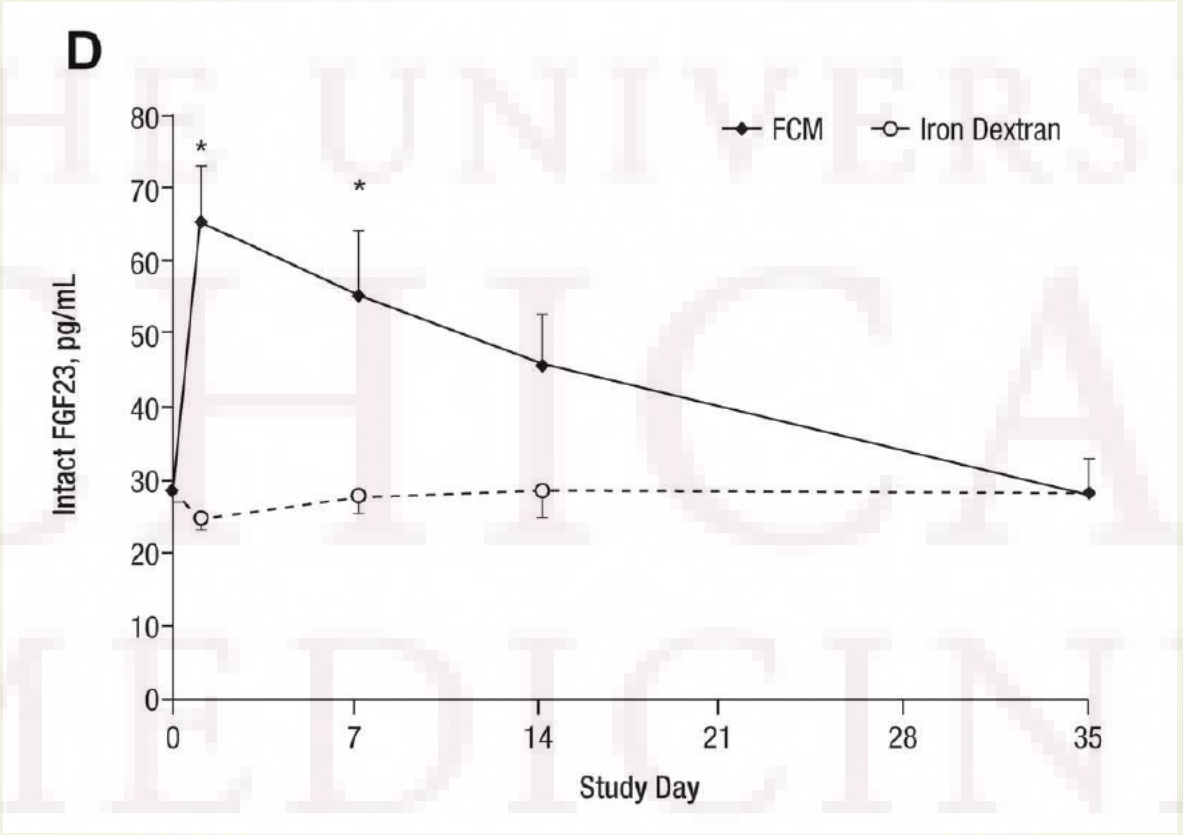
[1]Division of Nephrology and Hypertension, University of Miami Miller School of Medicine, Miami, FL, USA
[2]Luitpold Pharmaceuticals, Inc., Norristown, PA, USA
[3]Department of Pathology, Albert Einstein College of Medicine, New York, NY, USA


A
Heavy uterine bleeding
Hgb < 12 g/dL
&
Ferritin ≤ 100ng/mL
Or
Ferritin ≤ 300ng/mL
with TSAT ≤ 30%
Ferric carboxymaltose, 15 mg/kg up to 1000mg x 1 on study day 0
Randomization
Iron dextran, 15 mg/kg up to 1000mg x 1 on study day 0
0
1
7
14
21
28
35
Safety follow-up
Study Day

Effect of FCM and Iron Dextran on Phosphate and its Excretion



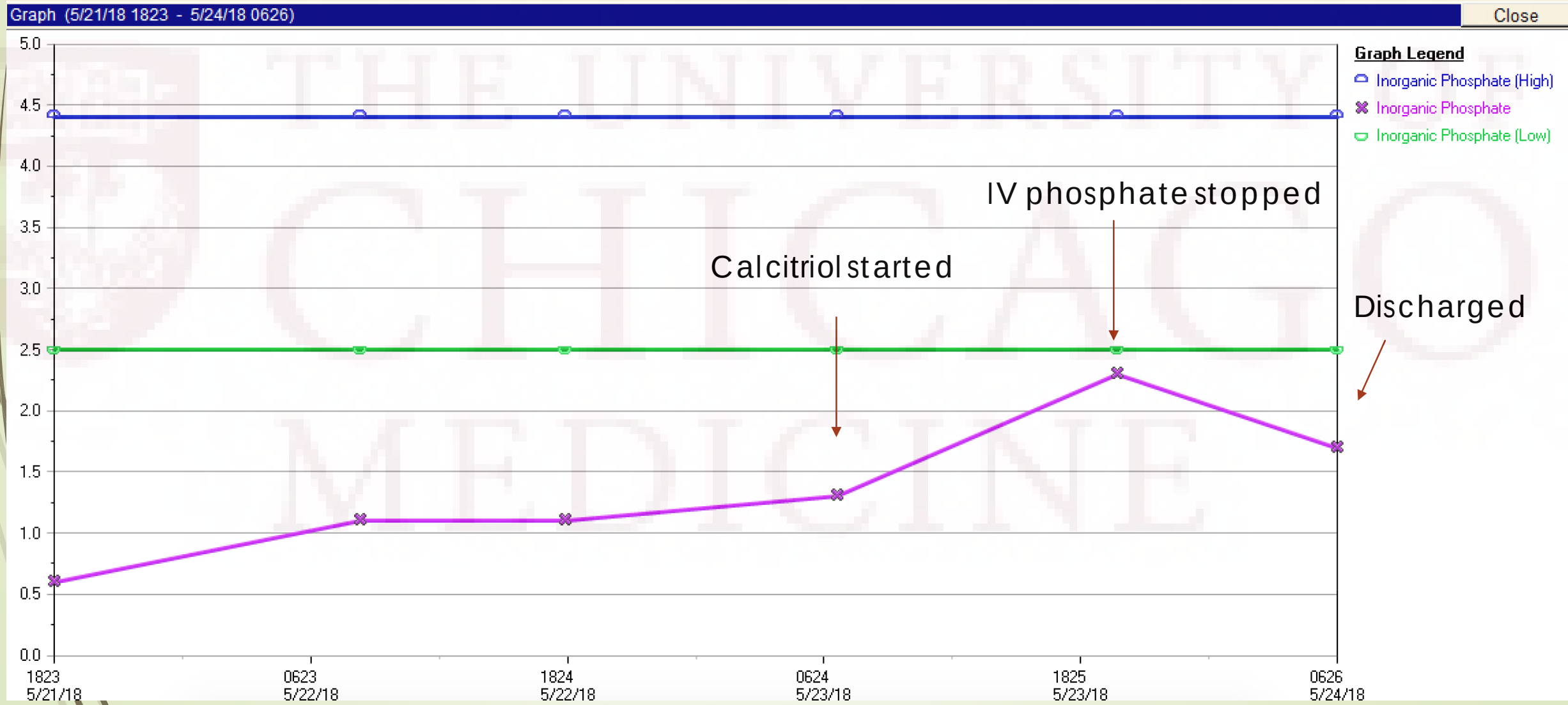
Effect of FCM and Iron Dextran on FGF23

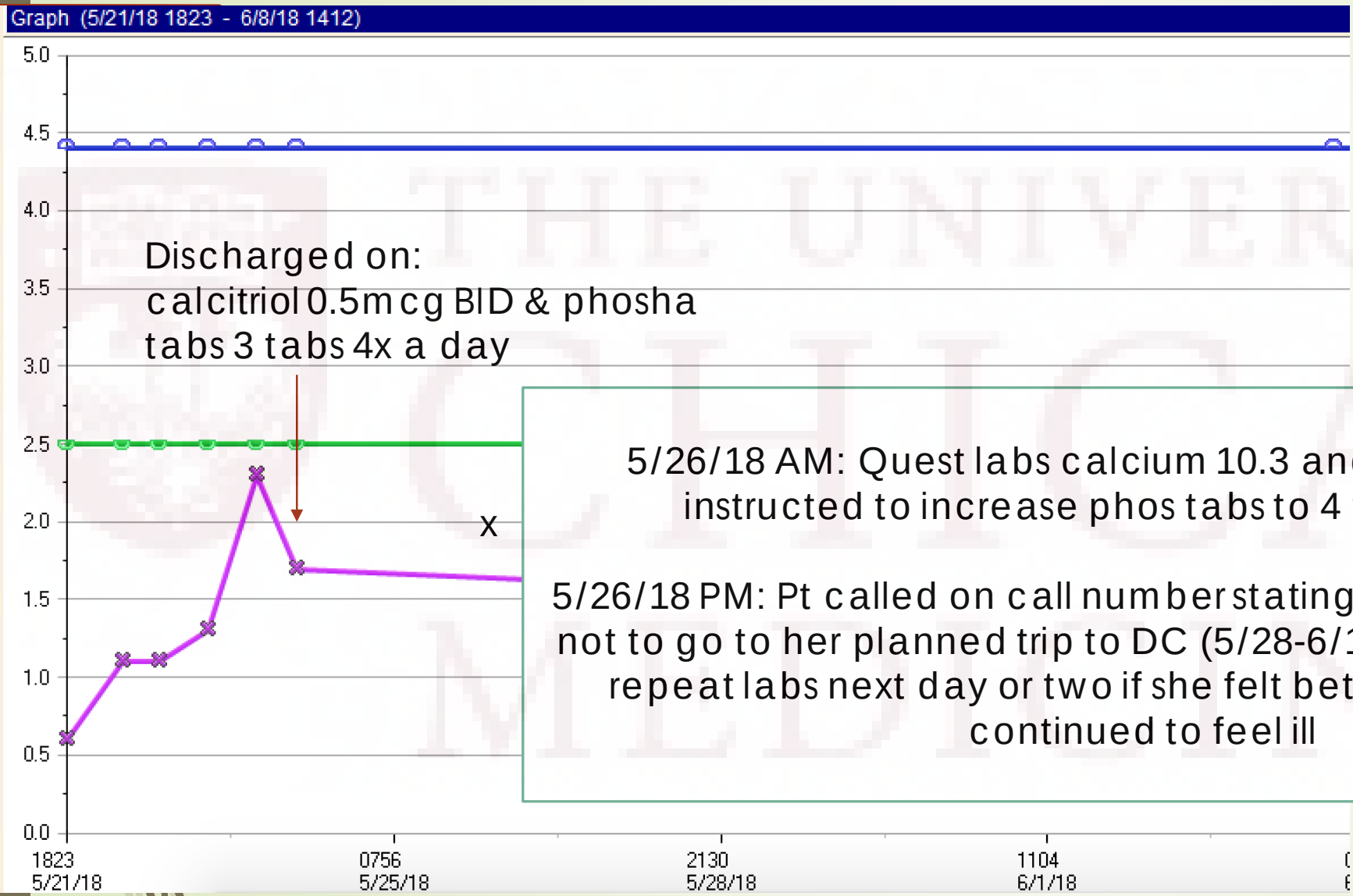


Conclusions from this study

- FCM but not iron dextran induced a significant increase in intact FGF23 by 24 hours, which was associated with an increase in fractional excretion of phosphate and decrease in serum phosphate, 1, 25 Vit D & calcium
  - Level of FGF23 was increased to levels seen in renal failure or hereditary rachitic diseases
- Additional research is needed into mechanisms of FGF23 synthesis and degradation and the role of iron deficiency and its treatment

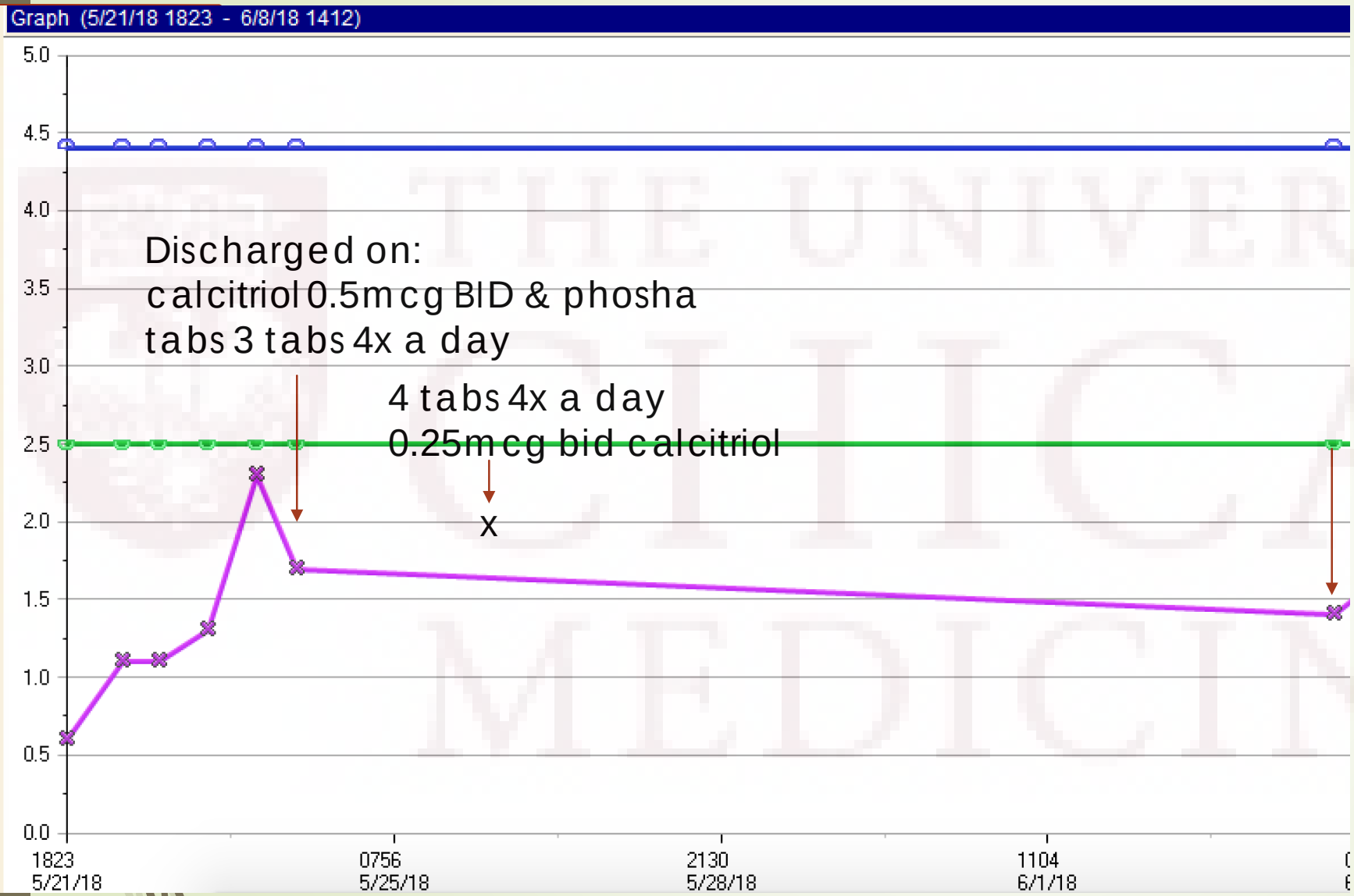
Patient Course

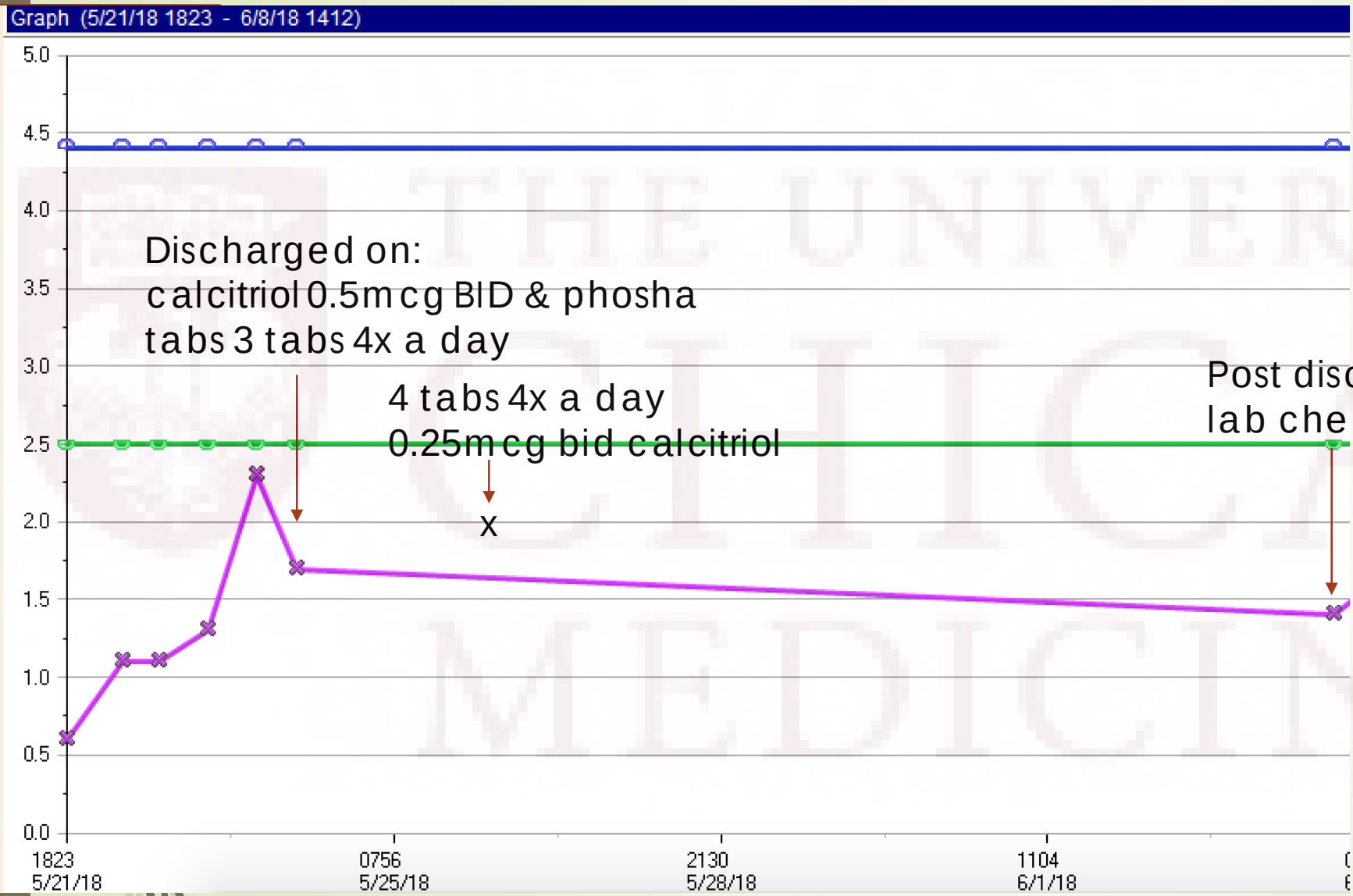


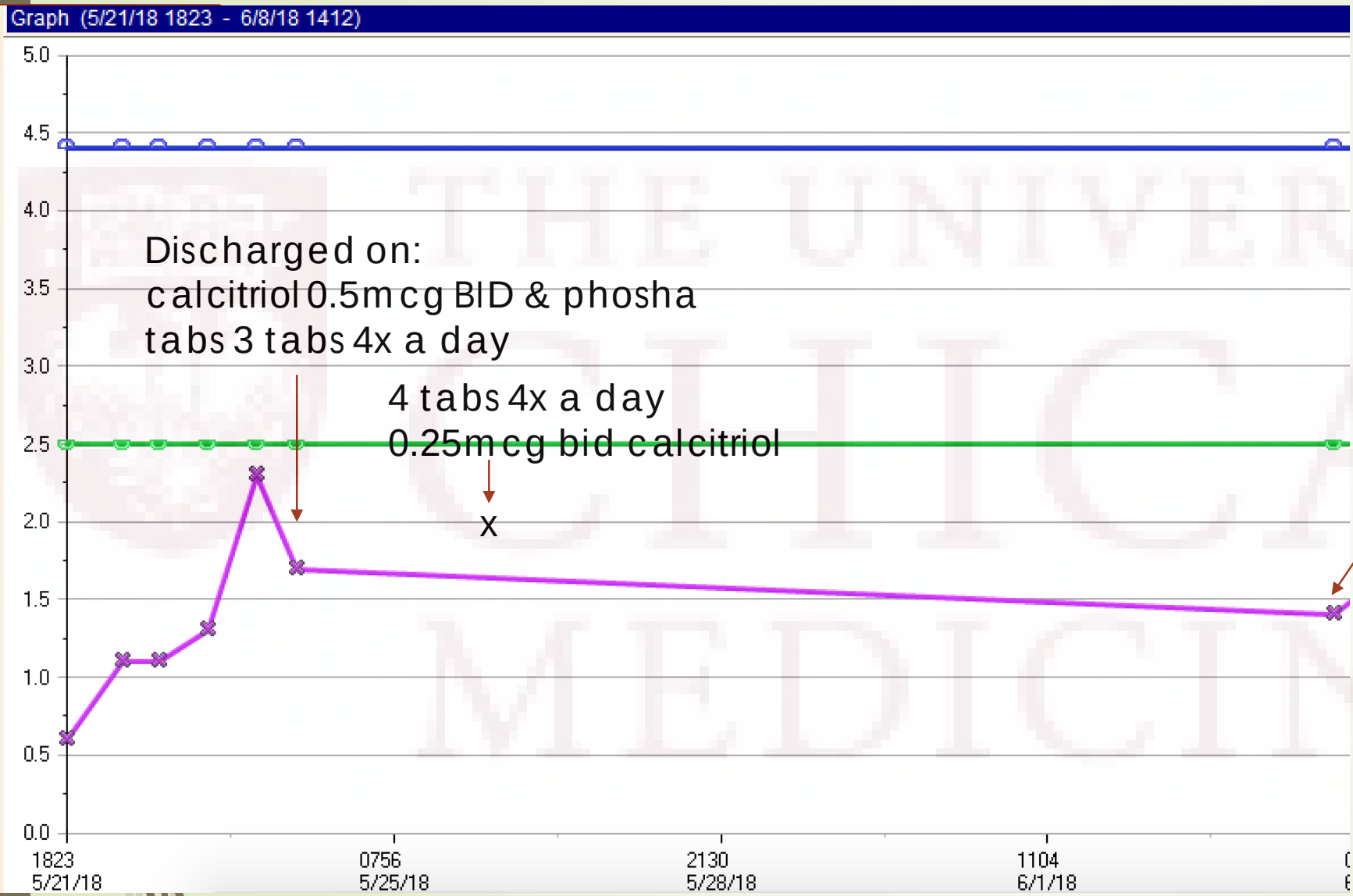


5/26/18 AM: Quest labs calcium 10.3 and phosphate 2.0; instructed to increase phos tabs to 4 tabs 4x a day

5/26/18 PM: Pt called on call number stating she felt ill. Instructed not to go to her planned trip to DC (5/28-6/1) and to come in for repeat labs next day or two if she felt better or to ED now if continued to feel ill


Graph (5/21/18 1823 - 6/8/18 1412)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Discharged on:
calcitriol 0.5mcg BID & phosha tabs 3 tabs 4x a day
4 tabs 4x a day
0.25mcg bid calcitriol
x
1823
5/21/18
0756
5/25/18
2130
5/28/18
1104
6/1/18


Graph (5/21/18 1823 - 6/8/18 1412)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Discharged on:
calcitriol 0.5mcg BID & phosha tabs 3 tabs 4x a day
4 tabs 4x a day
0.25mcg bid calcitriol
x
Post discharge lab check
1823
5/21/18
0756
5/25/18
2130
5/28/18
1104
6/1/18


Graph (5/21/18 1823 - 6/8/18 1412)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1823
5/21/18
0756
5/25/18
2130
5/28/18
1104
6/1/18
Discharged on:
calcitriol 0.5mcg BID & phosha tabs 3 tabs 4x a day
4 tabs 4x a day
0.25mcg bid calcitriol
x
Increase to 5 tabs 4x a day, calcitriol increased to 0.5mcg BID


Graph (5/21/18 1823 - 6/8/18 1412)
Close
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1823
5/21/18
0756
5/25/18
2130
5/28/18
1104
6/1/18
0038
6/5/18
1412
6/8/18
Graph Legend
Inorganic Phosphate (Hi
Inorganic Phosphate
Inorganic Phosphate (Lo
3 tabs 4x a day
0.25mcg bid calcitriol
4 tabs 4x a day
0.25mcg bid calcitriol
x
5 tabs 4x a day,
calcitriol 0.5mcg BID
Clinic visit:
Reduce to 3
tabs 4x day,
continue
current
calcitriol

Continued Course

- 6/13/18: Repeat FGF23 from 6/8 clinic visit resulted and showed it was back down to normal (277-> 150 (nml <180); Left voicemail for Pt to stop calcitriol
  - Of note PTH is even higher now at 250 (from 103), Ca 9.5, Phos 3.3
- She was due for repeat labs today

Conclusions

- Primary hyperparathyroidism presents with an elevated calcium and PTH; Sestamibi scan is reserved for Pts who will be considered for parathyroidectomy
- Causes of hypophosphatemia can be divided into:
  - Increased phosphate redistribution
  - Decreased phosphate absorption
  - Increased phosphate excretion
- Low 1,25 vit D in the setting of PHPT is unusual, and should prompt further evaluation for a contributing factor for phosphate excretion (or a severely low phosphate <1.0 mg/dL)
- Isolated urinary phosphate wasting is rare but can be observed in patients receiving certain forms of ferric carboxymaltose therapy
  - The mechanism appears to be increased FGF23 which reduces 1,25 vit D activity by inhibition of 1α-hydroxylase which causes a reduction of phosphate absorption and by FGF23 mediated phosphaturia

References

- Meyer, RA, Meyer MH, Gray RW: Parabiosis suggests a humoral factor is involved in X linked hypophosphatemia in mice. 1989. J Bone Miner Res 4:493-500
- Cai, Q, Hodgson SF, Kao PC. Brief report: Inhibition of renal phosphate transport by a tumor product in a patient with oncogenic osteomalacia. 1994. NEJM 330:1645-1649.
- THE ADHR CONSORTIUM: Autosomal dominant hypophosphatemic rickets is associated with mutations in FGF-23. Nature Genet 26:345–348, 2000
- White, KE,, Jonnson KB, Carn, G. The ADHR gene is a secreted polypeptide over expressed by tumors that cause phosphate wasting. 2001. JCEM 86:497-500.
- S.C. Schiavi and R. Kumar. The phosphatonin pathway: New insights in phosphate homeostasis. Kidney International, Vol. 65 (2004), pp. 1–14
- Myles Wolf, Todd A Koch, and David B Bregman. Effects of Iron Deficiency Anemia and Its Treatment on Fibroblast Growth Factor 23 and Phosphate Homeostasis in Women. Journal of Bone and Mineral Research, Vol. 28, No. 8, August 2013, pp 1793–1803
- A. Blazevic, J. Hunze, J.M.M. Boots. Severe hypophosphataemia after intravenous iron administration. The Netherlands J of Med. Jan 2014 (72):1
- Jenny E. Blau & Michael T. Collins. The PTH-Vitamin D-FGF23 axis. Rev Endocr Metab Disord Aug 2015

IV Iron Has Been Associated with Transient Hypophosphatemia

- Case 1: 45 Asian F with T1DM, ESRD s/p kidney Tx, iron def anemia from heavy menstrual bleeding (endometrial polyp). She received 1g infusion of Ferinject with phos of 0.25 mml/L) and high fractional excretion of phos. She was given IV phos and sent on oral supplementation. Readmited with n/vertigo/fatigue low phos again, found to have elevated FGF23 (202, <125RU/mL), Rx 6 wks.
- Case 2: 42 Caucasian female with SLE, APL syndrome, and iron def anemia due to heavy menstrual bleeding. Received 3 infusions at 6 wk intervals of ferric carboxymaltose. 3d after last infusion developed low phos (0.32 mml/L) and high phos excretion. Rx 4 wks and increased protein diet. Got Venofer iron and happened again.
- Case 3: 33yo Hindu F w Hx of Roux-N-Y gastric bypass, iron def anemia from heavy bleeding, vit D def, 2ry hyperparathyroidism, received 2 x 1g infusions of ferric carboxymaltose and developed low phos -> Rx 2 months
- Case 4: 47yo Caribbean F with Hx Graves dz, anemia due to fibroid received 1g ferric carboxymaltose x 3 and developed severe hypophosphatemia (0.28 mml/L). Rx 3 months.