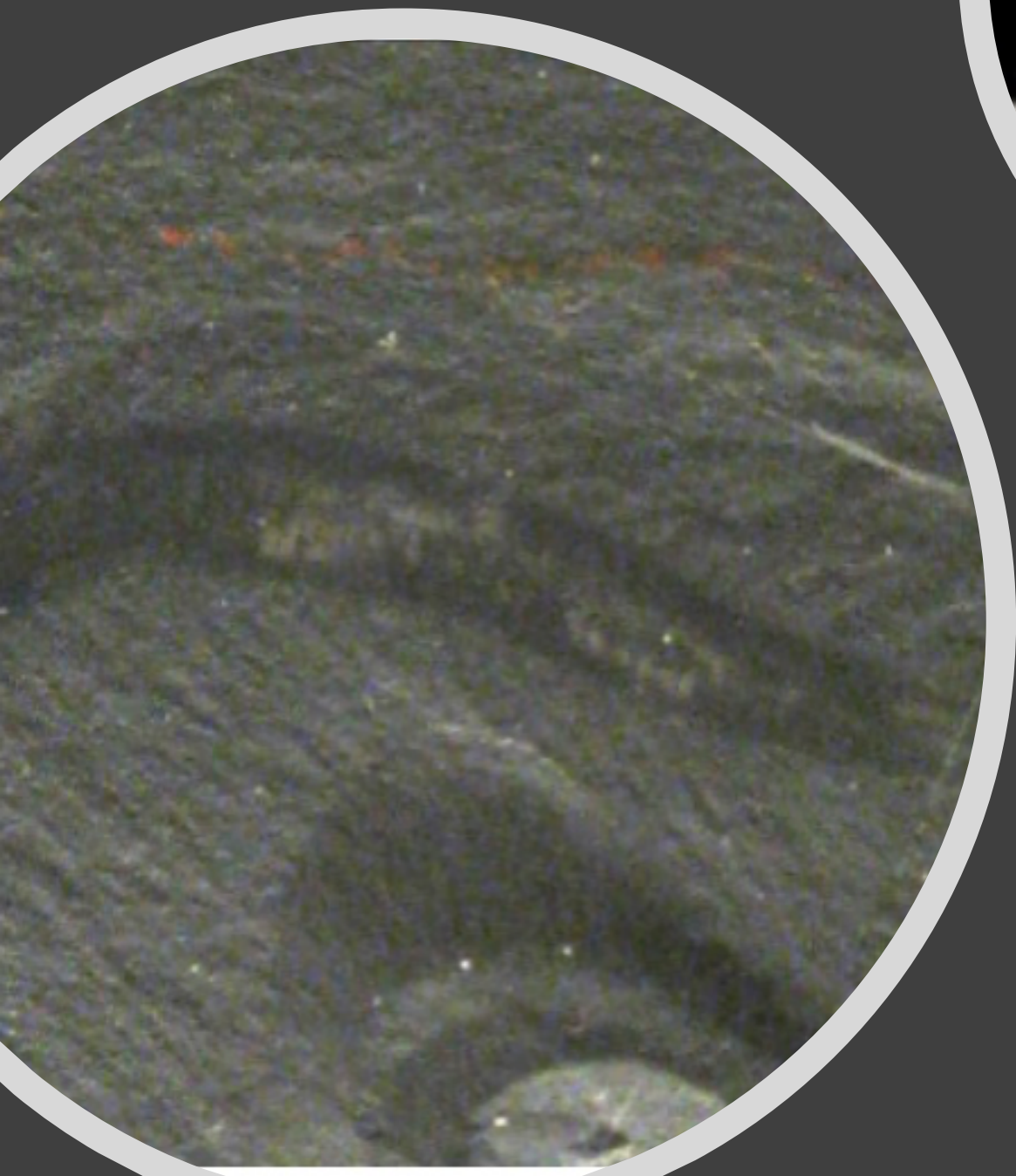




Skeleton Keys

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Disclosures:

none

The Bare Bones...

Objectives

- Discuss the epidemiology and clinical significance of osteoporosis in the US
- Identify common primary and secondary causes & risk factors for osteoporosis
- Describe the various treatment modalities for osteoporosis: nutritional, biomechanical, and pharmacologic
- Investigate post fracture management and treatment strategies related to bone health through case studies



I Love Lucy...

- Discovered in Ethiopia 1974
- 3.4 million years old
- 3'7", fully developed female hominid

Lucy's skeleton represents the earliest anthropological evidence of osteoporosis





With every bone in your body... The Burden of Osteoporosis

Chronic, progressive disease of either *quantity* (BMD) and/or *quality* (microarchitecture) of skeletal bone resulting from disruption of normal balance of bone remodeling.

- Osteoporosis is common, but not “normal”
- Over 50% of women & 30-45% of men >50 y/o have either osteopenia or osteoporosis
- 70% of adults >80 y/o have osteoporosis

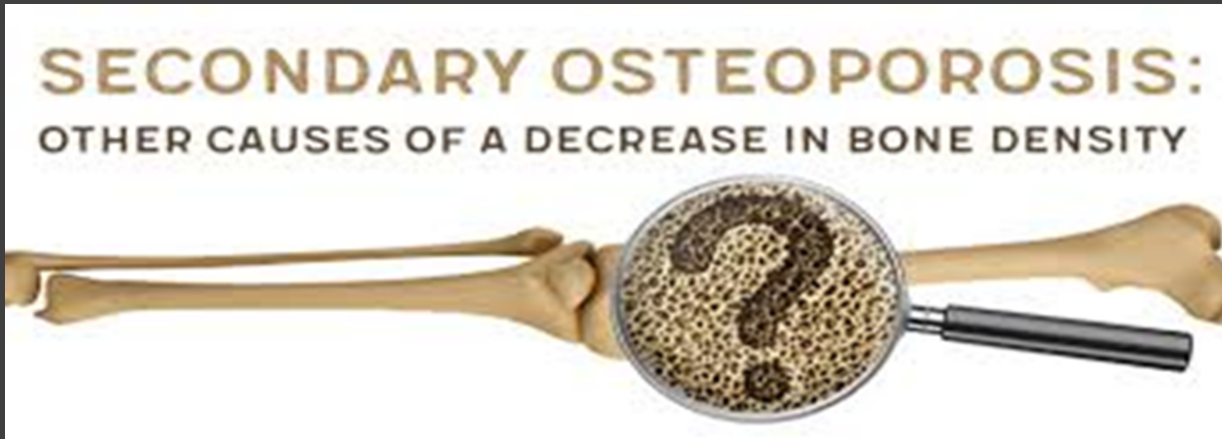


A bone to pick... Care Gaps

- 6% of hip fx patients admitted to tertiary care are adequately treated for osteoporosis at discharge.
- 14% of fx patients get osteoporosis care in primary care *within 5 years* of initial fx.
- 21% of Medicare beneficiaries with hip fx were provided Rx treatment

Skeletons in the closet...

Common risk factors for age related and secondary osteoporosis



- Age
- Hormone deficiency
- Family history
- Female osteologic sex
- Dietary insufficiencies
- Sedentary lifestyle/immobility
- Smoking, Alcohol abuse
- Low body weight
- Thyroid disorders
- Liver & kidney disease
- GI absorption disorders
- Medications (antiepileptics, glucocorticoids, aromatase inhibitors, heparin)
- Malignancies

Bad to the bone...

Screening & evaluating osteoporosis

IMAGING

Dual Energy X-ray Absorptiometry (DXA)

- Vertebral spine: +predictive value for vertebral fx risk
*falsely elevated scores w/ OA
- Femur and hip sites-best correlation w/ hip fx risk
- 1/3 Distal Radius: less predictive, but helpful for obtaining PAs
- Q5y in healthy pt, Q2y w/ hx osteopenia, osteoporosis or hx fragility fx

FRAX Scores

- Pt risk assessment associated with individual clinical risk factors & BMD

Trabecular Bone Scoring

- measure of bone texture correlated w/bone microarchitecture
- best available tool to estimate bone quality



Laboratory analyses

Primary utility is to exclude less common contributors:

Osteomalacia

Multiple myeloma

Primary hyperparathyroidism

Adynamic bone disease

Rare genetic disorders (x linked hypophosphatemia,
hypophosphatasia, familial hypercalciuria)

Always includes: CBC, CMP, PTH, Vit D25-OHD

May include: Alk Phos, TSH, Free T4, hormone levels, calcitonin

Consider: CTX, P1NP, NTX

Markers of bone turnover, have limited diagnostic value
Useful in monitoring effects of treatment than in diagnosis

Bones of Contention...

Current Guidelines



US Preventive Task Force (& AAFP)

Assessment:

- all women >65
- women <65 in context of 1 or more risk factors
- postmenopausal women with a history of fx
- “The current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis to prevent osteoporotic fractures in men.”

Treatment:

- T score <-2.5 and no additional risk factors
- T score <1.5 if any risk factor
- Everyone with prior vertebral/hip fx

American Academy of Clinical Endocrinologists

Assessment:

- All postmenopausal women aged ≥ 50
- Premenopausal or younger women based on clinical fracture risk profile
- Consider in men based on clinical fracture risk profile

Treatment:

- T score <-2.5 and no additional risk factors
- T Score > -2.5 with hx of fragility fx
- T-score -1.0 to -2.5 if the FRAX[®] 10-year probability for major osteoporotic fx is $\geq 20\%$ or 10-year probability of hip fx is $\geq 3\%$

The nearer the bone, the sweeter the meat...

Treating Osteoporosis



Treatment goal:

Decreased
fracture
incidence!



Surrogate outcome: BMD

Older women are at higher risk for fracture than younger women ***with the same BMD*** due to changes in bone microarchitecture.



Treatment options

Calcium, Vit D, Calcitonin
HRT/SERMs
Bisphosphonates
RANKL-I
Anabolics
Monoclonal antibodies

Calcium and Vitamin D

Use alone or with
other therapies

Reassess
adherence often

>50% of adults get insufficient amounts

Calcium and Vit D supplementation

↓ hip fracture risk in older adults!

Calcium goals: (from combo supplement and diet)

1000-1200 mg/day in women >50

1200-1500 mg/day in men >50

Vitamin D (25OH):

Treat to target 40-50.

Treat with D3 (D2 for vegans)

Higher risk: malabsorption (IBD, bariatric surgery, anorexia) renal & liver dz (2/2 Vit D synthesis)



Natural $\neq$ safe

Ask about supplements!

Calcitonin, HRT, SERMs

most appropriate for early tx of low risk pts

Calcitonin

- Minimally effective for fracture prevention
- 200 IU nasally/day (alternating nares)
- *May* decrease pain 2/2 VCF in acute phase

Estrogen

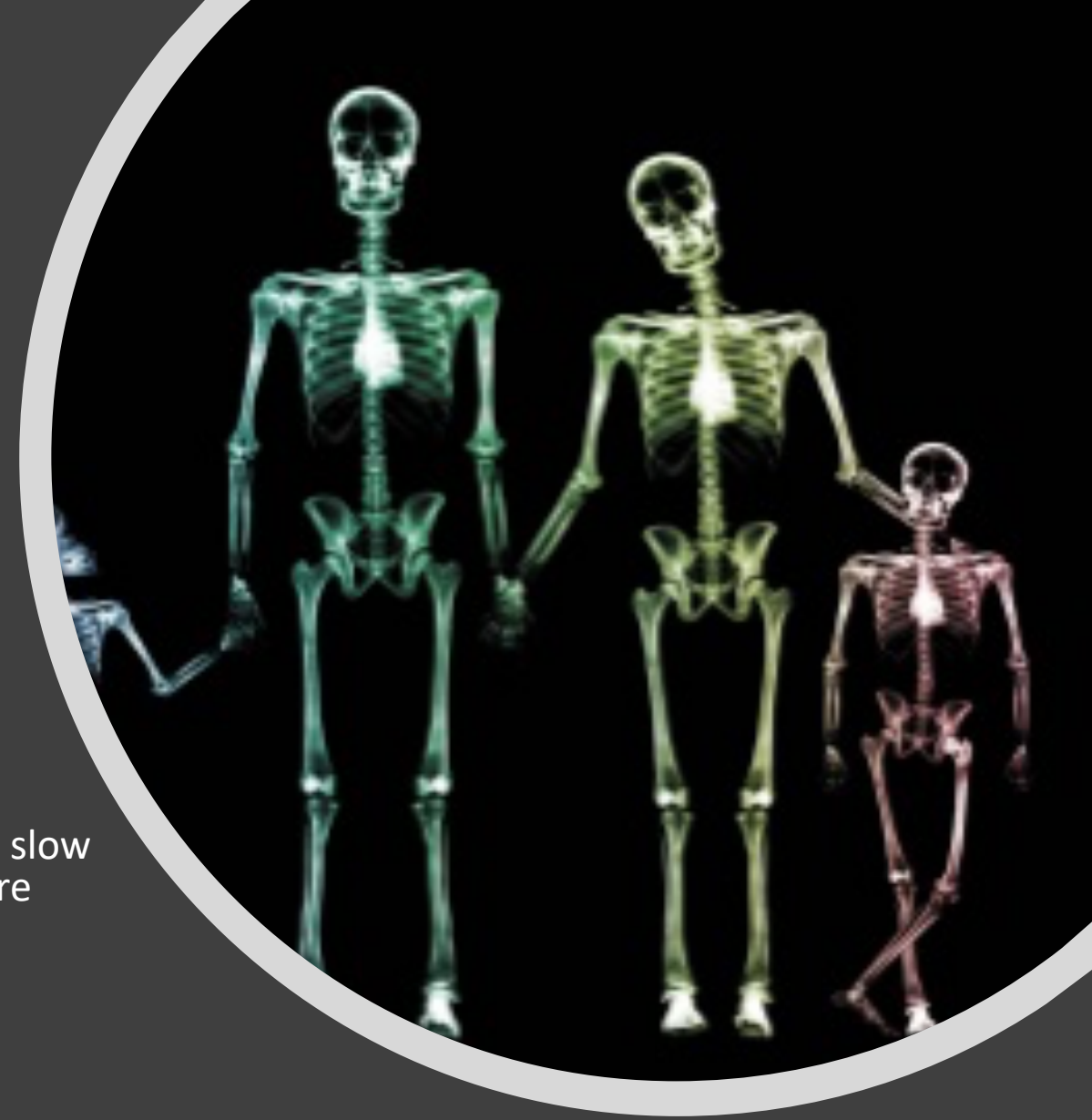
- Decrease bone resorption
- Best effect when initiated within 5 years onset perimenopause
- Increased risk for DVT & hormonally driven cancers in high risk pts

Testosterone

- Low T can contribute to early bone loss, and supplementation may slow bone loss, but testosterone has NO indication for secondary fracture prevention

Selective Estrogen Receptor Modulators

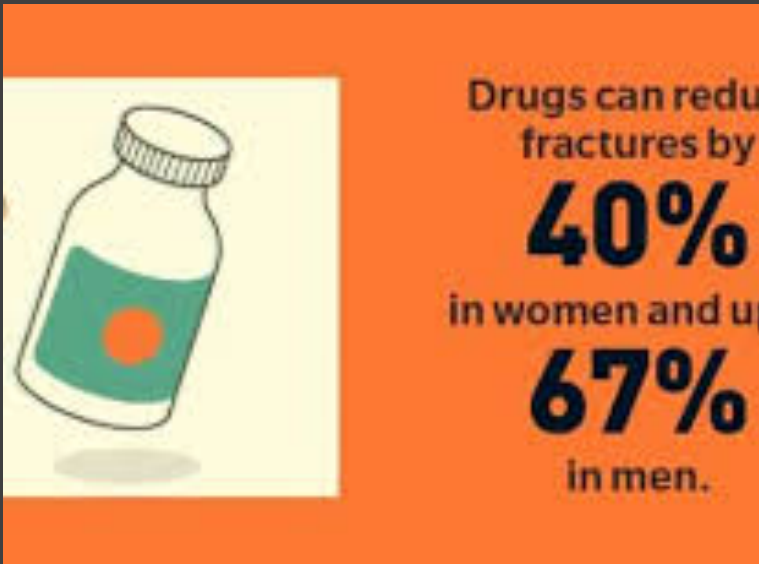
- Raloxifene (Evista)
- Decrease bone resorption similar to estrogen
- Decrease risk for breast cancer
- May lead to increased vasomotor symptoms associated with menopause



Bisphosphonates

BISPHOSPHONATES: antiresorptive

- Bind to bone surface & inhibit osteoclast activity
Their very long half life permits consideration of “drug holidays”
- Consistently demonstrate decrease in hip & vertebral fractures
 - Oral: Alendronate, risedronate , ibandronate.
 - Poor adherence and low GI absorption impacts efficacy
 - Contraindicated for refractory GERD, hx UGIB, Barrett's
 - IV: Zoledronic Acid
 - Commonly causes ‘acute phase reaction’
 - Infuse slowly, in well hydrated pt to avoid
 - Contraindicated in renal failure (minimum CrCl >29)



Rank ligand inhibitor

Prolia (denosumab)

- Administered in clinic subcutaneously Q 6 months
- Length of treatment 10 years, or more
- Bills through Medicare B or Major Medical coverage
- Profound suppression of RANKL = decreased bone remodeling
- “Rebound effect” at d/c, needs to be f/u with *something*;
 - Observing CTX trends is the best way to determine next steps
- No contraindications for CKD except w/ persistent, profound hypoCa⁺
- Risk for AFF (Significantly more common in Asian women).
 - Consider obtaining xrays of femurs when stopping therapy.
- Generally well tolerated
- May cause hypocalcemia; check serum Ca⁺ before injection



Alas, poor Yorick...

Medication Related Osteonecrosis of the Jaw

- RARE 4/10,000 in untreated population
5/10,000 in treated population
- Usually associated with significant underlying periodontal disease, metastatic disease, hx of radiation to head/neck
- More common with IV & SQ antiresorptives than PO
- Risk goes up with length of treatment
- AAOMS and ADA both support use of bisphosphonates for osteoporosis, and neither recommends deferring any indicated dental work during bisphosphonate therapy.



Anabolics: parathyroid hormone pulse therapy

PTH stimulates bone formation first, and later stimulates bone remodeling*

Abaloparatide (Tymlos)

Parathyroid hormone–related peptide

Daily SQ injection x18-24 months

Teriparatide (Forteo)

Parathyroid hormone analog

Daily SQ injection x24 months

Both agents demonstrate increased BMD at 90 days tx

Both demonstrate up to 90% decrease fx rate

Useful to expedite healing of nonunion fractures

Evolving peri-operative role in TJR

New investigations for use in OA related pain

Evolving data regarding use in avascular necrosis

BLACK BOX WARNING: REMAINS FOR TYMLOS ONLY, AND IS PENDING REMOVAL (OSTEOSARCOMA)





Anti-sclerostin Therapy: mAb

Romosozumab (Evenity)

- SQ injection in clinic monthly x12 months
- Dual anti-resorptive and anabolic effects
- Increases bone mass throughout skeleton
- Sclerostin antibody increases formation of cancellous bone
- May cause hypocalcemia

BLACK BOX WARNING:

AMI or CVA within preceding 12 months

Sticks & Stones...

Reducing Fractures

Nutritional education and support

Pharmacologic osteoporosis treatment

Weight bearing, resistance & balance training

Fall Prevention:

- Prior fall, or verbalized fear of falling
- Cognitive decline, especially presenting w/ impulsivity
- Loss of vision and/or hearing
- Peripheral neuropathy
- Weakness, sarcopenia, deconditioning
- Stroke, hemiplegia
- ETOH or drug abuse
- Medications (anticholinergics, tcas, opioids, benzos)
- Uncontrolled pain



Case Study #1: 65 y/o F w/o fx hx presents for routine annual exam, no acute complaints.

- PMHx: hypothyroid, postmenopausal (natural, mid 50s)
- PSHx: laproscopic cholecystectomy 2005
- Current med list: levothyroxine, MVI
- No previous fx, no FH osteoporotic fx
- BMI 26, Pilates 3x week, walks 1 mile daily, reports 1 glass wine “on holidays,” describes good diet and denies hx falls
- DXA Oct 2020: TScores LFN -2.6, LTH -2.2, LS -1.6; FRAX: HIP 1.4%, MOF 9.2%
- Current Labs:
 - Vit D 31 mg/dl, Creatinine, GFR, Ca, Mg, PO₄, PTH, TSH all WNL

- Diagnoses?
- Describe treatment options:



Case Study #2: 70 y/o F w/ 3 week hx LBP after lifting heavy pots while gardening. XR today w/ +VCFs at L1, L2

- PMHx: GERD, CDD, endometriosis, vaginal atrophy, +tobacco use 4-6 cigarettes/day x30y
- PSHx: TAH & BSO age 35 w/ oral HRT x5 years
- Current medication list: sertraline, omeprazole, vaginal estradiol cream
- No personal hx previous fx, no FH OP
- BMI 24, minimal physical activity/exercise, no alcohol, dairy free diet due to lactose intolerance and no hx previous falls
- DXA May 2019: TScores LFN -2.4, LTH -2.2, LS -1.5
- Current Labs:
 - Vitamin D 14 mg/dl, PTH 89 (9-77), Creatinine, GFR, Ca, Mg, PO4, TSH all WNL

- Diagnoses?
- Describe treatment options:



Case Study #3: 76 y/o M w/ nonunion s/p right ankle arthrodesis Dec 2019 due to intractable OA pain at old tibialtalar fracture site (college football injury)

- PMHx: prostate ca (2017) w/ external beam rad tx, advodart x30 months, 6 cycles of docetaxel completed July 2020, metastases to L1, L2 per bone scan 12/2020. Gleason 10. Hx also includes essential tremor, mild HTN.
- Previous fx hx: left DR 2/2 slip/fall on ice 2019
- Current medication list: Lupron, prednisone, propranolol, enalapril, latanoprost ophthalmic.
- BMI 21. Previously highly active, now sedentary 2/2 pain & instability, no alcohol, no tobacco, denies recurrent falls
- DXA 2019: T Scores LFN -3.0, LTH, -2.7, LS -2.1
- Current Labs:
Vitamin D 25 mg/dl, Ca 11.4, GFR 50, PTH, Creatinine, Mg, PO4, PTH, TSH all WNL

- Diagnoses?
- Describe treatment options:



QUESTIONS



Helpful Resources:

- <https://www.tandfonline.com/doi/full/10.1080/03007995.2020.1824897>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4620731/>
- https://www.aaoms.org/docs/govt_affairs/advocacy_white_papers/mronj_position_paper.pdf
- <https://www.sheffield.ac.uk/FRAX/tool.aspx?country=9>

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*If the bones are good,
the rest don't matter...*

<https://www.youtube.com/watch?v=urMgPHwE7Zk&feature=youtu.be>