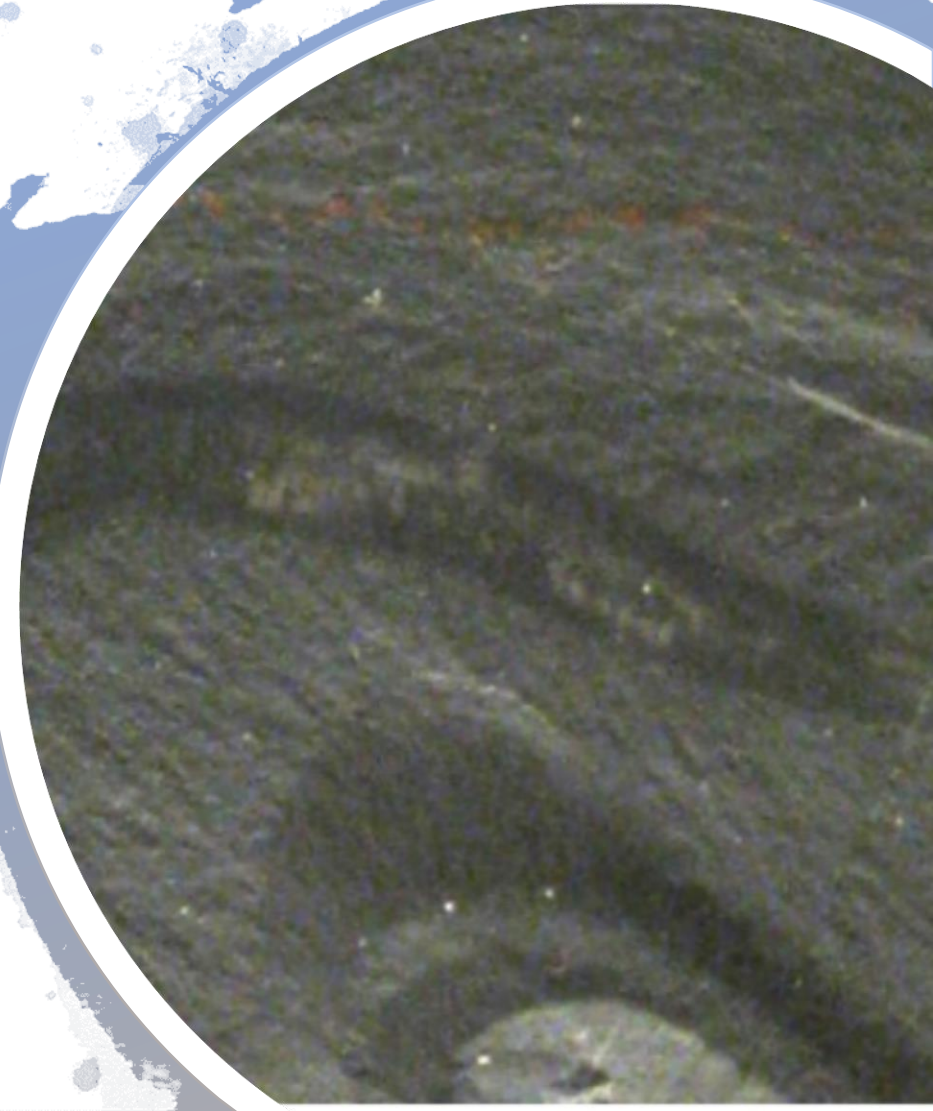# Skeleton Keys

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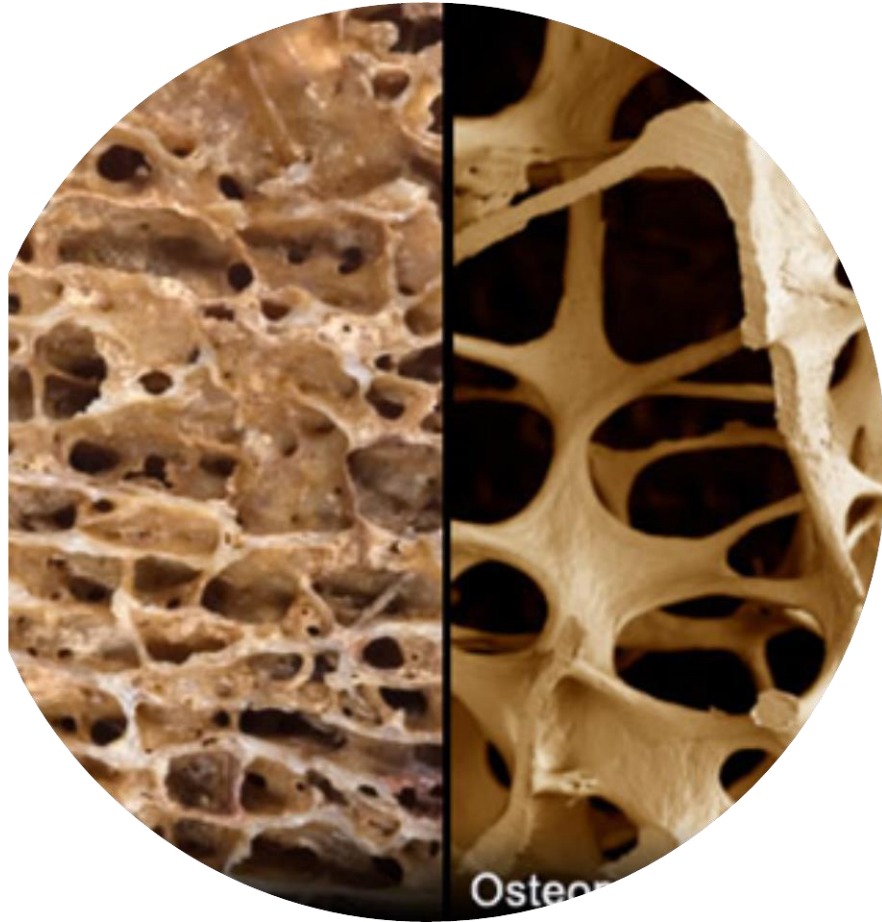Department of Orthopaedics

I Love Lucy

Discovered in Ethiopia 1974

3.4 million years old

3'7", thought to be fully developed female hominid

Earliest example of the biomechanical ability to walk upright due to the evolution of lumbar lordosis, never before seen in a biped

Lucy's skeleton represents the earliest evidence of osteoporosis

Bones of Contention…
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.

Most commonly related to aging.

➢ Decreased bone anabolism
➢ Accelerated bone catabolism
➢ Osteoporosis is common, but not "normal."
➢ Over 50% of women and 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

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 between −1.0 and −2.5 if the FRAX® 10-year probability for major osteoporotic fx is ≥20% or the 10-year probability of hip fx is ≥3%

Skeletons in the closet…
Common risk factors for age related and secondary osteoporosis

SECONDARY OSTEOPOROSIS:
OTHER CAUSES OF A DECREASE IN BONE DENSITY

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

A bare bones approach... Diagnosing Osteoporosis

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, LFTs, SPEP/UPEP, Bone specific Alk Phos, Celiac panel, U24Ca, Testosterone, female hormone panel, calcitonin.

➢ patient specific, per H&P and clinical judgement.

➢ Markers of bone turnover (CTX, P1NP, NTX):
- Limited diagnostic value
- more useful in monitoring effects of treatment than in diagnosis

Working our fingers to the bone…
Imaging to evaluate osteoporosis

Dual Energy X-ray Absorptiometry (DXA)

- Vertebral spine: +predictive value for vertebral fracture risk
  *falsely elevated scores w/ OA

- Femur and hip sites-best correlation w/ hip fracture risk

- 1/3 Distal Radius: less predictive, but often helpful for obtaining PAs

- Q5y in healthy patients, Q2y w/ hx osteopenia, osteoporosis or hx fragility fracture
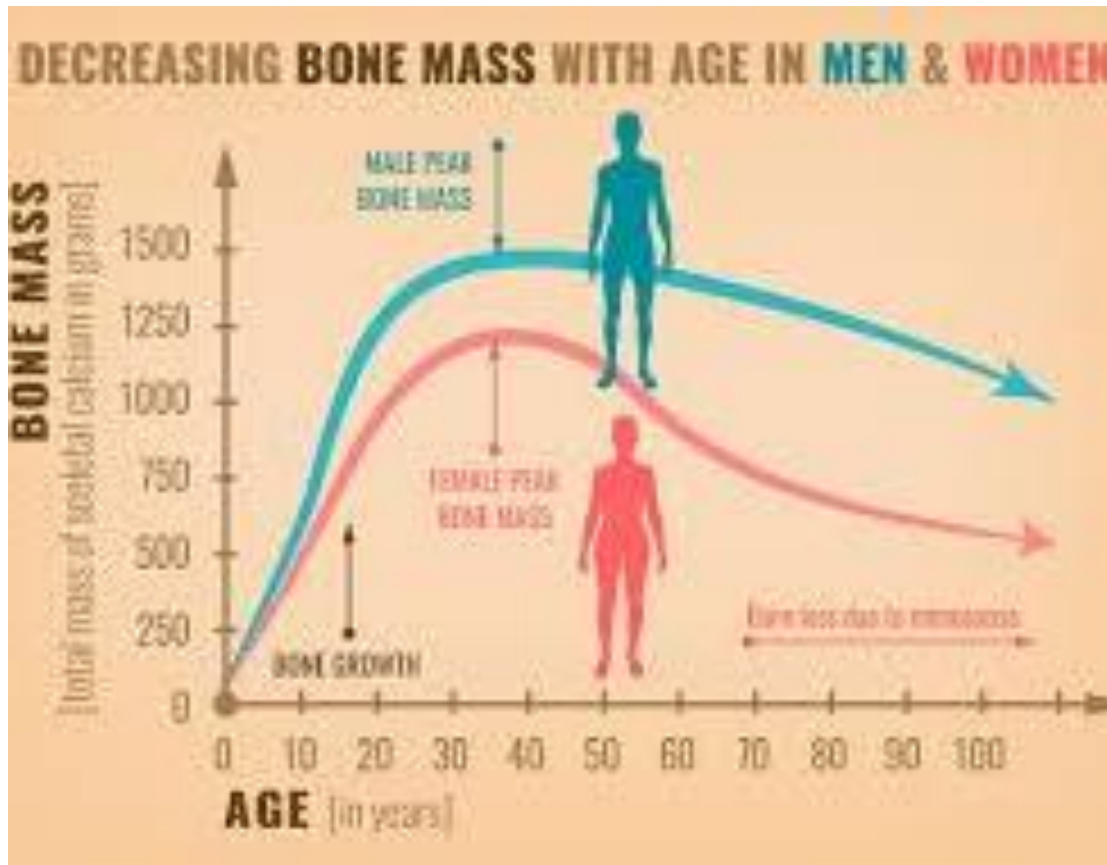
FRAX Scores

- patient risk assessment associated with individual clinical risk factors as well as BMD at the femoral neck

Trabecular Bone Scoring

- measure of bone texture correlated w/bone microarchitecture of trabecular, cortical,& integral bone

- best available tool to estimate bone quality

Quantitative Ultrasonography: 2D bone mass estimate. Low sensitivity and specificity. Poor predictive tool.

Quantitative CT: 3D technique for quantifying volumetric trabecular bone density that is not affected by spine degeneration. Highly sensitive and specific. QCT detects osteoporosis more frequently than spinal and hip DXA (45.1% versus 10.9%).

DECREASING BONE MASS WITH AGE IN MEN & WOMEN

- ➤T score: For use >50

  SD score of BMD compared to the mean sex matched 20 y/o

- ➤Z score: For use <50

  SD score compared to age matched controls

- ➤WHO Classifications:

  Osteopenia = T score -1 to -2.5

  Osteoporosis = T score <-2.5

- ➤Clinical Pearls:
  - For every SD decrease in T score, relative risk for fx increases 100%
  - *Regardless* of BMD, those w/ prior osteoporotic fx have 5x > risk for recurrent fragility fracture!

Weak in the knees...
Utilizing BMD in clinical decision making

With every bone in your body…
Treating Osteoporosis

Treatment goal:

Decreased fracture incidence!

Surrogate outcome: BMD

Older women are at <u>higher risk</u> 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)

Remind your patients
Natural ≠ safe

Don't overdo it
with supplements!

Calcitonin & HRT

most appropriate for early intervention in low risk patients

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: 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

- <u>Oral:</u> Alendronate, risedronate , ibandronate.
  - Poor adherence and low GI absorption impacts efficacy
  - Contraindicated for refractory GERD, hx UGIB, Barrett's

- <u>IV:</u> Zoledronic Acid
  - Commonly causes 'acute phase reaction'
  - Infuse slowly, in well hydrated pt to avoid
  - Contraindicated in renal failure (minimum CrCl >29)

Drugs can reduce fractures by **40%** in women and up to **67%** in men.

Alas, poor Yorick...
## A note about medication related Osteonecrosis of the Jaw

Fear regarding MR ONJ is the *single most commonly cited reason* for patient (and dentist*) determined treatment cessation

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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 bisphosphonates than PO

- Risk goes up with length of treatment

* The AAOMS and ADA both support use of bisphosphonates for osteoporosis, and *neither recommends deferring any indicated dental work* during bisphosphonate therapy.

https://www.aaoms.org/docs/govt_affairs/advocacy_white_papers/mronj_position_paper.pdf
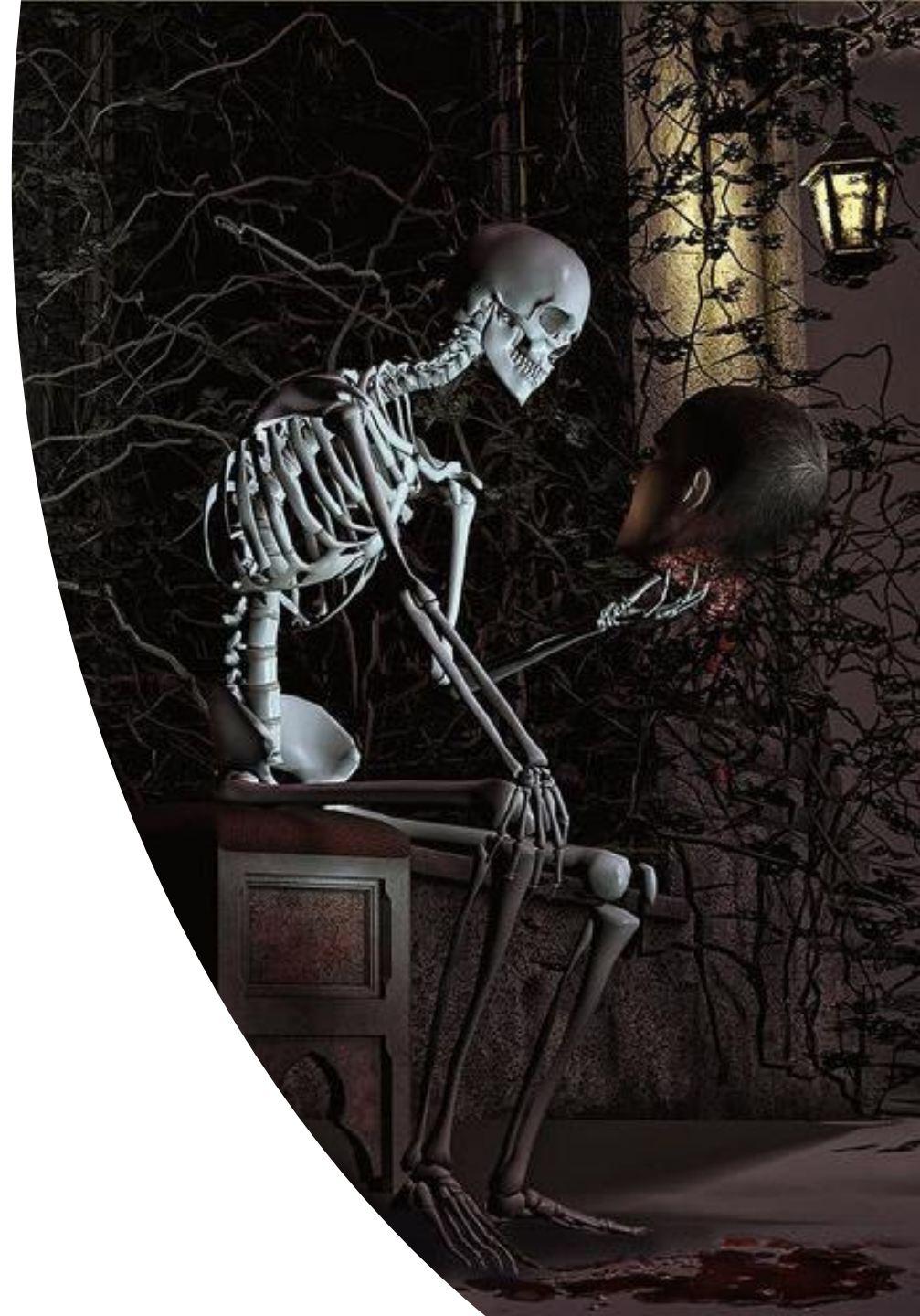
Prolia (denosumab)

➢ **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

Rank ligand inhibitor

Anabolics: parathyroid hormone pulse therapy
PTH stimulates bone formation first, and later stimulates bone remodeling*

- ## Abaloparatide (Tymlos)
Parathyroid hormone analog
Daily SQ injection x18-24 months

- ## Teriparatide (Forteo)
Parathyroid hormone–related peptide
Daily SQ injection x24 months

PTH simulates production of RANKL, while repressing OPG expression, which dually increases osteoclast activity. The anabolic window lasts approximately 18 to 24 months, before resorption exceeds bone formation and no net increase in BMD can be achieved, limiting therapeutic use to a maximum of 2 years.

Both agents demonstrate increased BMD at 90 days tx

Both demonstrate up to 90% decrease fx rate

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: osteosarcoma

Counsel/reassure patients regarding relative vs. actual risk

mAb Anti-sclerostin Therapy

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

Avoid osteotoxic drug when possible

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

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

https://youtu.be/urMgPHwE7Zk