HORMONE OPTIMIZATION
in Preventive/Regenerative Medicine
SECOND EDITION

A "NUTS AND BOLTS” Approach to Management

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Guidebook includes Treatment Algorithms and Abstracts
Parathyroid Hormone: The Forgotten Hormone in Anti-Aging Medicine
Ron Rothenberg MD

The following potential conflict of interest relationships are germane to my presentation.

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NA

Status of off-label use of devices, drugs or other materials that constitute the subject of this presentation
NA
Parathyroid Hormone: The forgotten hormone in Anti-Aging Medicine

Ron Rothenberg MD
Why is PTH Important in Anti-Aging Medicine?

• Symptoms of PHPT overlap with common complaints of many Anti-Aging patients:
  – Fatigue
  – Cognitive Problems
  – Osteoporosis
  – GI symptoms

• Anti-Aging physicians are the experts in advanced endocrine optimization

• Functional/Nutritional Connections
• High PTH is independent predictor of all cause and CV mortality
• We can measure PTH in our baseline assessments
• We can optimize PTH
• Vitamin D and PTH
• Phosphorus and PTH
Case Studies

• 59 y/o female with cognitive dysfunction, depression, anxiety getting worse over 1 year
• Had extensive workup with MRI, genetic testing, neurotransmitters and hormones etc. Ca^{++} 10.1 albumin 3.4, positive for ApoE double allele
• Hormones optimized, “brain boosters” used, adrenal fatigue addressed not much change
• Dx: ?
• 50 y/o male with chronic abd pain x 1 year
• Lab normal except for low hormones.
• Ca^{++} 10.2 , Albumin 4.0, 25-OH Vit D 105,
• CT abd: Stones in renal pelvis bilateral, no hydronephrosis or ureteral stones
• Meds: Omeprazole, Tramadol
• Supplements: Vitamin D 10K/day, Multi Vitamins, probiotics, digestive enzymes, Betaine HCl
• Hormones optimized, dysbiosis corrected
• Dx ?
Anatomy/Histology of Parathyroid

• 4 glands with inferior and superior attachment to each lobe of the thyroid gland

• 2 main epithelial cells
  – Chief or Principle Cells
    – Synthesize, process, and store PTH
    – Respond within seconds to falling calcium
  – Oxyphyl Cells –
    – No known function
    – Appear at puberty and increase with age
    – Densely populated with mitochondria
PTH

• 84–amino-acid single-chain peptide
  – Osteoclastic stimulation- calcium out of bones
  – Reabsorb calcium in kidneys
  – Converts 25OH D3 to 1,25-dihydroxyvitamin D3
  – Stimulates GI absorption of calcium

• Low circulating concentrations of calcium stimulate PTH secretion

• High circulating concentrations of calcium depress PTH secretion

• Metabolized in the liver and kidneys

• Half-life is two to five minutes.
PTH

Low concentration of calcium in blood

Release of parathyroid hormones

Efflux of Calcium from bone
Decreased loss of calcium in urine
Enhanced absorption of calcium from intestines

Increased concentration of calcium in blood
**PTH effects on the Kidney**
- Increases Calcitriol Formation
- Decreases excretion of calcium
- Increases excretion of phosphorus

**PTH effects on bone**
- Releases calcium and phosphorus
- Sense low serum calcium and increase PTH secretion

**PTH effects on the Small Intestine**
- Increases absorption of dietary calcium and phosphorus

**Red inhibits**
- Black stimulates

**Magnesium**
A useful way of looking at how hormones affect tissues to preserve calcium homeostasis is to examine the effects of calcium deprivation and calcium loading. The following table summarizes body responses to conditions that would otherwise lead to serious imbalances in calcium and phosphate levels in blood.

<table>
<thead>
<tr>
<th></th>
<th>Low Calcium</th>
<th>High Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTH</td>
<td><strong>Increased</strong></td>
<td><strong>Decreased</strong></td>
</tr>
<tr>
<td>Activated Vitamin D</td>
<td><strong>Increased</strong> synthesis by increased PTH secretion</td>
<td>Synthesis <strong>decreased</strong> due to low PTH secretion</td>
</tr>
<tr>
<td>Calcitonin</td>
<td><strong>Decreased</strong> secretion</td>
<td><strong>Increased</strong> secretion</td>
</tr>
<tr>
<td>Intestinal absorption CA</td>
<td><strong>Increased</strong></td>
<td><strong>Decreased</strong></td>
</tr>
<tr>
<td>Release of CA and phosphate from bone</td>
<td><strong>Increased</strong> by increased PTH hormone and vitamin D</td>
<td><strong>Decreased</strong> due to low PTH hormone and vitamin D</td>
</tr>
<tr>
<td>Renal excretion of calcium</td>
<td><strong>Decreased</strong> due to enhanced tubular reabsorption stimulated by elevated PTH and vitamin D</td>
<td><strong>Increased</strong> due to decreased PTH-stimulated reabsorption.</td>
</tr>
<tr>
<td>Renal excretion of phosphate</td>
<td><strong>Strongly increased</strong> by PTH; this phosphaturic activity prevents adverse effects of elevated phosphate from bone resorption</td>
<td><strong>Decreased</strong> due to hypoparathyroidism</td>
</tr>
</tbody>
</table>
How elevated Phosphorus increases PTH

- Phosphorus levels high
- Phosphate-calcium complexes are formed
- Serum calcium levels reduced
- Decreased calcium level stimulates PTH production in order to raise calcium
- If phosphorus is chronically elevated - persistent elevation in PTH levels
- P Reference range 3.0 - 4.5 mg/dL
- Continuous increased PTH secretion causes Parathyroid hyperplasia
- Elevated P and CA lead to vascular calcification
How does high P weaken bones

• High Phosphorus turns on PTH
• Calcium removed from bone
• Increased Ca++ and P → calcification
• Calcification
  – Red eye syndrome, painful joints, itchy skin
  – Cardiovascular
Other PTH Regulators

- **Hypermagnesemia**
  - Inhibits PTH secretion

- **Hypomagnesemia**
  - Stimulates PTH secretion
  - Very low Mg paradoxically blocks PTH leading to low Mg and Ca

- **Catecholamines**
  - Stimulates PTH secretion - Acting on β adrenergic receptors
Inflammatory cytokines

NF Kappa Beta

Inflammatory Enzymes

COX, LOX

Arachidonic acid

Bad Eicosanoids

TXA2, ASCVD

PGE2, LTB4

Pain PGE2, LTB4

Chronic Illness

Acute phase proteins

CRP, Fibrinogen

EPA, DHA

Good Eicosanoids

Wellness

Trans Fats

High Glucose and Insulin

Hormone Decline

Lack of Exercise

Aging

High Homocysteine

Frans Fats

Nutrition

Glucose and Insulin control

Stress

Infection

Depression

Vitamin D

CRP

Red inhibits

Yellow activates

Resveratrol

EPC’s

Unified Theory of Wellness

Chronic Inflammation Is the Cause and the Effect of the Diseases of Aging

Angiotensin II

Phosphate

PTH

RANKL

Magnesium

Catecholamines

Anti-Inflammatory Cytokines

Adhesion molecules

VCAM1, ICAM1, MCP1, MadCAM1

PGI2 = prostacyclin

good eicosanoids

Resveratrol

Red inhibits

Yellow activates

EPC’s

Gp4

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Catecholamines
Classic Hyperparathyroidism - HPT

• Moans, Groans, Stones and Bones
  – Seen in past - serum calcium was not commonly measured - serum calcium became markedly elevated.
  – Abdominal pain – Moans
    • Peptic ulcer disease
      – Increased gastric acid secretion by elevated Ca
    • Pancreatitis
  – Cognitive changes - Groans
  – Kidney stones - Stones
  – Osteoporosis – Bones
**Classic HPT**

- **Renal**
  - Polyuria
  - Kidney stones
  - Hypercalciuria
  - Rarely nephrocalcinosis

- **Gastrointestinal**
  - Anorexia
  - Nausea
  - Vomiting
  - Abdominal pain
  - Constipation
  - Peptic ulcer disease
  - Acute pancreatitis
• Neuromuscular
  – Proximal myopathy
  – Weakness
  – Easy fatigability
• Psychological – can be subtle
  – Depression
  – Inability to concentrate
  – Memory problems
  – Loss of initiative
  – Anxiety
  – Irritability
  – Sleep disturbance
• Cardiovascular
  – Hypertension
  – Bradycardia
  – Shortened QT interval
  – Left ventricular hypertrophy
HPT today

• Incidentally found when elevated serum calcium levels evaluated
• Usually “asymptomatic” on initial presentation
• Subtle cognitive changes
• Kidney stones may give you a clue
• Awareness is key to diagnosis with borderline Calcium
• Order ionized Calcium and iPTH
Primary Hyperparathyroidism - PHPT

- Most common cause of hypercalcemia in outpatients
- 100,000 patients a year
- 0.1 to 0.3% of the general population
  - 1/500 women
  - 1/2000 men
- Under referred and undertreated surgically
- Dx – chem panels
- Dx screening in patients with
  - High or borderline calcium, ionized calcium
  - Osteoporosis, osteopenia, kidney stones
  - Lab: ionized calcium iPTH, 25-OH D3
Primary Hyperparathyroidism

– Increased production of PTH
– Elevated Calcium
– Adenoma - most common cause– 85%
– Hyperplasia of two + glands - 15%
– Malignancy is rare - < 0.5%
– Over 50, rare in childhood
– Asymptomatic - 75 to 80 percent
Secondary Hyperparathyroidism (SHPT)

- Overproduction of PTH due to abnormal stimulus for its production
  - Most common causes
    - Chronic Renal Failure
    - Vitamin D deficiency
      - Calcium is never high
    - Low Calcium intake
    - Low GI absorption Calcium
- Renal SHPT
  - Develops early in CKD
  - Most patients with ESRD have SHPT
SHPT - Vitamin D deficiency

- 25 (OH) D low, Ca++ low or normal
- 25 (OH) D can be normal with SHPT from renal failure
- Severe 1,25 vitamin D deficiency
- Severe calcium deficiency either inability to absorb in intestines or lack of intake
- Low Vitamin D ↔ Low calcium ↔ PTH stimulation
- Treatment: Vitamin D3 150,000 IU/day x 3 days then 50-100K per week
Vitamin D and PTH

• PTH decreases linearly with vitamin D supplementation

Testing
Serum iPTH (Intact PTH) reference range

- 10-60 pg/mL
- pg/mL divided by 9.43 = pmol/L
- Should upper limit be decreased to 46 pg/mL?
- Consider elevated at 65 pg/ml if...
  - Increased body weight
  - Advanced age
  - Reduced renal function
  - Low dietary calcium
  - Low 25OH vitamin D

PTH testing

- PTH levels are subject to diurnal variation.
- Peaks around 2:00 AM - lowest around 2:00 PM
- Usually checked in am
- Normal PTH  10-65 Pg/ml
- **Optimal intact PTH – 10-30 pg/ml**
  - Divide by 9.43 to conversion to pmol/l
PTH evaluation

- Ca^{++} elevated
- Parathyroid abnormality suspected
- Monitoring for known disease
- Intraoperative to see if surgery was successful
- Preventive and regenerative medicine hormone evaluation
• Drugs that increase PTH levels
  – Phosphates
  – Anticonvulsants
  – Steroids
  – Isoniazid
  – Lithium
  – Rifampin

• Drugs that decrease PTH include
  – Cimetidine
  – Propranolol and Beta Blockers
Ionized Calcium

• Ionized calcium – more accurate measure of physiologic calcium
• Involved in intracellular signaling, enzyme activation and muscle contractions.
• Total Calcium
  – 50% ionized,
  – 40% bound to albumin and
  – 10% other anions (citrate, bicarb, etc)
Calcium and Ionized Calcium

- Normal Levels
  - 8.5-10.2 mg/dl Total
  - 4.5-5.6 mg/dL Ionized

To convert Serum Calcium results:
\[
\text{mg/dL} = \frac{\text{mmol/L}}{4}
\]
Formula for Calculating Ionized CA

- Formulas are not accurate but may give you a clue.
- When in doubt, measure ionized
- Calculation
  \[ \text{Calcium} + (\text{Normal Albumin} - \text{Serum Albumin}) \times 0.8 \]
  - Normal albumin is often 4.0
Phosphate

- Serum phosphorus level
  - 2.5 - 4.5 mg/dL
- In Primary hyperparathyroidism - low due to decreased renal reabsorption
- In Secondary – can be high due to decreased renal excretion
- 85% is present in the mineral phase of bone
Phosphorus - food

• Most foods contain some phosphorus
• High phosphorus content
  – Dairy products
  – Organ meats
• Phosphorous based chemicals in foods are not legally required to be listed
  – Phosphoric acid
  – Calcium and Tricalcium phosphate
• Sodas contain highest inorganic P
• These inorganic phosphate additives raised serum P more rapidly than P in food
  – have more effect on raising PTH
High Phosphorus Intake

- Phosphorus-containing food additives used in processing of most foods and sodas
- Causes SHPT and bone loss in animal models
- Impairs synthesis of 1,25 dihydroxy vitamin D and disrupts calcium homeostasis
- Higher Phosphate diets raised PTH 5-6 ng/dL
- Higher food additive phosphates raised PTH 6-10 ng/dl
- Calvo MS et al., Changing phosphorus content of the U.S. diet: potential for adverse effects on bone. *J Nutr.* 1996 Apr;126(4 Suppl):1168S-80S
- Calvo MS. Dietary considerations to prevent loss of bone and renal function. *Nutrition.* 2000;16(7-8):564-566
Does High Phosphorus Cause High PTH?

- Decreased Ca^{++} stimulates PTH to raise calcium levels by causing a release of calcium from the bone
- When phosphorus chronically elevated, it can cause a persistent elevation in PTH levels
- When phosphorus levels are high, phosphate-calcium complexes are formed, reducing serum calcium levels
- High phosphorus intake is often accompanied by a low calcium intake, accentuating the imbalance.
High Phosphorus Diet /PTH

• Lower Calcium, elevated phosphorus and PTH
• BMD decreased
• Receptor activator of NF-kappaB ligand (RANKL) increased
• Conclusion: secondary hyperparathyroidism due to a high-P diet leads to bone loss via an increase in bone turnover
  – increase in osteoclast number was caused by RANKL

Unified Theory of Wellness

Chronic Inflammation Is the Cause and the Effect of the Diseases of Aging

Vitamin D

CRP

Red inhibits

Yellow activates

Resveratrol EPC’s

EPA, DHA

Good Eicosanoids

Wellness

TXA2

Atherosclerosis

P53

Angiotensin II

Pain

ASCVD
Vitamin D

• Optimal level is = Concentration of Vitamin D that maximally suppresses PTH

25 OH Vitamin D3

- Low vitamin D3 leads to secondary hyperparathyroidism and increased bone loss
- Supplementation with D3 leads to suppression of PTH

25OH D vs PTH

• Serum 25-OH D concentration for optimal health: level at which PTH declines to a minimum
• Increasing 25-OH D continuously lower PTH continuously
• Striking percentage of elevated PTH with sub-optimal 25-OH D

• Valcour A et al. Effects of Age and Serum 25-OH-Vitamin D on Serum Parathyroid Hormone Levels. J Clin Endocrinol Metab, November 2012, 97(11)
Graph showing the relationship between PTH Median Value pg/mL and 25-OHD Frequency Class Mean ng/mL. The equation is:

\[ Y = 11.9 + 140.6 \times [25-OHD]^{-0.46} \]

with an \( R^2 = 0.994 \).
Hypotheses

1. Prolonged 25-OH D deficiency could induce secondary HPT, which could ultimately become autonomous

2. Long-term vitamin D deficiency could cause parathyroid gland tissue hyperplasia or induce somatic mutations leading to the development of parathyroid adenomas
Pathogenesis - PHPT

• PHPT often is present for many years before clinical diagnosis and often asymptomatic
• Possible early warnings
  — Unexplained elevated calcium with normal (low)iPTH
    Can lead to hyperplasia of parathyroids
  — Normal calcium with iPTH > 35
    Can lead to parathyroid adenoma
• Can early treatment with Vit D3 change this process?
• PTH levels in the upper third or higher
  — May be an indicator for later development of PHPT, especially in the setting of a replete vitamin D status.
• Rejnmark L et al. Further Insights into the Pathogenesis of Primary Hyperparathyroidism: A Nested Case-Control Study J Clin Endocrinol Metab, January 2013, 98(1):
Vitamin D Safety in PHPT

- PHPT
- 25 OH Vitamin D  15 ng/dl
- Treated with D3 50K/week
  - 25 (OH) D3 increased to 43 ng/dl
- No change in Ca++ or iPTH
- No new kidney stones or other complications
Parathyroid hormone-related protein (PTHrP)

• Ca high and iPTH low?
• Member of PTH superfamily
• Same N terminal end as PTH
• Hypercalcemia of Malignancy
  – Paraneoplastic phenomenon
  – Lung, Breast, Renal, squamous cell
  – Others
• Normal functions
  – Tooth eruption
  – Mammary gland development
  – Lactation calcium supply
Any Suspicion of Hyperparathyroidism?

• To Scan or not to scan
Parathyroid Scan

- Technetium sestamibi
  - Increased absorption in hyperparathyroid chief cells, almost no absorption in the oxyphil cells
Surgery
Incision used for a minimally invasive parathyroidectomy.

Intraoperative parathyroid hormone (IOPTH) measurements showing an appropriate decrease in PTH levels 5 minutes and 10 minutes after excision of an adenoma.

Conventional Standards for Surgery

• Surgery
  – Ca > 1 mg/dl above range
  – 24 hour urinary CA > 400 mg
  – Creatinine Clearance < 30% of normal
  – BMD < -2.5 at any site
  – Age < 50
  – Coexisting disease
  – Unable to have consistent follow up

Optimal Results

- Everyone

- Surgery can usually be done in less than 20 min under local anesthesia
Osteoporosis Connections

- PTH
- Phosphorous
- Estradiol
- RANKL- Receptor activator of nuclear factor kappa-B ligand
- NFkB
- Inflammation
- Fruits and Spices
Treatments for Osteoporosis Reversal

- Teraparitide
- Vitamin D3 (5-10K IU)
- Growth Hormone (0.2-.6 mg)
- Calcitonin (200 IU)
- Magnesium
- Omega 3 fish oil
- Estradiol (0.1-2 mg)
- Progesterone (50-300mg)
- Testosterone (1-5mg)
- Boron (6-9 mg)
- Strontium (700 mg)
- Vitamin K (45 mg)
- Calcium
  - Diet preferred not supps
- Dried Plum
- Exercise
Calcium supps – more MI’s?


- Bolland et al. Vascular events in healthy older women receiving calcium supplementation: randomised controlled trial. BMJ. 2008;336:262-266
Dried Plums and Osteoporosis

• 12 month study postmenopausal women, DEXA
• Dried plum (100 g/d) 500 mg Ca plus 400 IU vitamin D daily, exercise recorded, Dried apple control group
• Dried plum significantly decreased serum levels of bone turnover markers
• Dried Plums significantly improved BMD ulna and spine
• Suppressed the rate of bone turnover.

Dried Plum and IGF1, RANKL

- Increases IGF-1
- Decreases RANKL and NFKB

Inhibition of bone resorption in rats by 24 fresh food items and the red wine residue.

COMB protocol for bone health

- DHA (from Purified Fish Oil): 250mg/day
- Vitamin D₃: 2000IU/day
- Vitamin K₂ (non-synthetic MK₇ form): 100ug/day
- Strontium citrate: 680mg/day
- Elemental magnesium: 25mg/day
- Dietary sources of calcium recommended
- Daily impact exercising encouraged
## Results of COMB

<table>
<thead>
<tr>
<th>Percent change</th>
<th>COMB protocol: one year whole group (postmenopausal females)</th>
<th>Comparison to Strontium Ranelate at one year [21]</th>
<th>Comparison to Alendronate at one year [44]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral neck</td>
<td>4%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Total hip</td>
<td>3%</td>
<td>3-4%</td>
<td>2%</td>
</tr>
<tr>
<td>Lowest hip site</td>
<td>4%</td>
<td>Not calculated</td>
<td>Not calculated</td>
</tr>
<tr>
<td>Total spine</td>
<td>6%</td>
<td>5-6%</td>
<td>4%</td>
</tr>
<tr>
<td>Lowest spine site</td>
<td>8%</td>
<td>Not calculated</td>
<td>Not calculated</td>
</tr>
</tbody>
</table>
Conclusions

• The COMB study demonstrated that this combination of micronutrients along with regular weight-bearing exercise is as or more effective than bisphosphonates.
Fractures and Bisphosphonates


Teriparatide (PTH 1-34)

- SQ injection, 1 hour half life
- 20 mcg SQ daily
- Used with caution on patients on digoxin due to rise in calcium and potential for toxicity
- Expensive
- Osteosarcoma in rats, Black Box warning
  - 2 cases in > 430,000 humans

Teriparitide

- Anabolic agent stimulates bone formation within 1 month
- Peaks and plateaus developing resistance to treatment within 2 years
- Used for osteonecrosis of jaw treatment with good effect
- Effective in reducing fracture risk
- Greater increases in BMD as compared to bisphosphonates.
- Synergistic with BHRT

Elevated PTH Associated with multiple poor health outcomes

- Brain
- Bone
- Atherosclerosis
- Cardiovascular
- Inflammation
PTH – Independent risk factor for poor health outcomes

- Benefits Overlap with Vitamin D and some might be though Vitamin D receptor (VDR)
- Other benefits are independent of Vitamin D
PTH and Inflammation

- PHPT increases gene expression of inflammation with inflammatory cytokines
- Acute phase response
- Increased risk of CVD

- McCarty, Mark. Secondary Hyperparathyroidism promotes the acute phase response- a rationale for supplemental vitamin D in prevention of vascular events in the elderly. *Medical Hypotheses*. Volume 64, issue 5, pg 1022-1026.2005
Inflammatory cytokines
NF Kappa Beta
Inflammatory Enzymes COX, LOX
Coxibs block vioxx
PGI2=prostacyclin good eicosanoids
Good Eicosanoids
EPA, DHA
Pro-oxidants Viral Infections
Anti-oxidants Glutathione
EPA, DHA
Good Eicosanoids
PGE2: Pain Cancer Skin aging
ASCVD
Chronic Illness
Wellness
Angiotensin II
Phosphate
RANKL
Immune
Catecholamines
Wellness
Unified Theory of
Inflammation Is the Cause and the Effect of the Diseases of Aging
PTH and brain

- Age-induced increased PTH associated with cognitive decline and dementia
- PTH <30 had increased BMD, less P300 latency relative to those with levels >30.

Conclusion:
- Increased PTH may be biological marker for dementia and osteoporosis
- Control of PTH may be important for protecting against dementia
- Calcium overloading from PTH crossing BBB can damage neurons

Braverman, E et al. Age-related increases in parathyroid hormone may be antecedent to both osteoporosis and dementia. *BMC Endocrine Disorders*. 2009, 9:21
Mild PHPT
Anxiety/Depression

• Women with mild PHPT had more depression, anxiety and memory deficits than controls

• After parathyroidectomy depression and memory improved equal to controls

• Wide range of memory tests done
PTH - Mortality

• PHPT - increased mortality, improved by parathyroidectomy

• Even small PTH elevation predicts increased hospital mortality
  – Higher APACHE II score

• Vascular calcification higher with higher PTH
  – Calcific Aortic stenosis
  – Vascular calcification in renal failure
  – Inversely related to Magnesium

• Peiris, A et al. Secondary Hyperparathyroidism: Benign Bystander or Culpable Contributor to Adverse Health Outcomes? Southern Medical Journal. Volume 105, Number 1, January 2012
Highest Quartile PTH (in reference range) 2 x mortality

Hypertension

• >50% of patients of PHPT have HTN
  – Increased calcium levels
  – Increased peripheral resistance
  – Increased activity of the renin–angiotensin–aldosterone system

• Treatment of PHPT by surgery
  – decline in BP
  – decrease in plasma renin activity

• Sandeep Chopra et al. The thyroid hormone, parathyroid hormone and vitamin D associated hypertension. *Indian J Endocrinol Metab.* 2011 October; 15(Suppl4): S354–S360
PTH and CV Mortality

- 958 men – mean age 71
- PTH increase- vascular calcifications, LVH and myocardial fibrosis
- Higher PTH- higher risk for CV mortality – HR 1.38 p<.001

**Conclusion:** PTH levels predict CV mortality even when in normal levels

Phosphorus and CVD

- 3368 Framingham Offspring study participants mean age 44, free of CVD and CKD.

CONCLUSION: Higher serum phosphorus levels are associated with an increased CVD

PTH and Cartilage

• Conclusions:
  – Higher iPTH - less knee cartilage volume in women 35-49
  – Animal studies - higher PTH concentrations reduce the healing ability of cartilage

Adiposity and PTH

• Body fat associated with PTH in healthy adults with PTH in “normal” range.


• Bolland MJ et al. Fat mass is an important predictor of parathyroid hormone levels in postmenopausal women. *Bone*. 2006 Mar;38(3):317-21
PTH - weight gain

- Increased free intracellular calcium in adipocytes blunts catecholamine response
- PHPT and SHPT associated with weight gain
Functional Considerations

• Look for elevated Ca\(^{++}\) on metabolic panel
• Be aware that low albumin raises ionized Ca\(^{++}\)
• Be aware that HPT symptoms can be subtle
• Be aware that non-specific complaints such as fatigue, anxiety, lack of well being can be due to PHPT
• Higher PTH:
  – multiple adverse health outcomes and increased inflammation
  – Independent of vitamin D and Calcium
Optimize PTH: <30 ng/dL

• Adequate calcium intake from diet
  – But not too much
• Optimal Vitamin D status
• Optimal Magnesium status
• Optimal Phosphate status
  – Low inorganic phosphate intake
  – Limit sodas and processed foods
  – Limit animal protein to what is required
• Control catecholamines
  – Stress reduction
  – Meditation
• Optimize renal function
  – Adequate hydration
  – Limit NSAID’s
  – Optimal Blood Pressure
  – Optimal Glucose and Insulin Status
• Comprehensive Evaluation should include PTH and phosphate
• Limit inflammation
  – Omega 3 supplement
  – Limit omega 6
  – Anti-inflammatory nutrition, supplements and lifestyle
“Asymptomatic” PHPT

• Reasons for surgical treatment
  – Subtle cognitive changes may be present in “asymptomatic” patients
  – Most patients have disease progression
  – BMD Improves after surgery
  – Cardiovascular risks with elevated PTH
  – Patients just feel better and have better Q of L
  – Ask an “asymptomatic” patient with PHPT how she felt after surgery
Advantages of surgery in “asymptomatic” patients

- Improvement in bone density
- Reduced frequency of kidney stones
- Neuro improvement
- Improved Quality of Life
Case Studies

- 59 y/o female with cognitive dysfunction, depression, anxiety getting worse over 1 year
- Had extensive workup with MRI, genetic testing, neurotransmitters and hormones etc. Ca\(^{++}\) 10.1 albumin 3.4, positive for ApoE double allele
- Hormones optimized, “brain boosters” used, adrenal fatigue addressed not much change
- Ionized Ca\(^{++}\) = 6.9 (4.5-5.6) mg/dl
- iPTH – 197 pg/ml
- Dx: parathyroid adenoma
- surgery –”Dementia” cured
• 50 y/o male with chronic abd pain x 1 year
• Lab normal except for low hormones.
• Ca++ 10.2, Albumin 4.0, 25-OH Vit D 105,
• CT abd: Stones in renal pelvis bilateral, no hydronephrosis or ureteral stones
• Meds: Omeprazole, Tramadol
• Supplements: Vitamin D 10K/day, Multi Vitamins, probiotics, digestive enzymes, Betaine HCl
• Hormones optimized, dysbiosis corrected
• Ionized Ca++ = 7.1 (4.5-5.6) mg/dl
• iPTH – 119 pg/ml
• Dx Parathyroid Adenoma-surgery symptoms resolved
Elevated Calcium Workup

Elevated Screening Calcium

Recheck PTH i, ionized CA, Phosphate, Mag, Creatinine, 25OH D

Taking D supplement? Is 25OH D > 120 ng/dl? Hold D supplement

Asymptomatic, Normal PTHi and Ionized Calcium

YES

Monitor, optimize D and calcium, low phosphate diet

NO

PTHi elevated or upper 2/3 RR and/or Is calcium elevated over 10.2

Parathyroid Scan

positive scan?

YES

Primary HPT-adenoma

Surgery- micro

NO

24 hour urine Calcium

Low Calcium

FHH suspect-genetic screening

PTHi low

Measure PTHrP and Vitamin D panel

If PTHrP elevated

Malignancy possible - eval for SCC/Breast CA

If 1,25 vit D elevated

Chest xray

Evaluate for sarcoid, lymphoma, granulomatous disease
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SECOND EDITION

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Guidebook includes Treatment Algorithms and Abstracts