Parathyroid 101

Steven Ing, MD, MSCE
February 20, 2016

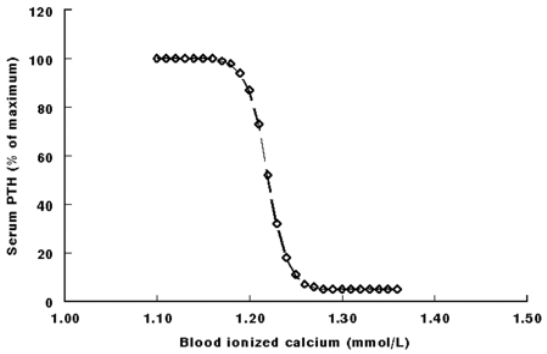
The Ohio State University
Wexner Medical Center

Objectives

- Review common presentations in which PTH is abnormal (and abnormally normal)
  - Hypoparathyroidism
  - Secondary Hyperparathyroidism
  - Primary Hyperparathyroidism

2

Regulation of PTH by Calcium



Am J Physiol Renal Physiol 286: F1005-F1011, 2004

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Case CB

9/2015 Initial Visit (transfer from fellows clinic)
56 y.o. African American man
Laryngeal squamous cell carcinoma
3/2012 Extensive resection

Laryngopharyngectomy with right radical neck dissection levels 1-5, sacrificing sternocleidomastoid and internal jugular vein
Left selective neck dissection levels 2-4
Right oropharyngectomy including tonsil, tonsillar pillars and portion of soft palate (radical tonsillectomy)
Upper cervical esophagectomy
Pharyngectomy requiring closure with fasciocutaneous free flap
Tracheoesophageal puncture with insertion of voice prosthesis
Total thyroidectomy with paratracheal dissection
Esophagoplasty
Dermal graft to right carotid artery 10 x 4 cm
Left fasciocutaneous radial forearm free flap 14 x 9 cm to reconstruct pharyngoesophageal defect

7/2012 Chemo-radiation completed

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Case CB

9/2012 Admission for hypocalcemia (Ca 5.8)

11/2012 Admission for hypercalcemia (Ca 20.9)

8/2013 Admission for hypocalcemia (Ca 5.6)

10/2013 Ca 12.7, managed as outpt

Case CB

Calcium citrate (elemental Ca 200 mg per tab) 4 tabs tid

Ensure 1 bottled tid

Calcitriol 0.25 mcg qD

Vitamin D 1000 units qD

HCTZ 25 mg qD

Levothyroxine 137 mcg 1 tab Mon-Sat, 2 tabs Sun (separates from Ca)

No paresthesia, muscle cramps, fatigue, brain fog, musculoskeletal pain

No recurrence of cancer

Labs

Test	Result	Reference Range
Calcium	8.4	8.6-10.0 mg/dl
Albumin	4.2	3.4-4.8 g/dl
Ionized Calcium	4.08	4.60-5.30 mg/dl
Phosphorous	5.2	2.7-4.5 mg/dl
Creatinine	0.84	0.60-1.10 mg/dl
eGFR	>60	>60 ml/min/1.73M^2
Intact PTH	<6.3	14-72 pg/ml
25 OH vitamin D	56.6	30-100 ng/ml
TSH	1.746	0.55-4.78 uIU/ml

Case CB (Cont'd)

"Doc, can I come off of some of these pills?"

The Ohio State University
Wexner Medical Center

Acute symptomatic hypocalcemia

- IV Calcium gluconate
  - 1 amp (=90 mg elemental Ca) in 50-100 ml D5W
  - Bolus infusion: 1-2 amps over 10-20 minutes
  - Continuous infusion: 1-2 mg/kg/hr
  - Cardiac monitoring
  - Monitor ionized Ca
- Initiate: symptoms, prolonged QTc, Ca <7 who may develop severe complications if untreated

Chronic Management

- Calcium Carbonate
  - Oscal, Caltrate, Viactiv, Tums
  - Take with food
- Calcium Citrate
  - Citracal
  - Achlorhydria, PPI
- Wide spectrum of needs 1-9 g/day

Chronic Management

- Calcitriol
  - 0.25 to 2 mcg/day
- Vitamin D
  - Smoother control due to longer half life
  - 800 IU daily to 50,000 IU weekly
- Thiazide
  - HCTZ, chlorthalidone (25-100 mg/day)

The Ohio State University
Wexner Medical Center

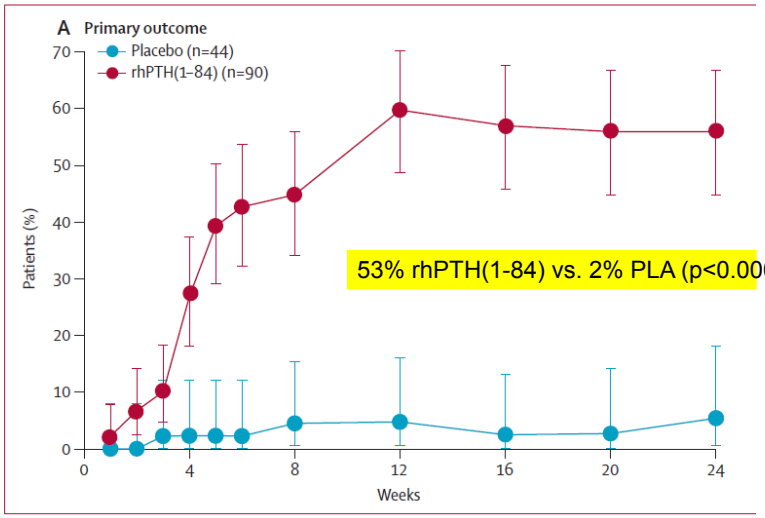
"REPLACE" RCT

- Safety and efficacy of PTH1-84 in adults with chronic hypoparathyroidism
- 50, 75, 100 mcg SQ qD
- 1° Endpoint: ↓50% in Ca and active vitamin D
- 2 ° Endpoint: Stop all active vitamin D, ↓Ca ≤ 500mg qD

The Ohio State University
Wexner Medical Center

Mannstadt M, et. al. Lancet Diabetes Endocrinol 2013;1:275-2

1° EndPoint:
≥50% ↓in Ca and active vitamin D



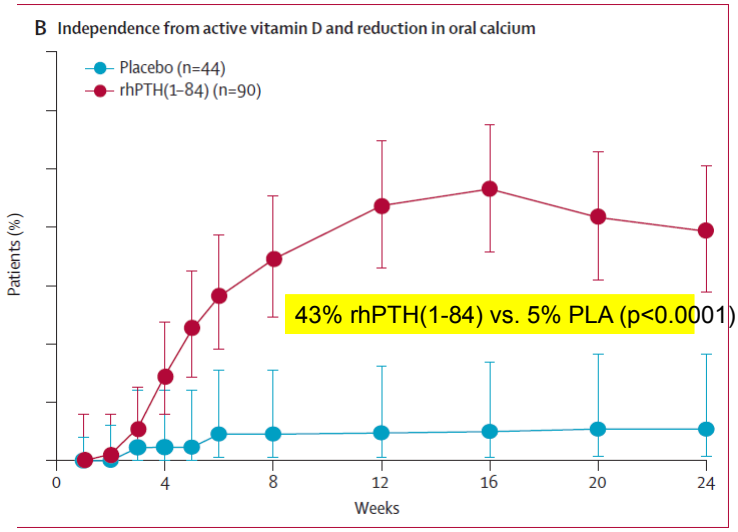
48/90

53% rhPTH(1-84) vs. 2% PLA (p<0.0001)

1/44

Mannstadt M, et. al. Lancet Diabetes Endocrinol 2013;1:275-283

2 ° Endpoint:
Off active vitamin D, Ca ≤500mg qD



36/84

43% rhPTH(1-84) vs. 5% PLA (p<0.0001)

2/37

Mannstadt M, et. al. Lancet Diabetes Endocrinol 2013;1:275-283

Case CB (Cont'd)

10/5 Started Natpara 50 mcg qD,
d/c calcitriol, cont Ca 2 tabs tid
10/26 Ca 10.4, reduce Ca 1 tab tid
11/9/2015 Ca 8.7
11/23/2015 Ca 7.4, phos 5.9 (missed Natpara doses)
12/10/2015 Ca 8.7, phos 3.8, plan to ↑ Natpara
1/13/2016 ↑ Natpara 75 mcg qD, d/c Ca citrate
1/19/2016 Ca 7.9, phos 4.4, Ensure tid only
1/27/2016 Ca 8.5, phos 4.4, Ca citrate 1 tab tid

Case KG

- First visit 1/2012
- 84 y.o. caucasian woman
- ALE 2000 x years
- TPTD x 3M (2008), d/c due to high cost
- ZOL 2009, 2010
- Worsening BMD 2009-2011→ refer

Case KG: DXA Scan

9/28/2011

	BMD	T-score	Z-score
Lumbar spine	0.694	-3.2	-0.4
Left femoral neck	0.337	-4.5	-2.1
Left total hip	0.462	-3.9	-1.6

	2009 BMD	2011 BMD	% Change
Lumbar spine	0.694	0.694	0.0%
Left total hip	0.522	0.462	-7.3%

Case KG

No personal or parental hx of fxr

No family hx osteoporosis

2" ↓ height vs. historical young adult height (4' 11")

Menarche 15, menopause 38

Took Premarin until age 64 for uterine cancer

Calcium-rich foods: soy milk 1 glass, Lactaid milk 1 glass, cottage cheese daily.

Calcium carbonate (elemental Ca 300mg) 1 cap bid, vitamin D 5000 IU qD taking faithfully for past year

Weight bearing exercise: walking 6 miles daily until recent surgery:

12/2010 ERCP/sphincterotomy for CBD stones

Complicated by duodenal perforation, transferred to OSU for exploratory laparotomy, lysis of SB adhesions, SB excision (43 cm)

Chronic loose BMs (12x/day) since, managed with tincture of opium (8x/day)

Tests?

Tests?

Test	Result	Reference Range
Calcium	8.9	8.6-10.0 mg/dl
Albumin	4.3	3.4-4.8 g/dl
Phosphorous	3.9	2.7-4.5 mg/dl
Creatinine	1.15	0.60-1.10 mg/dl
eGFR	45	>60 ml/min/1.73M^2
Intact PTH	230.4	14-72 pg/ml
25 OH vitamin D	17.6	30-100 ng/ml
Urinary Calcium	ND	100-300 mg/24hr

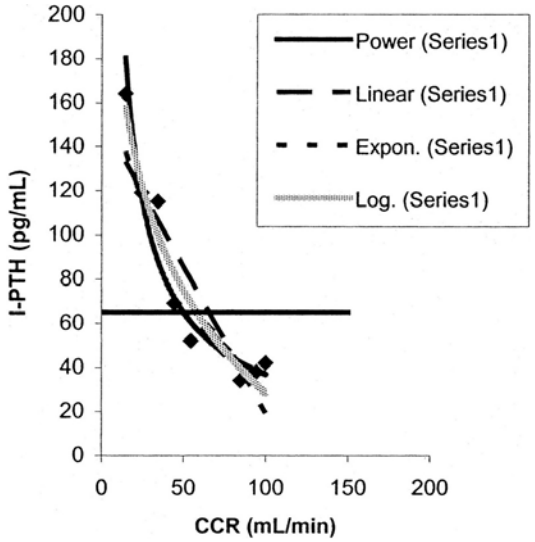
Case EH: Additional Labs

Test	Result	Reference Range
SPEP/immunofixation	Normal	
UPEP/immunofixation	Normal	
Transglutaminase IgA Ab	<1.2	<1.2
Transglutaminase IgG Ab	<1.2	<1.2
CTX	404	25-573 pg/ml
P1NP	46	19-83 mcg/L

Causes of SHPT

- Renal failure
  - Impaired calcitriol production
  - Hyperphosphatemia
- Decreased calcium intake
- Calcium malabsorption
  - Vitamin D deficiency
  - Bariatric surgery
  - Celiac disease
  - Pancreatic disease (fat malabsorption)
- Renal calcium loss
  - Idiopathic hypercalciuria
  - Loop diuretics

PTH x CrCl



KDOQI Guidelines; accessed 2/17/2016
http://www2.kidney.org/professionals/KDOQI/guidelines_pedbone/guide1.htm

DXA Scan

	4/14/2009	9/28/2011	10/1/2013
Lumbar Spine BMD T-score	0.694	0.694 -3.2	0.675 (-2.7%) -3.4
Left Total Hip BMD T-score	0.522	0.462 (-7.3%) -3.9	0.414 (-10.4%) -4.3
Right Total Hip BMD T-score			

Case EH (Cont'd)

Date	25 OH vitamin D	PTH	While Taking
1/13/2012	17.6	230.4	5k IU qD
4/27/2012	16.7	132.2	10k IU qD
7/30/2012	19.3	127.5	50k IU 3x/week
12/14/2012	20.8	179.2	50k IU 5x/week
4/11/2013	64.1	66.8	50K IU qD
7/29/2014	74.2		50K IU qD
2/3/2015	61.1		50K IU 3x/week
2/9/2016	52.8		50K IU 3x/week

Forteo 12/2013-1/2016

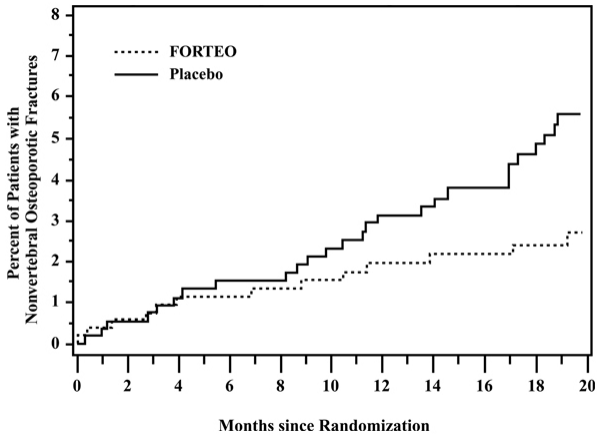
THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER

DXA Scan

	4/14/2009	9/28/2011	10/1/2013	10/6/2015
Lumbar Spine BMD T-score	0.694	0.694 -3.2	0.675 (-2.7%) -3.4	0.798 (+18.2%) -2.3
Left Total Hip BMD T-score	0.522	0.462 (-7.3%) -3.9	0.414 (10.4%) -4.3	***
Right Total Hip BMD T-score				0.448 -4.0

10/2014 Fragility hip fracture: walking in the dark without Turning on lights, reached into an empty door, tripped and fell

THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER



THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Case EH

- First visit 9/2013
- 63 y.o. woman
- PMH: Crohn's disease 1990
- Prednisone 2012-2013: 3 tapers, ~2 Mo each
- Humira 2012, Crohn's disease now controlled

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Case: DXA scan

4/19/2013

Region	g/cm2	T-score	Z-score
Lumbar Spine	0.885	-2.7	-1.3
Left Femoral Neck	0.674	-2.6	-1.3
Left Total Hip	0.830	-1.4	-0.4
Right Femoral Neck	0.703	-2.4	-1.1
Right Total Hip	0.802	-1.6	-0.6

	Prior BMD (T-score) 8/10/2012	Current BMD (T-score) 4/19/2013	Change	% Change
Lumbar Spine	1.009 (-1.7)	0.885 (-2.7)	-0.124	-12.3%
Left Total Hip	0.893 (-0.9)	0.830 (-1.4)	-0.063	-7.1%
Right Total Hip	0.885 (-1.0)	0.802 (-1.6)	-0.083	-9.4%

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Case EH (Cont'd)

- No personal/parental hx fracture
- Mother takes osteoporosis medication
- Menstrual hx unremarkable
- Ensure 2 cans qD, women's MVI qD
- No prior osteoporosis med
- 2012 EGD: +severe reflux esophagitis
- 2012 abd CT: 1cm kidney stones bilat, (aSx)

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Case EH: Labs?

Case EH: Labs

Test	Result	Reference Range
Calcium	10.9	8.6-10.0 mg/dl
Albumin	3.9	3.4-4.8 g/dl
Phosphorous	2.3	2.7-4.5 mg/dl
Creatinine	0.8	0.60-1.10 mg/dl
eGFR	>60	>60 ml/min/1.73M^2
Intact PTH	88.9	14-72 pg/ml
25 OH vitamin D	32.9	30-100 ng/ml

Case EH: Additional Labs

Test	Result	Reference Range
SPEP/immunofixation	Normal	
UPEP/immunofixation	Normal	
Transglutaminase IgA Ab	<1.2	<1.2
Transglutaminase IgG Ab	<1.2	<1.2
CTX	570	25-573 pg/ml
P1NP	82	19-83 mcg/L
Urinary Calcium FECa	157 0.011	100-300 mg/24hr

The Ohio State University Wexner Medical Center

Guidelines for Surgery

Age		<50
Hypercalcemia	Calcium >ULN	1.0 mg/dl
Skeletal	DXA scan	BMD T-score ≤-2.5 @ LS, TH, FN, or Distal 1/3 radius
	Fracture	Vertebral fracture by x-ray, VFA, (CT, MRI)
Renal	GFR	CrCl <60 ml/min
	Urinary Ca	>400 mg/24hr & ↑ stone risk
	Stone	Nephrolithiasis or nephrocalcinosis by x-ray, US, CT

4th International Workshop on PHPT, JCEM 2014;99:3561-3569

The Ohio State University Wexner Medical Center

Guidelines for Monitoring

	2013
Serum Ca	Annually
Skeletal	DXA q1-2 yr (3-site) X-ray or VFA if clinically indicated (e.g. height loss, back pain)
Renal	eGFR annually If stones suspected → 24 hr biochemical stone profile Renal imaging by x-ray, US, or CT

4th International Workshop on PHPT, JCEM 2014;99:3561-3569  The Ohio State University Wexner Medical Center

Evaluation

- Ca, phos, ALP, BUN, Cr
- iPTH
- 25 OH vitamin D
- DXA (3-site)
- Spine x-ray or VFA
- 24 hr urinary Ca, Cr, CrCl
- Abdominal x-ray, US, or CT

4th International Workshop on PHPT, JCEM 2014;99:3561-3569 The Ohio State University Wexner Medical Center

Surgical Indications During Monitoring

- Ca >1 mg/dl above ULN
- Significant ↓ BMD & T-score -2.5 at that site
- Fragility fracture
- New kidney stone
- CrCl <60 ml/min

4th International Workshop on PHPT, JCEM 2014;99:3561-3569

Case (Cont'D)

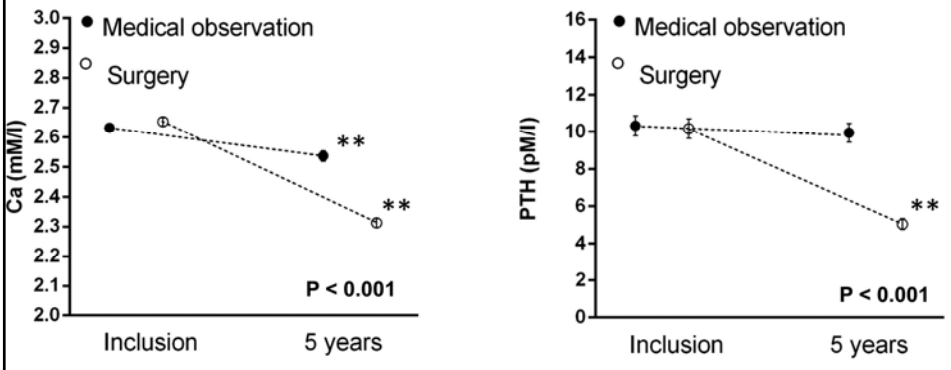
- Refer to surgery (GI→endo→surgery)
- Sestamibi-SPECT: +uptake right thyroid bed
- 1/2014 PTX: right superior parathyroid adenoma, 0.7 g (1.6 x 1.1 x 0.6 cm)
- Intraop PTH: 91.4→77.0→285.1→31.4→14.1

Case F/U DXA (Cont'd)

	8/10/2012	4/16/2013	2/6/2015
Lumbar Spine BMD T-score	1.009 -1.7	0.885 -2.7 (-12.2%)	0.983 -1.9 (+11.1%)
Left Total Hip BMD T-score	0.893 -0.9	0.830 -1.4 (-7.1%)	0.836 -1.4 (+0.7)
Right Total Hip BMD T-score	0.885 -1.0	0.802 -1.6 (-9.4%)	0.848 -1.3 (+5.7%)

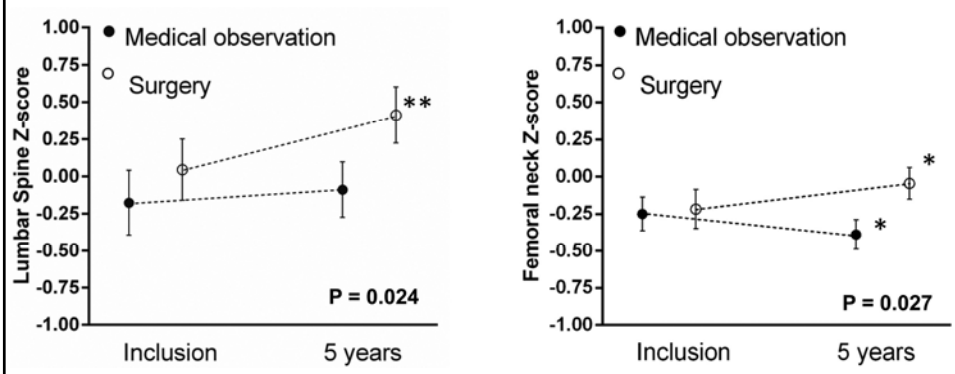
Does parathyroidectomy off other bone-protective effects?

RCT: Observation vs PTX in mild asymptomatic PHPT @ 5 years



Lundstam K, et. al. JCEM 2015 (100):1359-1367

RCT: Observation vs PTX in mild asymptomatic PHPT @ 5 years



Lundstam K, et. al. JCEM 2015 (100):1359-1367

RCT: Observation vs PTX in mild asymptomatic PHPT @ 5 years

	Observe n=55	Surgery n=51
Baseline Vert Fxr # patients # Vert Fxr	 4 (7.3%) 6	 5 (9.8%) 5
New Vert Fxr # patients # Vert Fxr	 5 (9.1%) 5	 0 0

Lundstam K, et. al. JCEM 2015 (100):1359-1367