

What the DXA Scan Doesn't Tell You

How hormones, delivery methods,
and metabolic factors shape bone in midlife

Deb Matthew, MD

America's Happy Hormones Doctor

Bone health is more than bone density

DENSITY

is one measurement

≠

STRENGTH

is the clinical outcome

Architecture • Matrix • Turnover • Muscle • Falls

Walker & Shane, N Engl J Med 2023

What does DXA actually measure?



DXA estimates the mineral contained in a projected area of bone.

It is areal—not volumetric—density.

T-score and Z-score answer different questions

T-SCORE

Compared with a healthy young adult

NORMAL
 ≥ -1.0

OSTEOPENIA
 -1.0 to -2.5

OSTEOPOROSIS
 ≤ -2.5

Z-SCORE

Compared with age-matched peers

≤ -2.0 = **below expected range for age**

DXA cannot tell us whether bone is strong or fragile

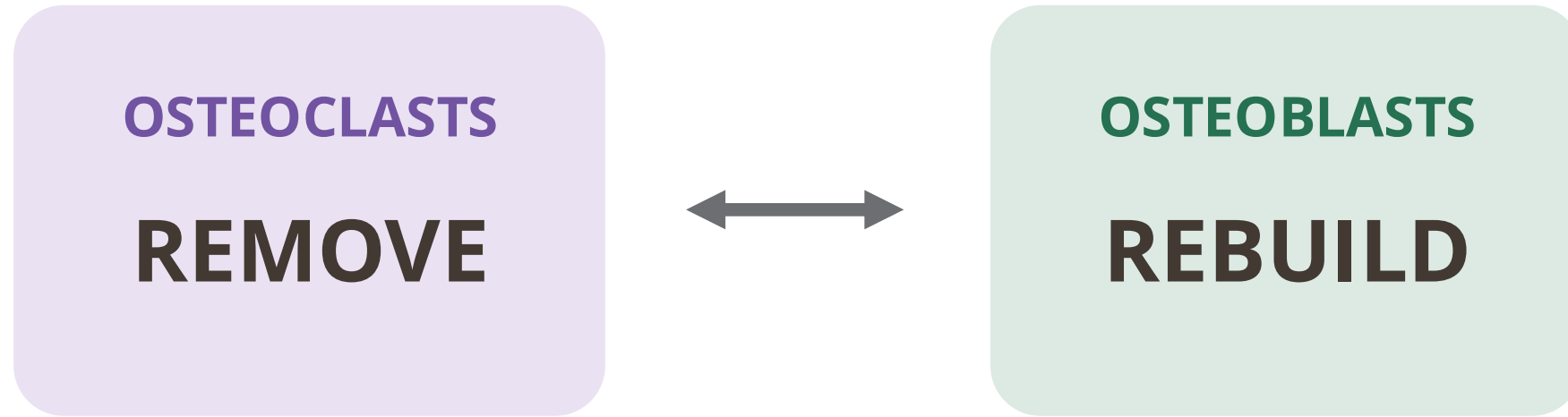
MINERAL DENSITY

The number we see

- Microarchitecture
- Collagen quality
- Bone turnover
- Cortical porosity
- Accumulated damage

Walker & Shane, N Engl J Med 2023

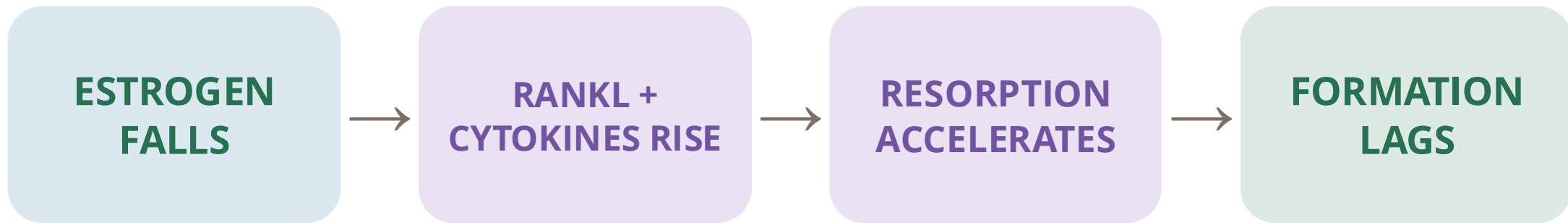
Bone is living endocrine tissue



Osteocytes sense load and coordinate the balance

Walker & Shane, N Engl J Med 2023

Menopause uncouples remodeling



More remodeling (removing bone). Less complete replacement.

Gosset et al., Best Pract Res Clin Endocrinol Metab 2021

Bone loss accelerates before menopause



Years since last period may matter more than chronological age

Sowers et al., JCEM 2013; Shieh et al., JCEM 2022

FSH may be more than a menopause marker

EMERGING EVIDENCE

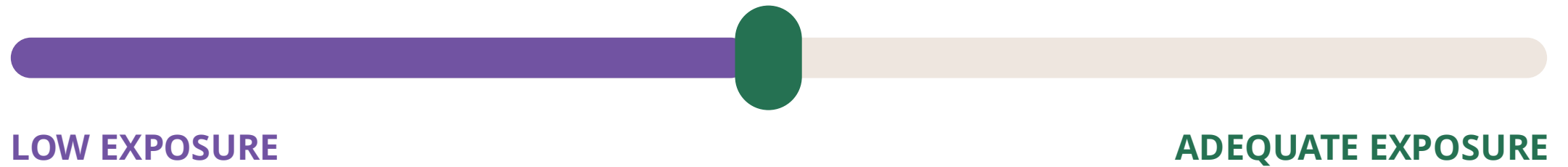
FSH ↑

Possible direct signaling
to osteoclasts

Rising FSH may help identify rapid bone losers during the transition.

Sun et al., Cell 2006; Sowers et al., JCEM 2006

Estradiol appears to have a threshold effect



Below a critical exposure, bone loss accelerates.

We may just need to exceed the threshold (60pg/ml?)
May not be a linear dose-response

Kim et al Sci Rep. 2021, Reginster et al., Maturitas 1992; Tian & Zhang, Sci Rep 2025

We don't treat the estradiol number alone

DOSE **+** **ABSORPTION** **+** **METABOLISM** **+** **TISSUE RESPONSE**

Interpret the level plus:
Symptoms, SHBG, metabolism, turnover markers, and longitudinal response

Cauley et al., JCEM 2019; Greendale et al., Obstet Gynecol 2000

For bone, systemic exposure matters

**ORAL
ESTRADIOL**

**TRANSDERMAL
ESTRADIOL**

Both can preserve bone when the delivered dose is adequate.

Ettinger et al., Obstet Gynecol 2004; Mizunuma et al., Maturitas 2010

Oral and transdermal estradiol are not identical

ORAL

Hepatic first pass
SHBG ↑
IGF-1 often ↓

TRANSDERMAL

Bypasses first pass
Less SHBG effect
Preserves IGF-1

Ropponen et al., JCEM 2005; Bellantoni et al., JCEM 1996

Estrogen metabolism may shape skeletal exposure

EMERGING EVIDENCE

2-OH

Weaker signaling
Faster inactivation

16 α -OH

More persistent
estrogenic activity,
may have
bone benefits

4-OH

Catechol + quinone
handling

The same estradiol level may not create the same tissue signal.

Lim et al., JCEM 1997; Leelawattana et al., JBMR 2000

Progesterone supports bone formation

EMERGING EVIDENCE

PROGESTERONE

Stimulates osteoblasts

**Loss of ovulation may matter
before estradiol is consistently low.**

Prior, Endocr Rev 2018; Prior et al., PLoS One 2017

Testosterone supports the musculoskeletal unit and provides bone strength

**ANDROGEN
RECEPTOR**

**AROMATIZATION
TO ESTRADIOL**

**MUSCLE +
MECHANICAL
LOAD**

Bone and muscle should be evaluated together.

Zhang et al., Sci Rep 2022

DHEA supports bone through intacrine conversion

EMERGING EVIDENCE



The diagram consists of a light purple rounded rectangle containing the text 'DHEA' in bold purple font. A downward-pointing arrow is positioned below this rectangle, pointing towards the text 'ESTROGENS • ANDROGENS • IGF-1'.

DHEA

ESTROGENS • ANDROGENS • IGF-1

Small BMD gains have been reported in older women.

Jankowski et al., Clin Endocrinol 2019

Cortisol excess shifts bone toward breakdown

CORTISOL ↑

Osteoblast activity ↓

Calcium absorption ↓

Muscle mass ↓

Trabecular bone is especially vulnerable.
Higher fracture risk before DXA looks dramatic

Zavatta et al., J Clin Endocrinol Metab 2023

Bone remodels on a clock

EMERGING EVIDENCE



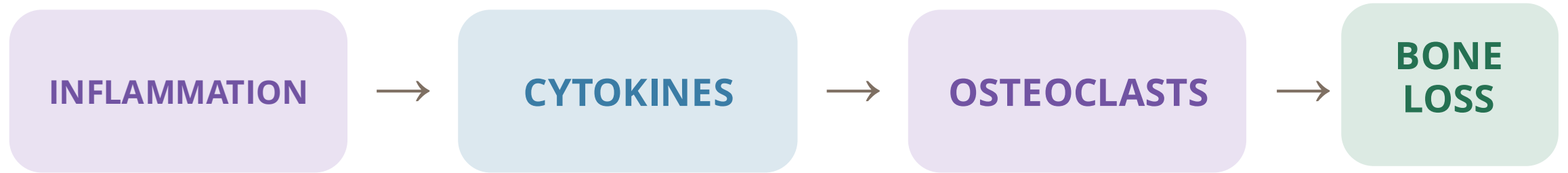
24h
RHYTHM

Sleep disruption + circadian misalignment may uncouple formation from resorption.

Cortisol timing may be part of the story.

Depner et al., Bone 2021

Inflammation amplifies osteoclast signaling



Estrogen normally helps restrain this pathway.

Barbour et al., J Bone Miner Res 2014

Other hormones can override the estrogen plan

THYROID EXCESS

PTH EXCESS

CORTISOL EXCESS

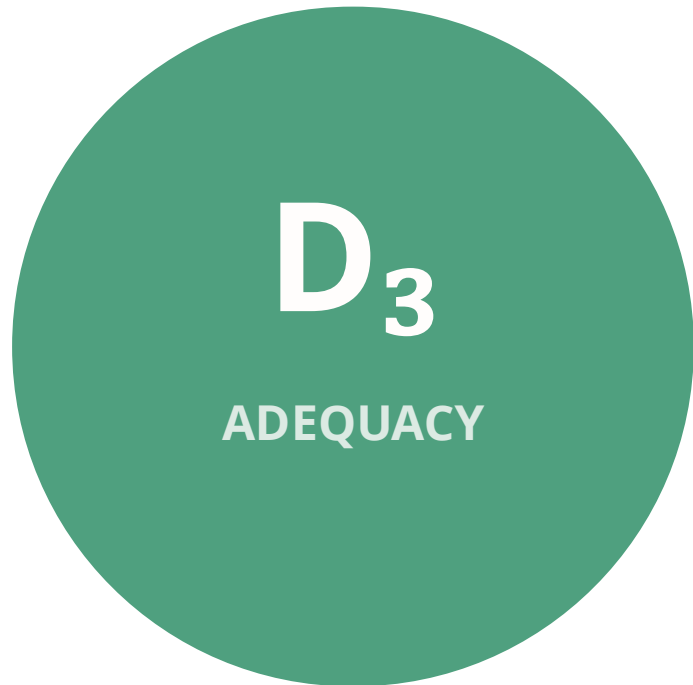
INSULIN RESISTANCE

LOW IGF-1

RENAL / PHOSPHATE

Walker & Shane, N Engl J Med 2023

Vitamin D enables mineralization



Calcium absorption



Phosphate availability



Mineralization

At least correct deficiency,
but optimal level for bone remains debated...

LeBoff et al., J Gerontol A 2023

Vitamin K activates calcium-binding proteins

EMERGING



180–375 µg/day studied • Fat soluble - take with food
BMD results mixed

<https://pubmed.ncbi.nlm.nih.gov/23525894/>, Hamidi et al., J Clin Densitom 2013, Yasui et al., Menopause 2006;

Build the Whole System

**Muscle is part of the bone prescription.
Bone needs a reason to stay strong.**

ESTABLISHED

LIFT

Progressive
resistance

LOAD

Impact / weight-
bearing

STEADY

Balance +
coordination

**Resistance + impact tell bone where strength is needed.
Protect lean mass during midlife/aging and weight loss.**

Whitman et al., Bone 2025; Hansen et al., eClinicalMedicine 2024

Build the Whole System

Build the whole system: mineral, matrix and muscle

ESTABLISHED

Ca

Mineral

Calcium • phosphate •
vitamin D and K
physiology

I

Matrix

Type I collagen • cross-
linking • vitamin C



Muscle

Mechanical loading •
balance • fall protection

Closing the Loop

Measure whether the physiology is changing

**DXA
TREND**

**CTX
(breakdown)**

**P1NP
(Formation)**

Hormones

**Muscle
Mass**

Trends reveal response before the next fracture does.

Gutierrez-Buey et al., Clin Endocrinol 2019; Shieh et al., JCEM 2020

Optimize bone health (not just the T score...)

- Preserve hormonal signaling
- Control excessive resorption
- Support matrix + mineralization
- Build + load muscle
- Measure the response

Thank You!

Deb Matthew, MD

