A young man with hypertension, renal failure, hypercalcemia, and “no diagnosis”

Matt Ettleson, M.D.*

Endorama

October 24, 2019

M170

AT THE FOREFRONT
UChicago Medicine

TELETYPE URGENT

TO: SAC, SAN FRANCISCO (9-2296)

FROM: DIRECTOR, FBI (9-49911)

UNSUB; "VALLEJO TIMES-HAROLD," VALLEJO, CALIFORNIA-VICTIM,

EXTORTION.

REURTEL NOVEMBER SIX LAST.

LATENT FINGERPRINTS AND IMPRESSIONS THIS CASE NOT IDENTICAL

FINGERPRINTS OF [redacted] BORN [redacted]

[redacted] FBI NUMBER [redacted]

[redacted] BORN [redacted] FBI NUMBER

[redacted] OR [redacted] BORN [redacted]

[redacted] NO PALM PRINTS HERE FOR THESE INDIVIDUALS.

[redacted] AND [redacted] MAY BE IDENTICAL INDIVIDUALS NAMED RETEL.

NO FINGERPRINTS OUR FILES FOR [redacted]

GEG/lvc

Learning Objectives

- Briefly review the diagnosis and evaluation [redacted]
- Explain the mechanism of [redacted] and other [redacted]
- Discuss the fundamentals of [redacted]
- Identify [redacted] for [redacted]
- Speculate on role of [redacted] in this case [if time allows]

22 year old man presents with headache, vision changes, and progressive lower extremity weakness.

HPI: a chronology

2007

Presents with abdominal pain, possibly appendicitis. An abdominal CT scan demonstrates borderline prominent mesenteric lymph nodes in the RLQ which is consistent with mesenteric adenitis. No secondary signs of appendicitis.

16		
21.6		303

139	103	23	115
5.1	23	0.5	

calcium 9.9
albumin ?

Abdominal pain resolved. No further work up at that time.

HPI: a chronology

2016

Presents with R inguinal pain. He has multiple palpable inguinal lymph nodes. He undergoes CT imaging, which demonstrates lymphadenopathy (again) and ascites.

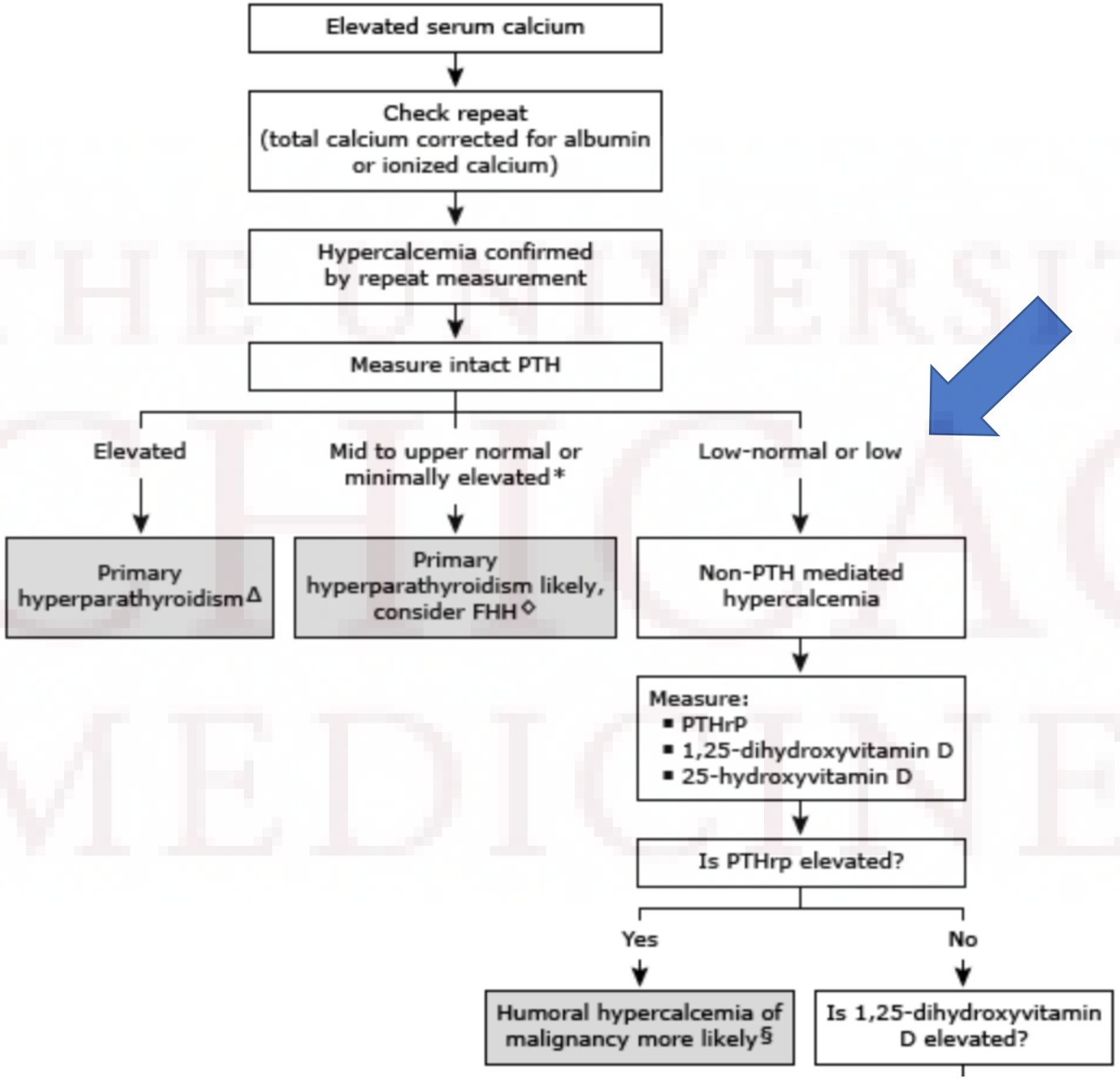
9.1	14	211

141	104	19	83
3.8	32	**2.1**	

calcium **12.8**
albumin 4.2
protein 7.0
alk phos 61
AST 15
ALT 11
mag 2.1
LDH 128

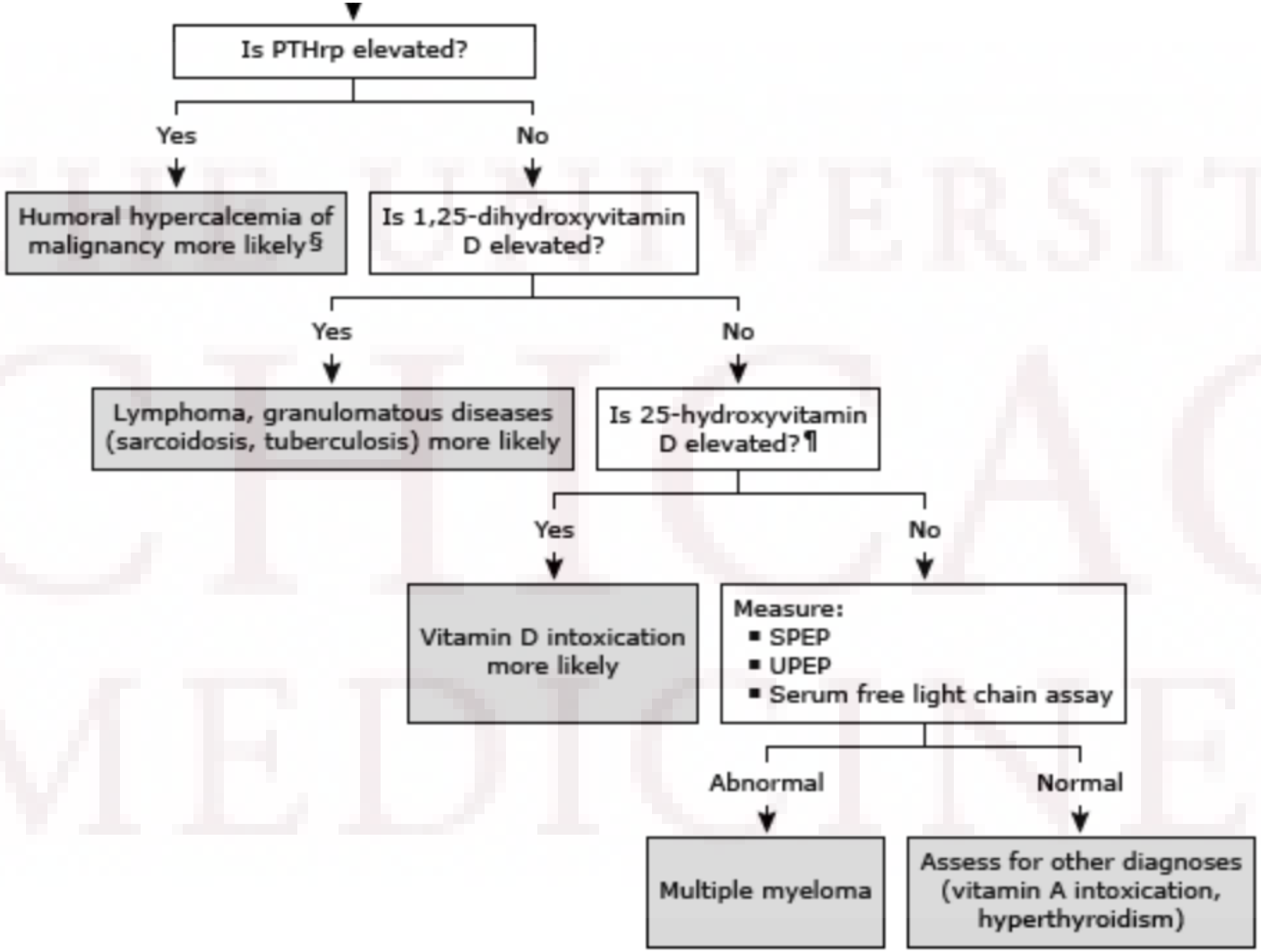
PTH **1.2**

review



"Diagnostic approach to hypercalcemia." Uptodate.com

review



“Diagnostic approach to hypercalcemia.” Uptodate.com

HPI: a chronology

2016

Presents with R inguinal pain. He has multiple palpable inguinal lymph nodes. He undergoes CT imaging, which demonstrates lymphadenopathy (again) and ascites.

9.1	14	211

141	104	19	83
3.8	32	**2.1**	

calcium **12.8**
albumin 4.2
protein 7.0
alk phos 61
AST 15
ALT 11
mag 2.1
LDH 128

PTH **1.2**
Vitamin D 25-OH 15.8
Vitamin D 1, 25-OH 68.5 (cr 1.6)

TSH 4.0
PTH-rp: **3.1**
SPEP: normal serum protein pattern, normal IF

HPI: a chronology

2016

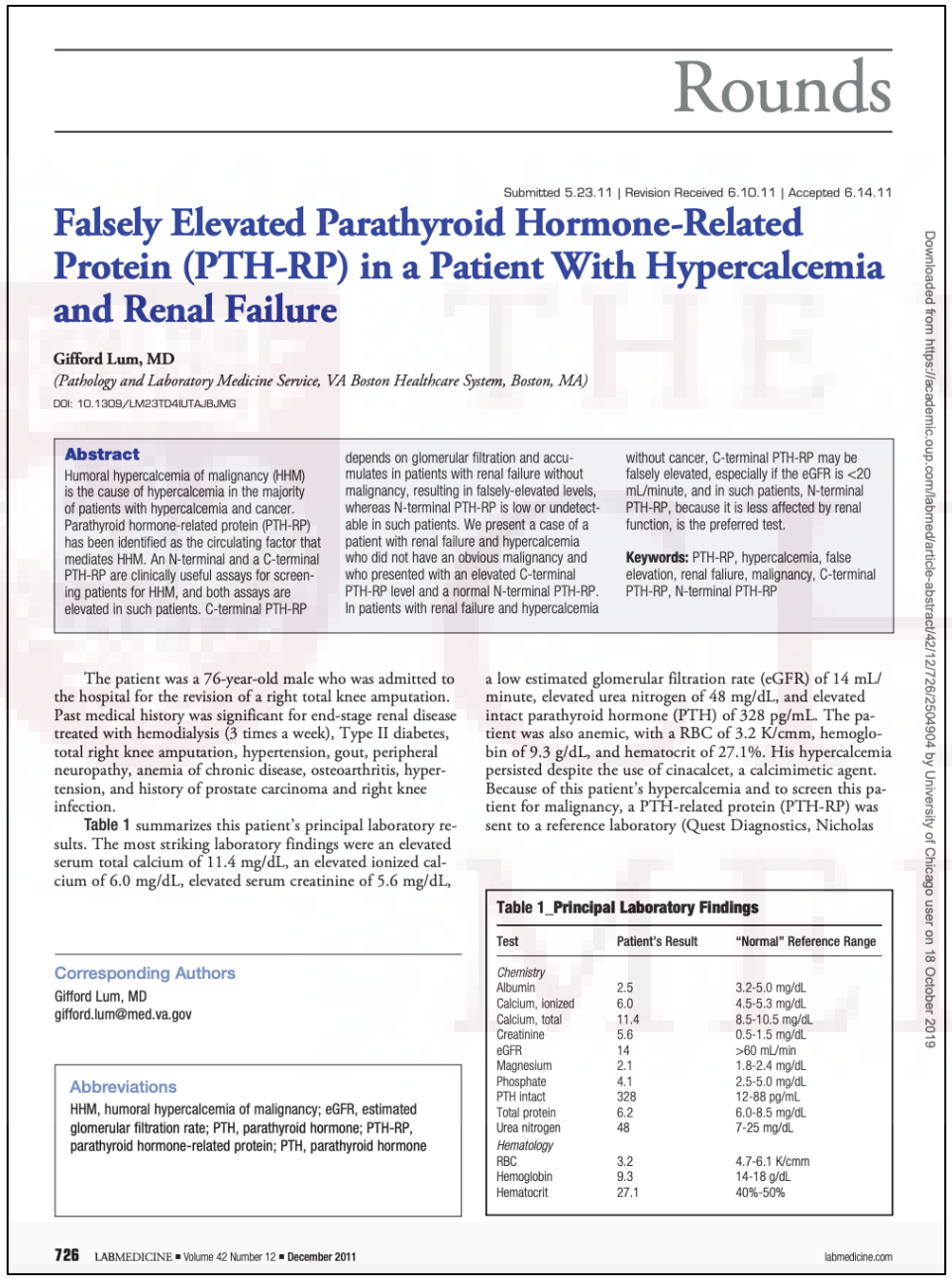
calcium **12.8**
albumin 4.2
protein 7.0
alk phos 61
AST 15
ALT 11
mag 2.1
LDH 128

PTH **1.2** →

TSH 4.0
Vitamin D 1, 25-OH 68.5
Vitamin D 25-OH 15.8
PTH-rp: **3.1**

How do you interpret these findings in the setting of the patient's acute kidney injury?

What are your next steps?



Rounds

Submitted 5.23.11 | Revision Received 6.10.11 | Accepted 6.14.11

Falsely Elevated Parathyroid Hormone-Related Protein (PTH-RP) in a Patient With Hypercalcemia and Renal Failure

Gifford Lum, MD

(Pathology and Laboratory Medicine Service, VA Boston Healthcare System, Boston, MA)

DOI: 10.1309/LM23TD4IUTAJBJMG

Abstract

Humoral hypercalcemia of malignancy (HHM) is the cause of hypercalcemia in the majority of patients with hypercalcemia and cancer. Parathyroid hormone-related protein (PTH-RP) has been identified as the circulating factor that mediates HHM. An N-terminal and a C-terminal PTH-RP are clinically useful assays for screening patients for HHM, and both assays are elevated in such patients. C-terminal PTH-RP depends on glomerular filtration and accumulates in patients with renal failure without malignancy, resulting in falsely-elevated levels, whereas N-terminal PTH-RP is low or undetectable in such patients. We present a case of a patient with renal failure and hypercalcemia who did not have an obvious malignancy and who presented with an elevated C-terminal PTH-RP level and a normal N-terminal PTH-RP. In patients with renal failure and hypercalcemia without cancer, C-terminal PTH-RP may be falsely elevated, especially if the eGFR is <20 mL/minute, and in such patients, N-terminal PTH-RP, because it is less affected by renal function, is the preferred test.

Keywords: PTH-RP, hypercalcemia, false elevation, renal failure, malignancy, C-terminal PTH-RP, N-terminal PTH-RP

The patient was a 76-year-old male who was admitted to the hospital for the revision of a right total knee amputation. Past medical history was significant for end-stage renal disease treated with hemodialysis (3 times a week), Type II diabetes, total right knee amputation, hypertension, gout, peripheral neuropathy, anemia of chronic disease, osteoarthritis, hypertension, and history of prostate carcinoma and right knee infection.

Table 1 summarizes this patient's principal laboratory results. The most striking laboratory findings were an elevated serum total calcium of 11.4 mg/dL, an elevated ionized calcium of 6.0 mg/dL, elevated serum creatinine of 5.6 mg/dL, a low estimated glomerular filtration rate (eGFR) of 14 mL/minute, elevated urea nitrogen of 48 mg/dL, and elevated intact parathyroid hormone (PTH) of 328 pg/mL. The patient was also anemic, with a RBC of 3.2 K/cmm, hemoglobin of 9.3 g/dL, and hematocrit of 27.1%. His hypercalcemia persisted despite the use of cinacalcet, a calcimimetic agent. Because of this patient's hypercalcemia and to screen this patient for malignancy, a PTH-related protein (PTH-RP) was sent to a reference laboratory (Quest Diagnostics, Nicholas

Table 1_Principal Laboratory Findings

Test	Patient's Result	"Normal" Reference Range
Chemistry		
Albumin	2.5	3.2-5.0 mg/dL
Calcium, ionized	6.0	4.5-5.3 mg/dL
Calcium, total	11.4	8.5-10.5 mg/dL
Creatinine	5.6	0.5-1.5 mg/dL
eGFR	14	>60 mL/min
Magnesium	2.1	1.8-2.4 mg/dL
Phosphate	4.1	2.5-5.0 mg/dL
PTH intact	328	12-88 pg/mL
Total protein	6.2	6.0-8.5 mg/dL
Urea nitrogen	48	7-25 mg/dL
Hematology		
RBC	3.2	4.7-6.1 K/cmm
Hemoglobin	9.3	14-18 g/dL
Hematocrit	27.1	40%-50%

Corresponding Authors

Gifford Lum, MD

gifford.lum@med.va.gov

Abbreviations

HHM, humoral hypercalcemia of malignancy; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone; PTH-RP, parathyroid hormone-related protein; PTH, parathyroid hormone

PTH-rp is widely expressed in normal and malignant tissues.

Most labs screen for C-terminal PTH-rp levels because it is more stable, but clearance depends on GFR.

PTH-rp can be falsely elevated in patients with renal failure without malignancy.

Laboratory Medicine, Volume 42, Issue 12, December 2011, Pages 726–728.

Vitamin D-Mediated Hypercalcemia: Mechanisms, Diagnosis, and Treatment

Peter J. Tebben, Ravinder J. Singh, and Rajiv Kumar

Divisions of Endocrinology (P.J.T., R.K.) and Nephrology and Hypertension (R.K.), and Departments of Pediatric and Adolescent Medicine (P.J.T.), Internal Medicine (P.J.T., R.K.), Laboratory Medicine and Pathology (R.J.S.), and Biochemistry in Molecular Biology (R.K.), Mayo Clinic College of Medicine, Rochester, Minnesota 55905

Hypercalcemia occurs in up to 4% of the population in association with malignancy, primary hyperparathyroidism, ingestion of excessive calcium and/or vitamin D, ectopic production of 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], and impaired degradation of 1,25$(OH)_2$D. The ingestion of excessive amounts of vitamin D_3 (or vitamin D_2) results in hypercalcemia and hypercalciuria due to the formation of supraphysiological amounts of 25-hydroxyvitamin D [25(OH)D] that bind to the vitamin D receptor, albeit with lower affinity than the active form of the vitamin, 1,25$(OH)_2$D, and the formation of 5,6-*trans* 25(OH)D, which binds to the vitamin D receptor more tightly than 25(OH)D. In patients with granulomatous disease such as sarcoidosis or tuberculosis and tumors such as lymphomas, hypercalcemia occurs as a result of the activity of ectopic 25(OH)D-1-hydroxylase (CYP27B1) expressed in macrophages or tumor cells and the formation of excessive amounts of 1,25$(OH)_2$D. Recent work has identified a novel cause of non-PTH-mediated hypercalcemia that occurs when the degradation of 1,25$(OH)_2$D is impaired as a result of mutations of the 1,25$(OH)_2$D-24-hydroxylase cytochrome P450 (CYP24A1). Patients with biallelic and, in some instances, monoallelic mutations of the *CYP24A1* gene have elevated serum calcium concentrations associated with elevated serum 1,25$(OH)_2$D, suppressed PTH concentrations, hypercalciuria, nephrocalcinosis, nephrolithiasis, and on occasion, reduced bone density. Of interest, first-time calcium renal stone formers have elevated 1,25$(OH)_2$D and evidence of impaired 24-hydroxylase-mediated 1,25$(OH)_2$D degradation. We will describe the biochemical processes associated with the synthesis and degradation of various vitamin D metabolites, the clinical features of the vitamin D-mediated hypercalcemia, their biochemical diagnosis, and treatment. (***Endocrine Reviews* 37: 521–547, 2016**)

I. Introduction

Hypercalcemia is encountered in 0.2 to 4% of community-dwelling subjects and hospital patients (1–8). The incidence of hypercalcemia is dependent upon whether serum calcium measurements are performed in free-living subjects in a community (1), in a hospital population (2–4), or in patients seen in an emergency department (5, 6, 8). Causes of hypercalcemia are listed in Table 1. Cancer-associated hypercalcemia and primary hyperparathyroidism are the most frequent causes of hypercalcemia. Their relative frequency depends upon whether the diagnosis of hypercalcemia is made in a hospital setting (where cancer-associated hypercalcemia is most frequent) or within the context of an outpatient practice (where the diagnosis of primary hyperparathyroidism predominates) (9).

From a diagnostic and therapeutic perspective, it is useful to think of hypercalcemia as a PTH-dependent or PTH-independent process. Increases in PTH concentrations in association with hypercalcemia indicate the presence of primary (10–14), tertiary (15–28), and post-transplant hyperparathyroidism (3, 21, 25, 26, 28–38) or severe neonatal hyperparathyroidism (associated with homozygous mutations of the calcium-sensing receptor) (39–42),

ISSN Print 0163-769X ISSN Online 1945-7189
Printed in USA

Received June 3, 2016. Accepted August 25, 2016.
First Published Online September 2, 2016

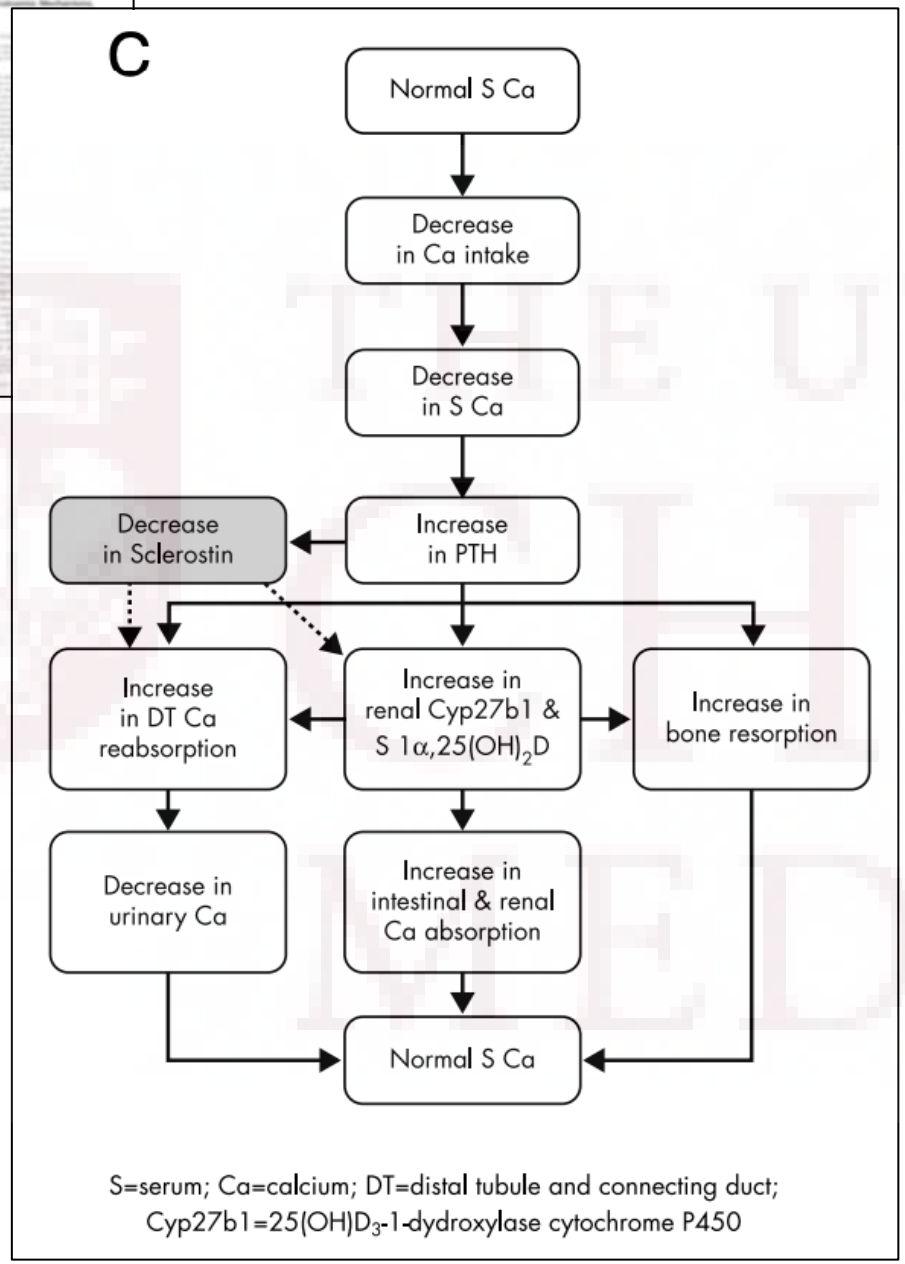
Abbreviations: HTLV, human T lymphotropic virus; IIH, idiopathic infantile hypercalcemia; 1,25$(OH)_2$D, 1,25-dihydroxyvitamin D; 25(OH)D, 25-hydroxyvitamin D; PAM, pulmonary alveolar macrophage; VDBP, vitamin D binding protein.

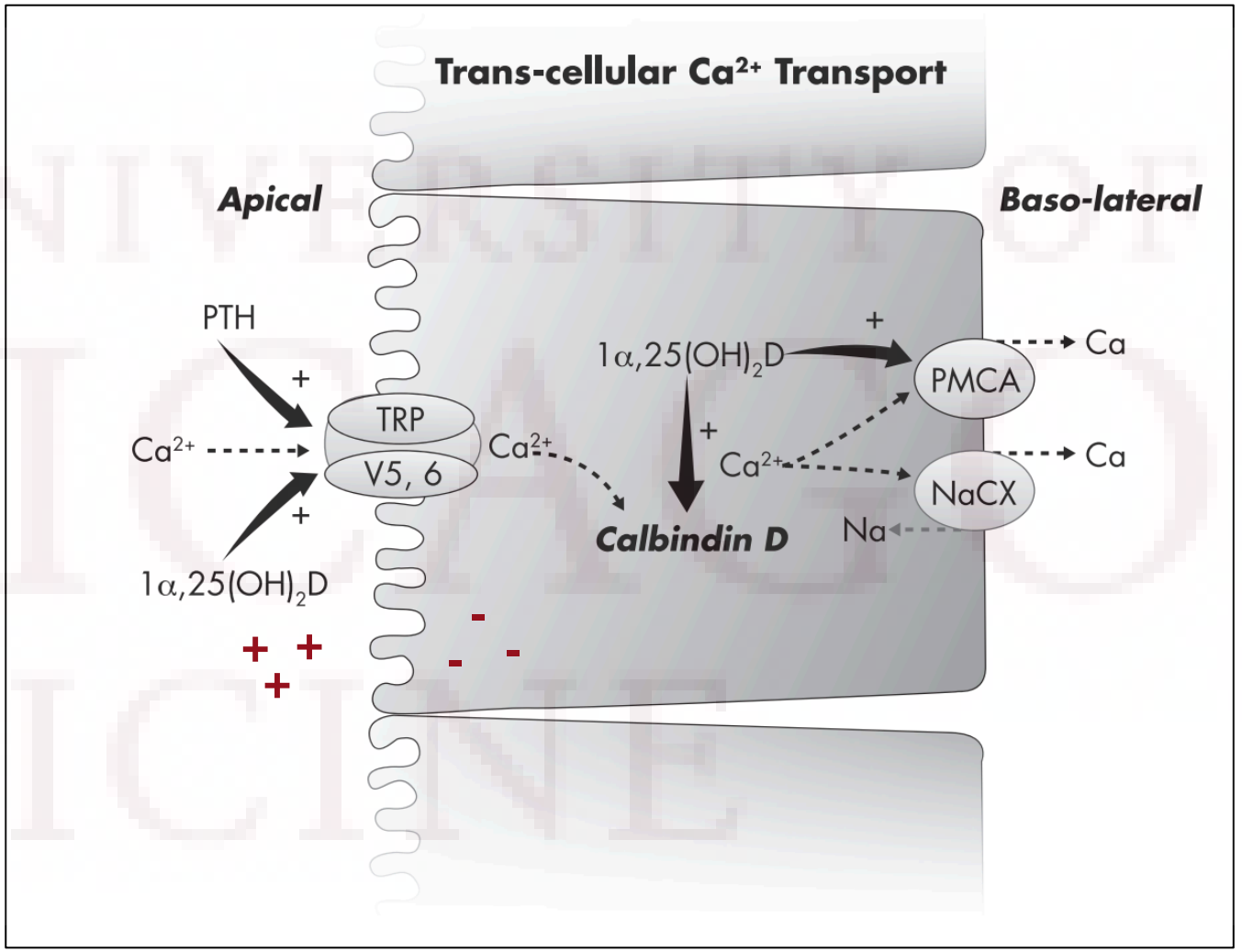
Endocr Rev. 2016 Oct;37(5):521-547.

Table 2. Vitamin D-Associated Hypercalcemia

Exogenous Vitamin D Toxicity
Administration of excessive amounts of vitamin D_3 or vitamin D_2
Administration of excessive amounts of $25(OH)D_3$
Administration of excessive amounts of $1\alpha,25(OH)_2D_3$, other 1α-hydroxylated vitamin D analogs such as $1\alpha(OH)D_3$, paricalcitol, and doxercalciferol in the context of chronic renal failure, end-stage renal disease, and hemodialysis therapy
Excessive Production of Vitamin D Metabolites
Congenital disorders: excessive production of 25(OH)D and $1,25(OH)_2D_3$, eg, in Williams-Beuren syndrome with mutations of the Williams Syndrome Transcription Factor
Granulomatous disease: excessive production of $1,25(OH)_2D_3$: sarcoidosis, tuberculosis, leprosy, histoplasmosis, coccidioidomycosis, paracoccidioidomycosis, candidiasis, cat-scratch disease, *Pneumocystis jiroveci* or *P. carinii* pneumonia, *Mycobacterium avium* complex, Wegener's granulomatosis, Crohn's disease, infantile sc fat necrosis, giant cell polymyositis, berylliosis, silicone-induced granuloma, paraffin-induced granulomatosis, talc granuloma.
Lymphomas and malignant lymphoproliferative disease: excessive production of $1,25(OH)_2D_3$: lymphoma, non-Hodgkin lymphoma, lymphomatoid, granulomatosis, inflammatory myofibroblastic tumor, dysgerminoma
Mutations in Enzymes Associated With Vitamin D Metabolite Degradation
Mutations of the *CYP24A1* gene: reduced degradation of $1,25(OH)_2D_3$: infantile and adult hypercalcemia

Endocr Rev. 2016 Oct;37(5):521-547.

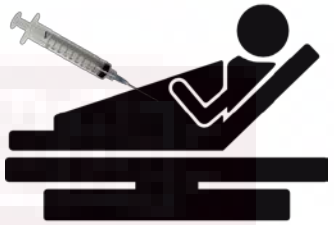




Endocr Rev. 2016 Oct;37(5):521-547.

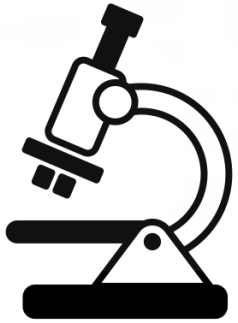
HPI: a chronology (continued)

2016



Paracentesis: no evidence of infection, cytology ‘negative for malignancy’

Bone marrow biopsy and peripheral smear: unremarkable



Core lymph node biopsy: reactive lymphoid tissue, no evidence of malignancy, no evidence of acid fast organisms or fungal elements.

HPI: a chronology (continued)

2018 - 2019  Further evaluation of secondary hypertension and renal disease

24 hour urine calcium: **535 mg/24h**

24 hour urine volume: 5050 mL/24h

24 hour urine creatinine: 1899 mg/24h

24 hour urine protein: 303 mg/24h

PTH **1.4**

Aldosterone: 5.5

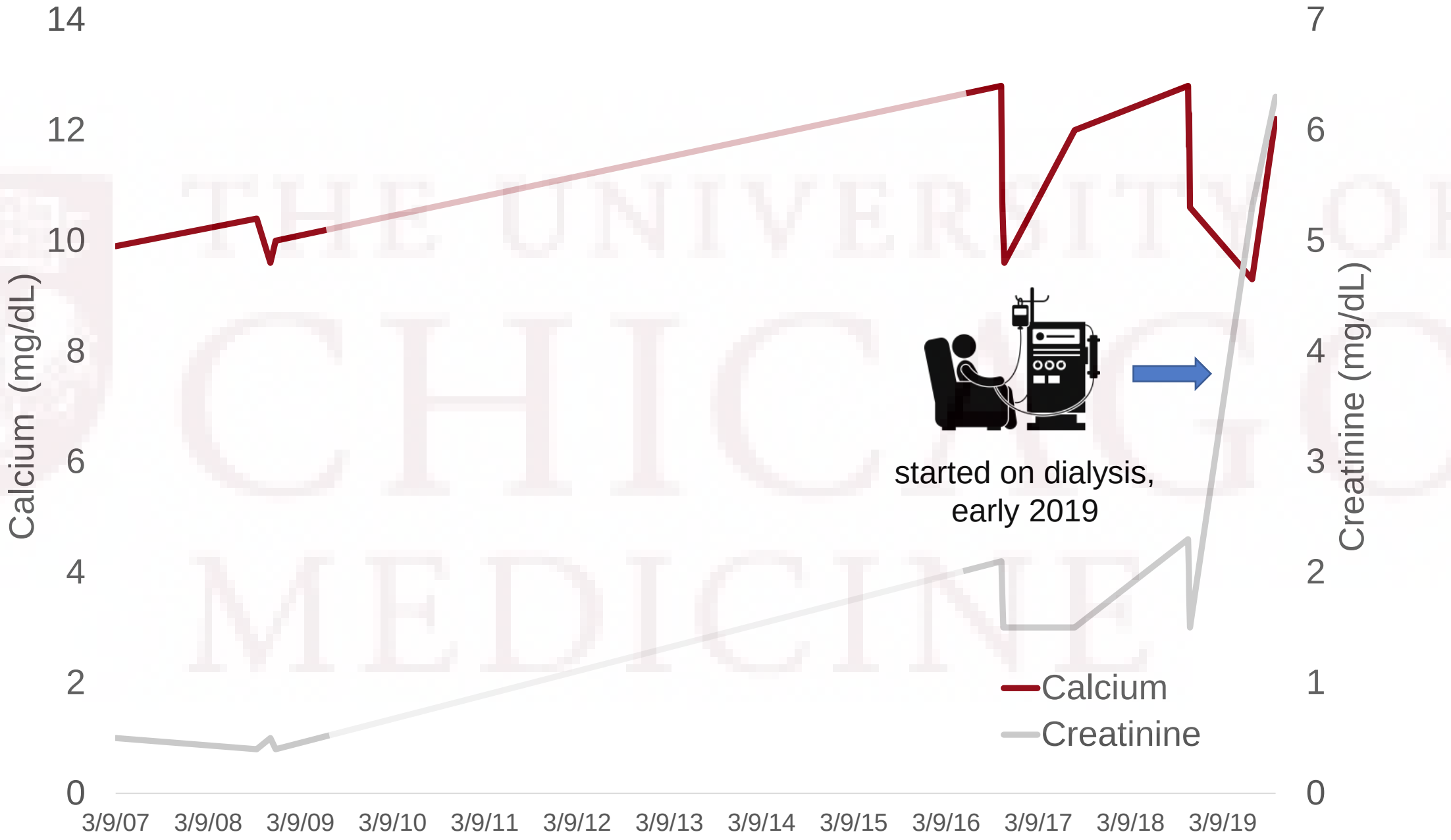
Renin: 28.4

Serum metanephrines: 0.11

Serum normetanephrines: 0.22

Renal ultrasound with doppler:
bilateral nephrolithiasis and mild hydronephrosis; normal renal peak systolic velocities and resistive indices

Echocardiogram:
Reduced systolic function, EF ~40%


14
12
10
8
6
4
2
0
Calcium (mg/dL)
7
6
5
4
3
2
1
0
Creatinine (mg/dL)
started on dialysis,
early 2019
Calcium
Creatinine
3/9/07
3/9/08
3/9/09
3/9/10
3/9/11
3/9/12
3/9/13
3/9/14
3/9/15
3/9/16
3/9/17
3/9/18
3/9/19

2019 The patient presents to  for evaluation headache, renal disease and weakness.

HPI

The patient presents with 3 weeks of weakness, nausea and weight loss. He is having trouble walking and has been falling at home. He has symptoms of lightheadedness but no vertigo. During his last session of dialysis, he had transient loss of vision and headache. He had one episode of emesis and has some non-specific abdominal pain that is near his baseline. He was seen recently in the cardiology clinic to establish care for a new diagnosis of heart failure. He has lost 25lbs in the last 2 months and has little appetite. He has no history of passing kidney stones. He denies constipation. He denies heavy calcium intake.

Emergency department evaluation

Vitals

Temp: 36.8
Pulse: 87
RR: 19
BP: 149/73
SO_2: 99%

Physical Exam

general: fatigued, does not engage in conversation
PERRL, EOMI
CTAB but decreased effort
RRR. No murmur appreciated
Tunneled catheter line in place with no skin changes
Diffusely tender to palpation in abdomen, scaphoid abdomen
2+ peripheral pulses
No costovertebral tenderness
No obvious skin changes.
Depressed mood. When directly asked, will answer questions appropriately

Emergency department evaluation

Current Medications

Amlodipine 10mg daily
Aspirin 81mg daily
B complex-vit C-folic acid daily
carvedilol 25mg BID
cholecalciferol 1000 units daily
Ferric citrate 420mg TID
hydralazine 25mg TID
isosorbide mononitrate 60mg daily

Biochemical evaluation

5.1	**11.0** / **83**

67% PMNs
15% lymphs

138	98	22	102
4.9	25	**6.3**	

calcium **12.2**
albumin 4.0
protein 6.8
alk phos 55
AST 16
ALT 13
mag 2.0
phos 4.4

iCal **5.85**
ESR 12
CRP **9**

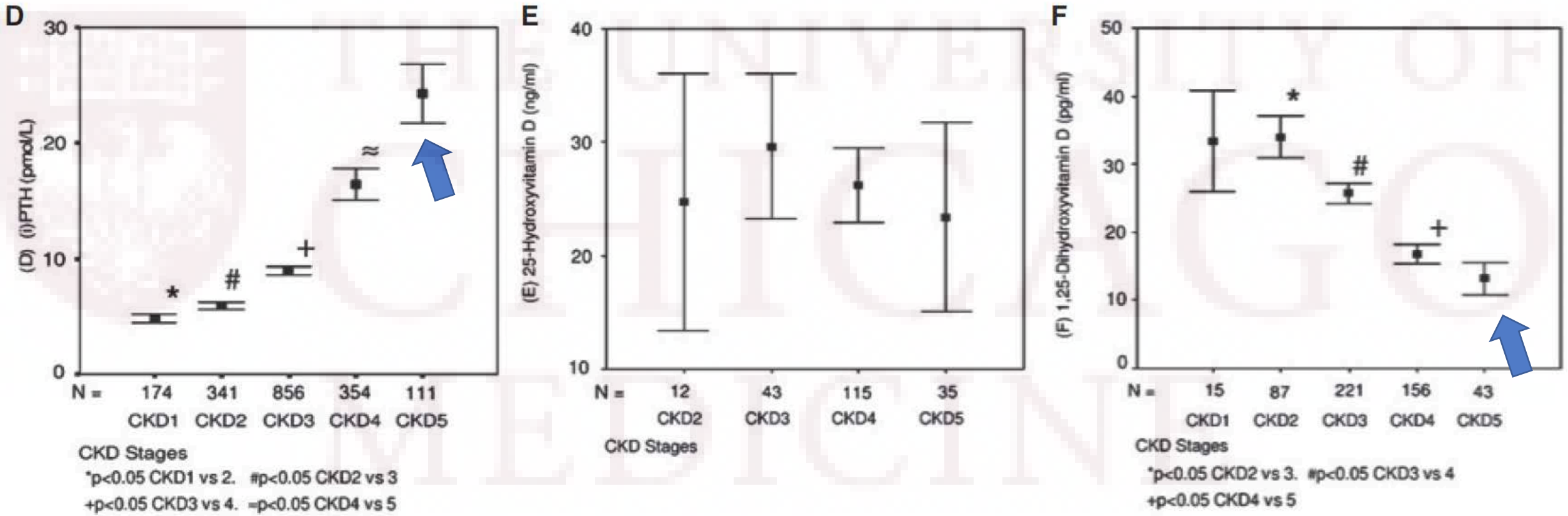
BNP **4143**
PTH **6**
PTH-rp 2.6

TSH 1.86
25-OH vitamin D 60
1, 25-OH vitamin D **191**

What is the significance of low PTH and alk phos in the setting of chronic renal failure?

Pathophysiology of Calcium, Phosphorus, and Magnesium Dysregulation in Chronic Kidney Disease

Arnold J. Felsenfeld,* Barton S. Levine,* and Mariano Rodriguez†
*Department of Medicine, VA Greater Los Angeles Healthcare System and the David Geffen School of Medicine at UCLA, Los Angeles, California, and †Nephrology Service, IMIBIC, Hospital Universitario Reina Sofia, University of Cordoba, Cordoba, Spain



*Typically, ESRD leads to decreased 1,25 – Vit D levels, causing hypocalcemia and secondary hyperparathyroidism. Our patient's PTH is **LOW**.*

Semin Dial. Nov-Dec;28(6):564-577.

Is this patient at risk of having adynamic bone disease?

Adynamic bone disease: “low or absent bone formation in conjunction with thin osteoid seams, decreased cellularity and minimal marrow fibrosis.”

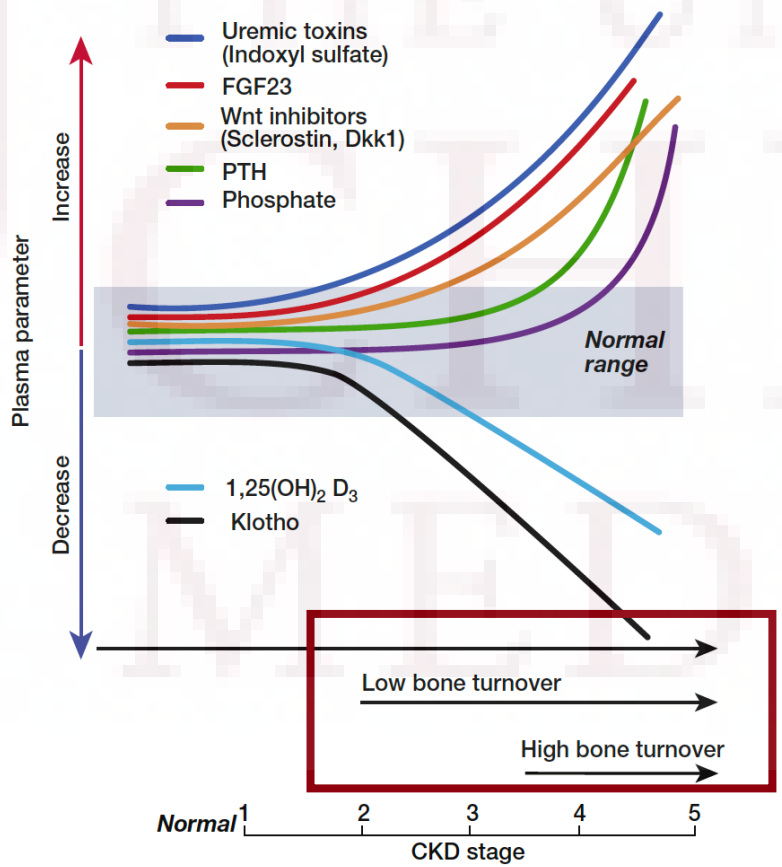


Figure 4 | Schematic view of the time profile of disturbances in mineral hormones and bone turnover with the progression of CKD. CKD, chronic kidney disease; Dkk1, Dickkopf-related protien-1;

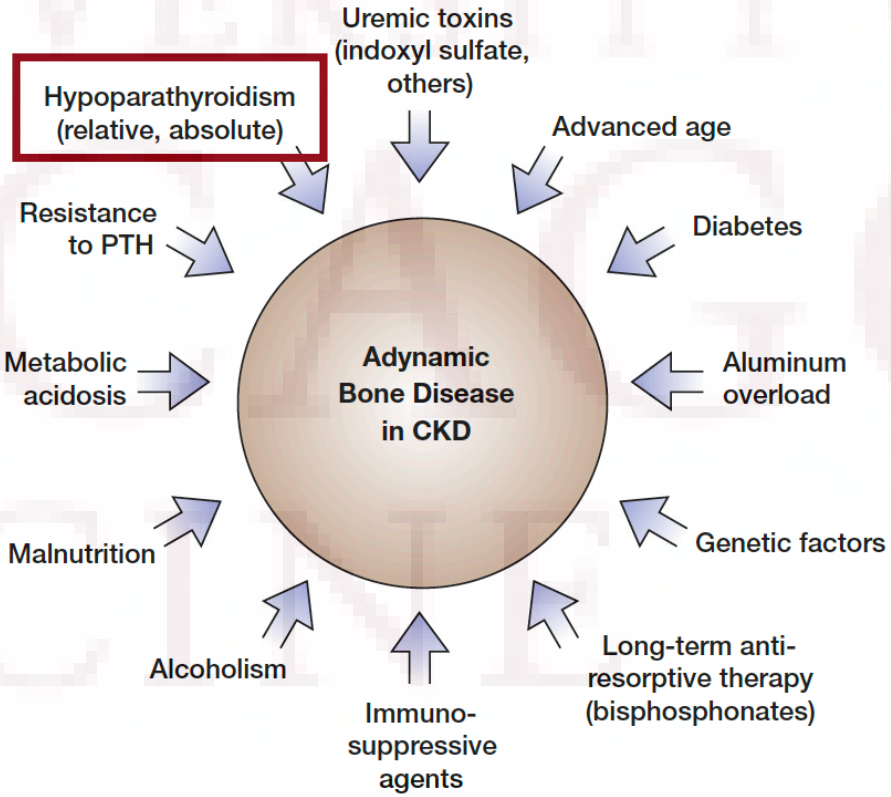


Figure 6 | Schematic representation of factors and conditions favoring low bone turnover (adynamic bone disease). Hypopara-thyroidism is generally considered to be the main cause. It may

Kidney International (2016) 89, 289-302.

Is this patient at risk of having adynamic bone disease?

Adynamic bone disease: “low or absent bone formation in conjunction with thin osteoid seams, decreased cellularity and minimal marrow fibrosis.”

“The principal factor underlying adynamic bone disease is either oversuppression of PTH release or resistance of PTH actions on the bone.”

PTH suppression can occur via use of calcimimetic agents, calcium-based phosphate binders or *relatively high doses of vitamin D analogs*.

It is noted that patients with CKD and adynamic bone disease have *relatively low* PTH levels, which are usually still above the upper limit of normal.

“Adynamic bone disease associated with CKD.” Uptodate.com

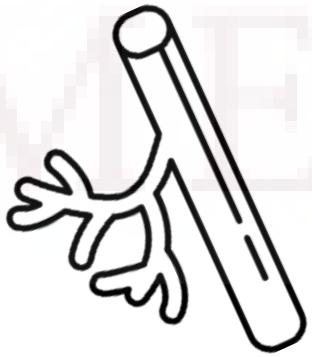
What are the clinical features of adynamic bone disease and how is the diagnosis made?

Most patients are asymptomatic. If symptoms are present, the most common are:

bone pain

fractures

hypercalcemia



vascular calcification

“Adynamic bone disease associated with CKD.” Uptodate.com

What are the clinical features of adynamic bone disease and how is the diagnosis made?

Among dialysis patients**, PTH levels less than 100 pg/mL** are consistent with ABD, especially if hypercalcemia is present.

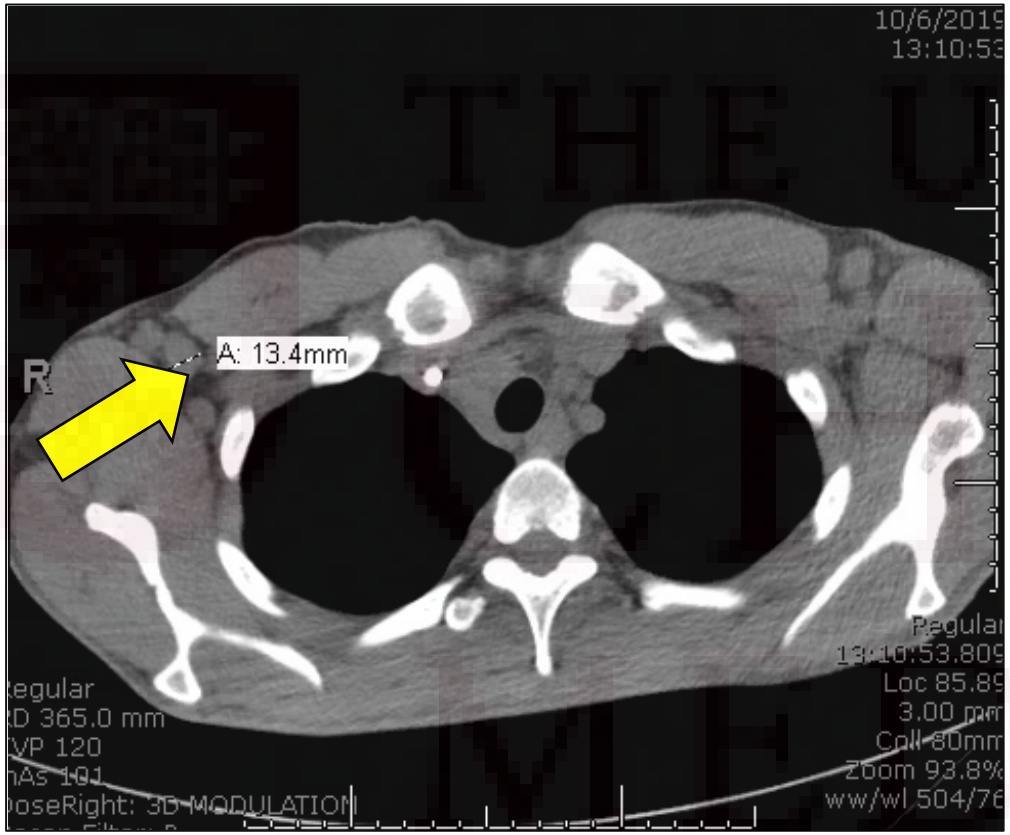
High levels of **bone specific alkaline phosphatase** (>20 ng/mL) make ABD very unlikely.

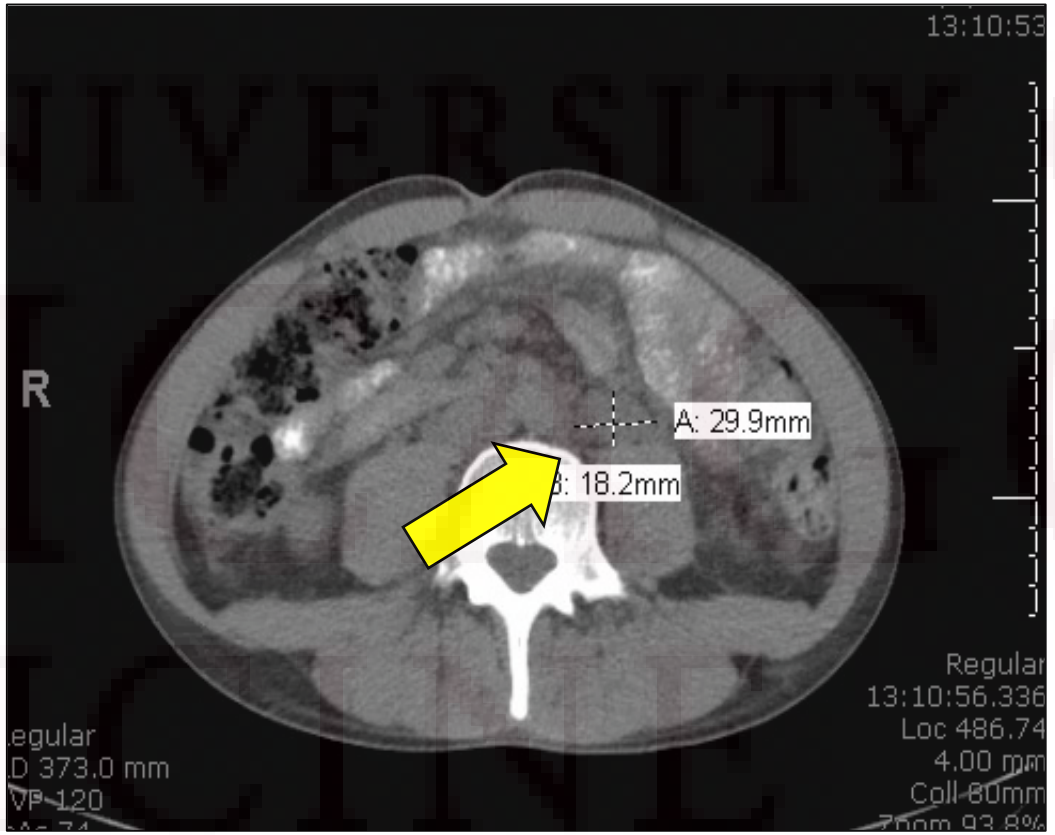
Definitive diagnosis is made on **bone biopsy**.

Our patient's bone-specific alkaline phosphatase: **8.5 ug/L** (0 – 20 ug/L).

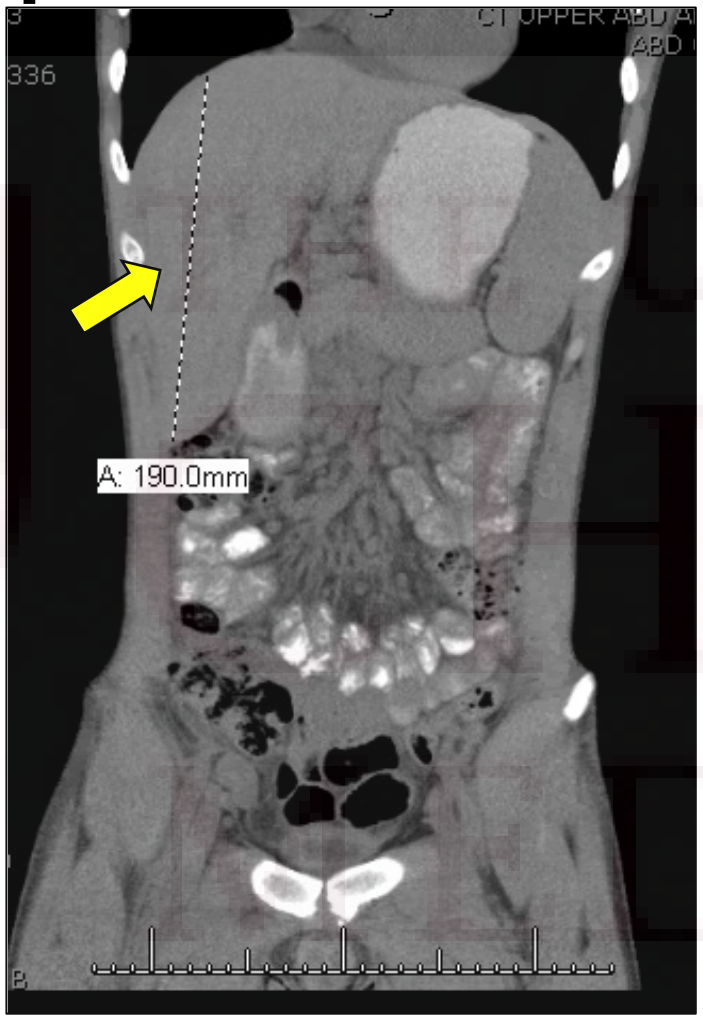
"Adynamic bone disease associated with CKD." Uptodate.com

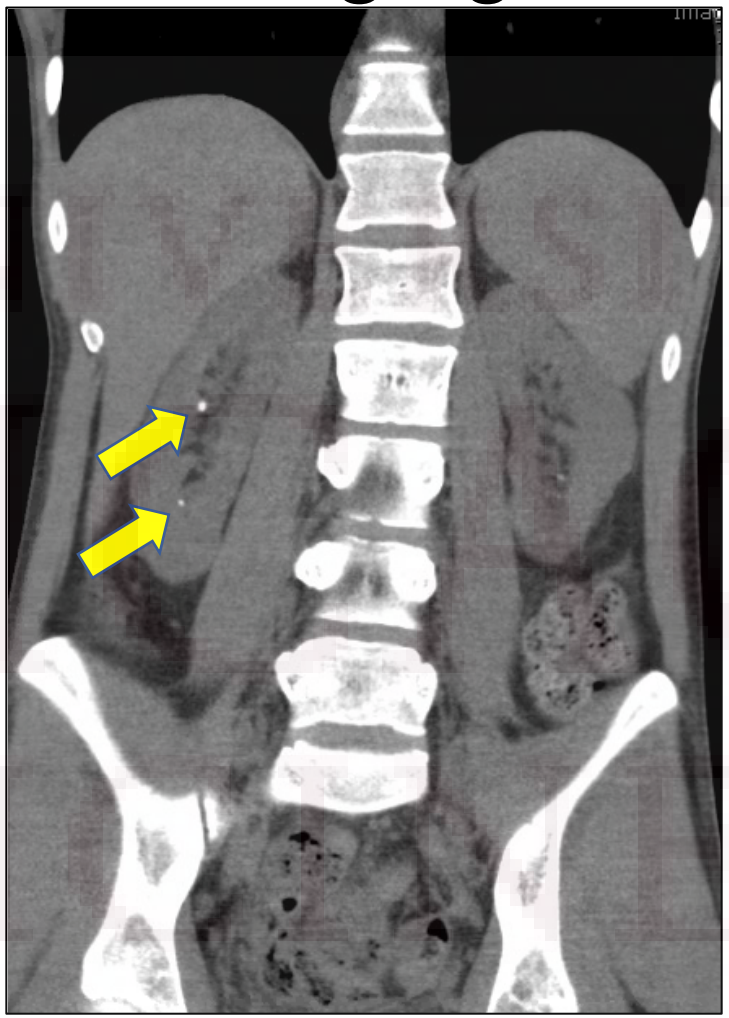
radiographic and cross sectional imaging





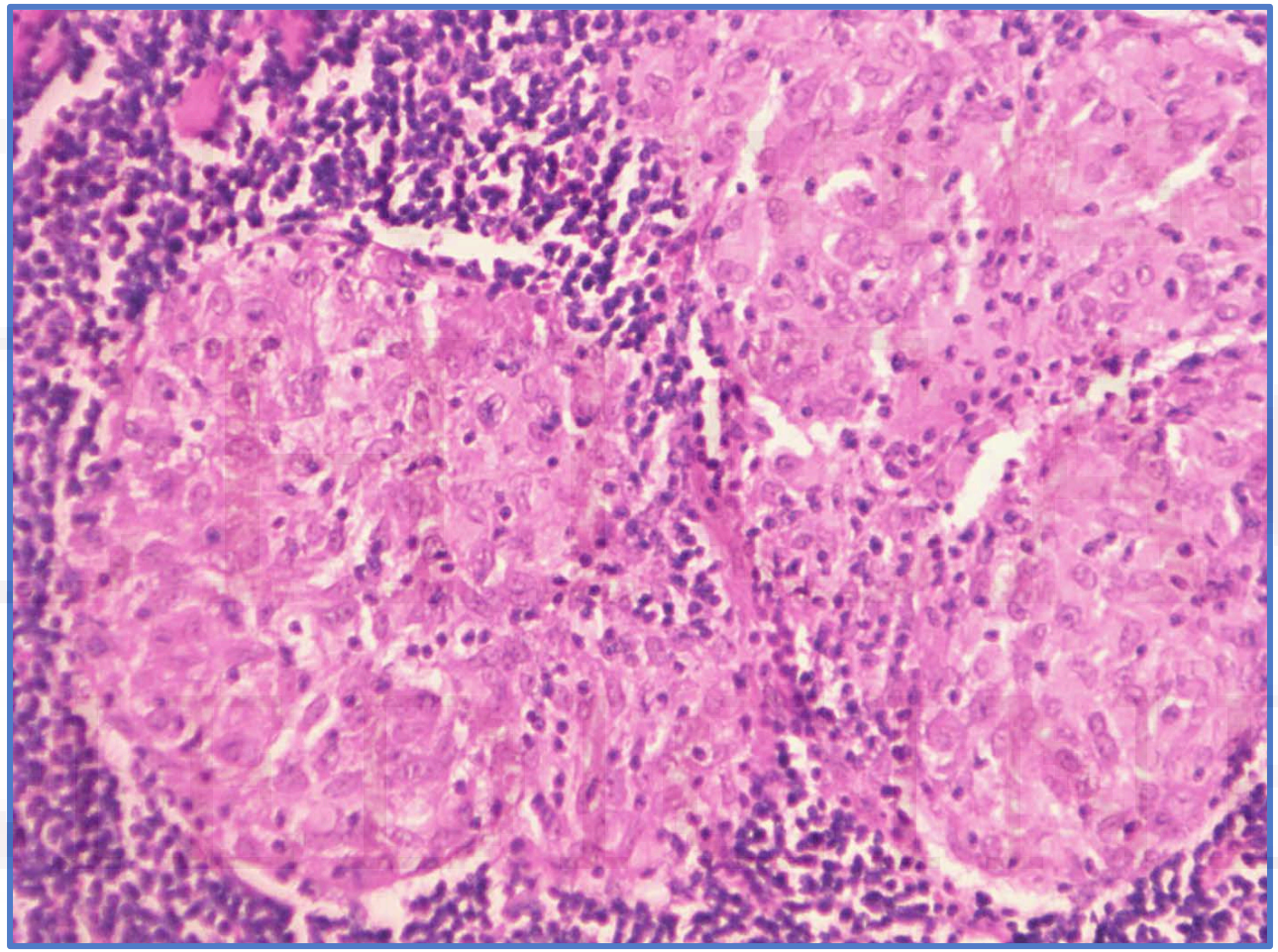
radiographic and cross sectional imaging





CT C/A/P: Prominent mediastinal, axillary, and supraclavicular lymph nodes, pleural effusions. hepatosplenomegaly, extensive mesenteric and retroperitoneal adenopathy, nonobstructive bilateral nephrolithiasis.

excisional inguinal lymph node biopsy



Left inguinal lymph node 1, 2 and 3: lymph nodes with non-caseating granulomas. Comment: The findings support the clinical impression of **sarcoidosis** assuming that cultures are negative for infectious etiologies.

22 year old man presents with headache, vision changes, and progressive lower extremity weakness.

Final diagnosis: SARCOIDOSIS

Started on 20mg prednisone daily.
Stopped vitamin D supplementation.

Metabolism of 25-Hydroxyvitamin D_3 by Cultured Pulmonary Alveolar Macrophages in Sarcoidosis

JOHN S. ADAMS, O. P. SHARMA, MERCEDES A. GACAD, and FREDERICK R. SINGER,
Bone and Connective Tissue Laboratory, Orthopaedic Hospital, and Department of Medicine, University of Southern California School of Medicine, Los Angeles, California 90007

Sarcoid associated pulmonary macrophages convert 25-OH vitamin D to 1,25-OH vitamin D via a specific hydroxylase that is not inhibited by vitamin D or calcium.

The process operates in a PTH-independent manner.

J Clin Endocrinol Metab. 1985 May;60(5):960-6.

J Clin Invest. 1983 Nov;72(5):1856-60.

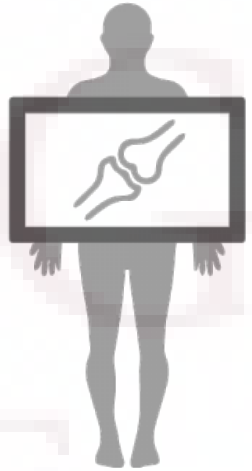
Table 3. Initial Therapy According to Organ and Clinical Status.*

Organ	Clinical Findings	Treatment
Lungs	Dyspnea plus FEV_1, FVC <70%	Prednisone, 20–40 mg/day
	Cough, wheezing	Inhaled corticosteroid
Eyes	Anterior uveitis	Topical corticosteroid
	Posterior uveitis	Prednisone, 20–40 mg/day
	Optic neuritis	Prednisone, 20–40 mg/day
Skin	Lupus pernio	Prednisone, 20–40 mg/day Hydroxychloroquine, 400 mg/day Thalidomide, 100–150 mg/day Methotrexate, 10–15 mg/wk
	Plaques, nodules	Prednisone, 20–40 mg/day Hydroxychloroquine, 400 mg/day
	Erythema nodosum	NSAID
Central nervous system	Cranial-nerve palsies	Prednisone, 20–40 mg/day
	Intracerebral involvement	Prednisone, 40 mg per day Azathioprine, 150 mg/day Hydroxychloroquine, 400 mg/day
Heart	Complete heart block	Pacemaker†
	Ventricular fibrillation, tachycardia	AICD
	Decreased LVEF (<35%)	AICD; prednisone, 30–40 mg/day
Liver	Cholestatic hepatitis with constitutional symptoms	Prednisone, 20–40 mg/day Ursodiol, 15 mg/kg of body weight per day
Joints and muscles	Arthralgias	NSAID
	Granulomatous arthritis	Prednisone, 20–40 mg/day
	Myositis, myopathy	Prednisone, 20–40 mg/day
Hypercalciuria and hypercalcemia	Kidney stones, fatigue	Prednisone, 20–40 mg/day Hydroxychloroquine, 400 mg/day

Other treatments:
Diet modification
Ketoconazole
(P450 inhibitor)

N Engl J Med 2007; 357:2153-2165.

Monitoring response and follow up?



Learning Objectives

- Briefly review the diagnosis and evaluation [redacted]
- Explain the mechanism of [redacted] and other [redacted]
- Discuss the fundamentals of [redacted]
- Identify [redacted] for [redacted]
- Speculate on role of [redacted] in this case [if time allows]

Learning Objectives

- Briefly review the diagnosis and evaluation of PTH-independent hypercalcemia
- Explain the mechanism of hypercalcemia in sarcoidosis and other granulomatous diseases
- Discuss the fundamentals of adynamic bone disease
- Identify treatment options for hypercalcemia in sarcoidosis
- Speculate on role of hypercalcemia as a driver of renal failure in this case [if time allows]

Postgraduate Medical Journal (1986) **62,** 937–938

Hypercalcaemia due to sarcoidosis corrects with bisphosphonate treatment

Charles J. Gibbs and Munro Peacock

MRC Mineral Metabolism Unit, The General Infirmary, Leeds LS1 3EX, UK.

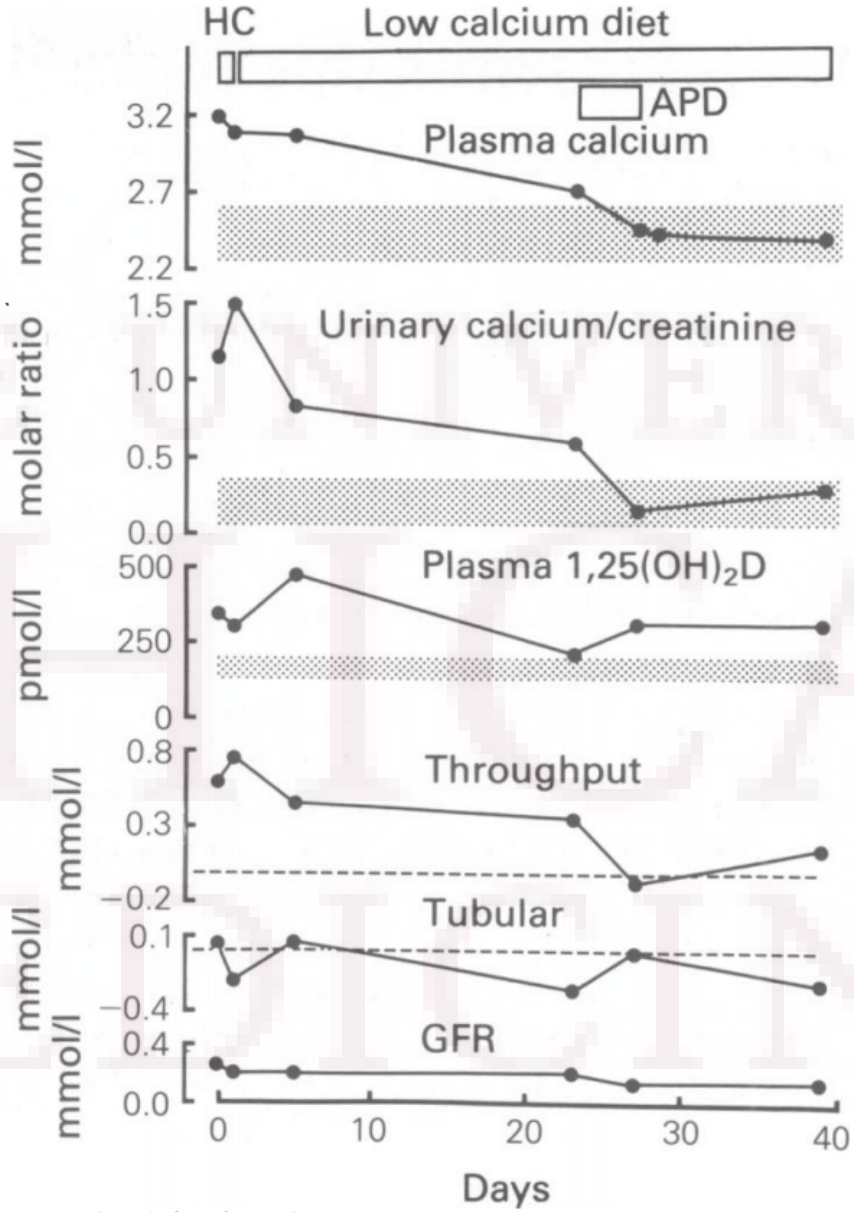


Figure 1 Biochemistry and components of hypercalcaemia during treatment with hydrocortisone (HC), low calcium diet and APD. The stippled areas represent normal ranges and the dotted lines indicate zero.

Postgrad Med J. 1986 Oct;62(732):937-938.

Is there a direct effect of hypercalcemia on the kidney that leads to loss of filtration?

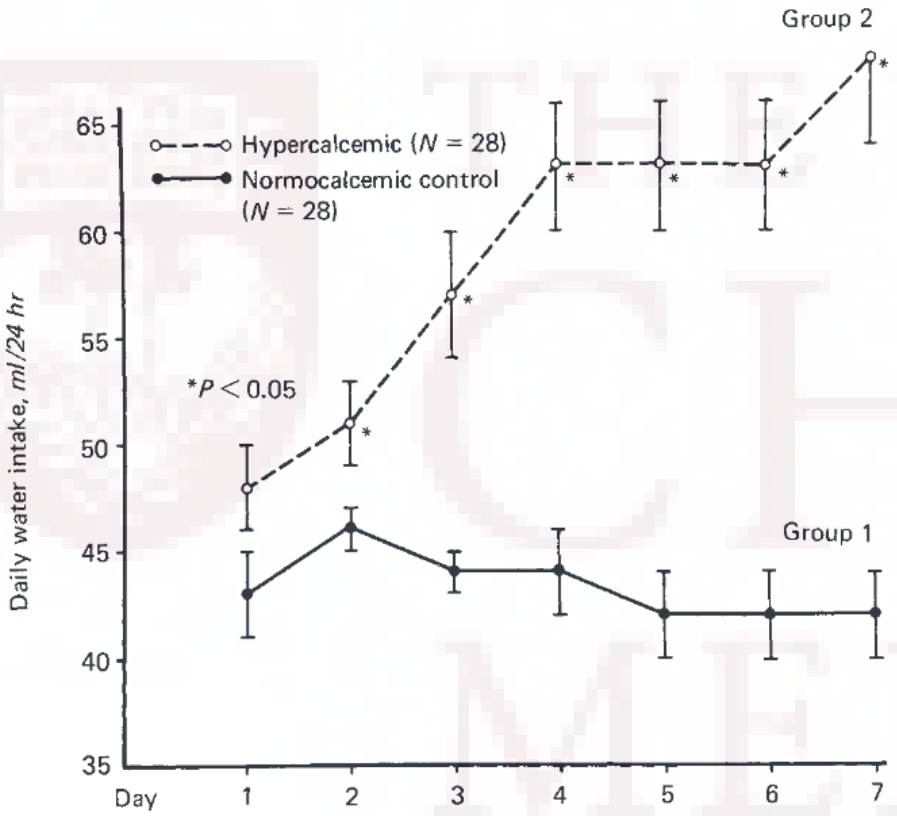
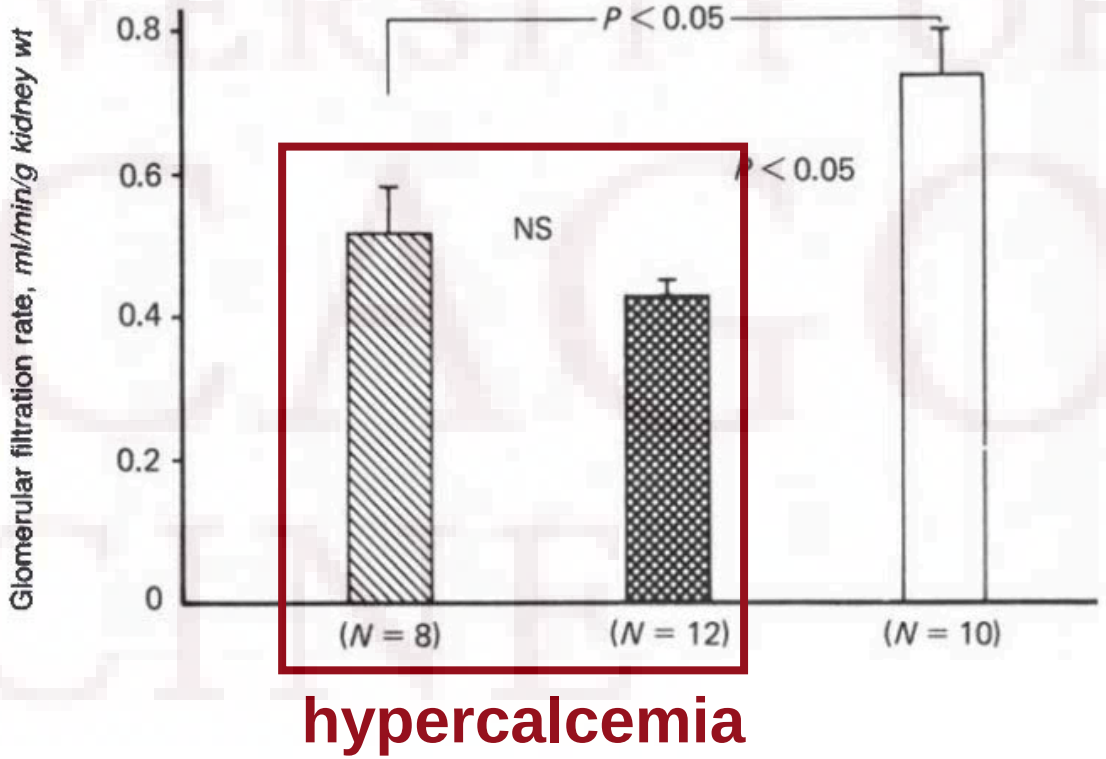


Fig. 1. *Daily water intake (ml/24 hr) of pair-fed normocalcemic rats* (Group 1) *and hypercalcemic rats* (Group 2).



hypercalcemia

Kidney Int. 1983 Mar;23(3):489-97.