Exposure to environmental endocrine disruptors: What may this mean for bone health?

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**Endocrine disruptor**: a chemical that can promote or inhibit the **production**, **elimination** or **action** of hormones and hormone-like chemicals.

http://www.untamedscience.com/biology/human/endocrine-system/
Hormones and their receptors regulate bone biology

Steroid receptors
- Estrogen receptor – Under-activation leads to bone loss
- Glucocorticoid receptor – Over-activation leads to bone loss
- Vitamin D receptor – Under-activation leads to failure to form bone
- PPARγ – Over-activation leads to bone loss

Vitamin/Metabolite/Hormone receptors
- VDR
- RAR α, β, γ
- PPAR α, β/δ, γ
- LXR α, β
- FXR
- SXR/PXR
- RXR α, β, γ
- CAR
- TR α, β

Environmental PPARγ Agonists?

• PPARγ – the master regulator of fat formation. Fat is found under the skin, around the organs and in the bone marrow

• Agonists – turn on fat cell formation and lipid storage programs by binding to PPARγ

• Where do we find PPARγ agonists? Everywhere!
How are we exposed to PPARγ agonists?

Critical risk factors for developing osteoporosis:
1) Bone loss at menopause
2) Failure to reach peak bone mass

**Men are NOT immune to bone loss.**

Shuler et al., 2012 Orthopedics. 35:798.
Analyses of bone quality in humans and mice

Dexa Scan – Bone Density

CT– Bone structure/Density

Normal bone

Osteoporotic bone

Serum Markers –
• Bone formation
  Bone alkaline phosphatase (BALP)
  N-terminal propeptide of type 1 procollagen (PINP)
• Bone breakdown
  C-terminal telopeptide of type 1 collagen (CTX)
  Trap5b

www.food4healthybones.com/blog/dxa-test-must-knows/
Lactation has a dramatic effect on bone

Control - End of lactation

Two week after lactation ends

C57BL/6J mouse – femur

In utero/lactational exposure (Vh or triphenyl phosphate)
Pups are weaned at 21 days of age

Schlezinger, Unpublished data
An environmental PPARγ ligand prevents recovery of bone after lactation

Flame retardant
Triphenyl Phosphate

End of lactation

Two weeks after lactation ends

Schlezinger, Unpublished data
Do early life EDC exposures impact bone quality?

Female pups at 16 weeks of age, fed a high fat diet after weaning

PINP - Bone Formation

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Trap5b - Bone Breakdown

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Schlezing, Unpublished data
What do we know? What don’t we know?

1. PPARγ, the protein which controls the formation of fat cells, plays an important role in regulating bone quality.

2. Drugs that turn on PPARγ reduce bone quality.

3. Environmental EDCs that turn on PPARγ can decrease bone formation and increase bone resorption. Are there other bone-relevant nuclear receptors that are targets of EDCs?

4. Lactation is a time of bone mobilization. Is recovery from lactation-induced bone loss impaired by EDC exposure?

5. The *in utero* environment is an important factor in determining bone quality. Are early life EDC exposures impairing the ability to achieve peak bone mass?