

Osteoporosis in Premenopause, Pregnancy and Lactation

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- Mineral metabolism during pregnancy, breast feeding and weaning
- Pregnancy associated osteoporosis
- Transient osteoporosis of the hip
- Premenopausal osteoporosis

Nutritional demands of pregnancy and lactation

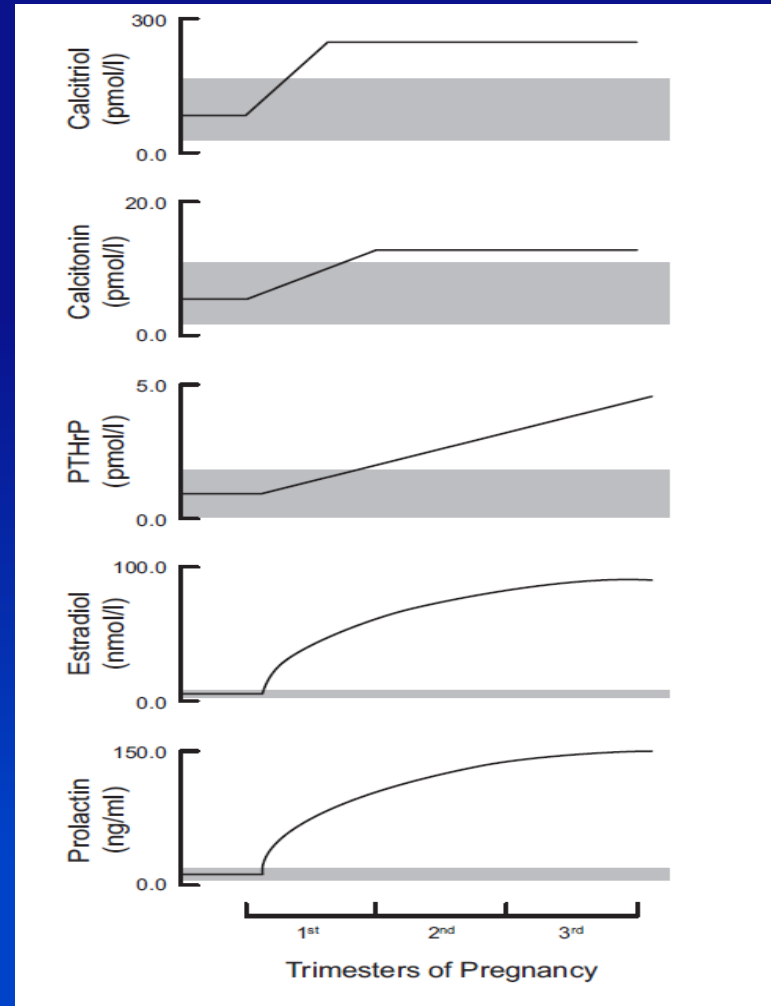
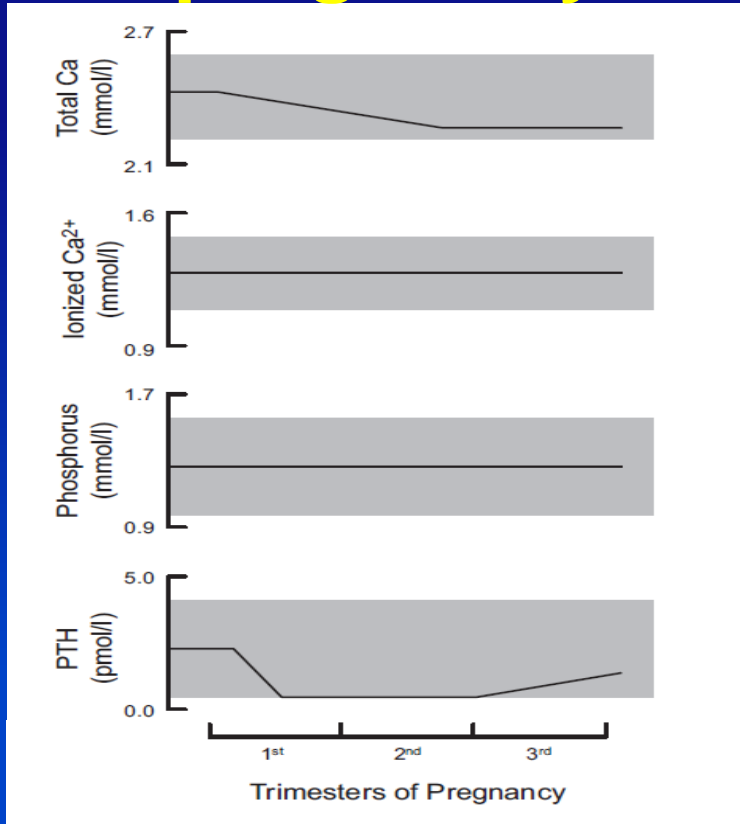
- Fetus contains 30g Ca, 20g phosphorus, 0.8g Mg
- 80% of mineral accretion in third trimester
- Ca transfer at 300-350mg/d in last 6 wks

- Neonate - 200mg ca per day 0-6 mths, 120 mg/d 6-12 mths

- 25% dietary calcium is absorbed

- Physiological adaptation
 - pregnancy - ↑ intestinal calcium absorption
 - lactation - ↑ bone resorption

Metabolic changes during pregnancy



Intestinal Calcium absorption

- Active transport duodenum and prox jejunum,
passive transport distal jejunum and ileum
- ↑Intestinal ca absorption 2-fold from 1st trimester
partly ↑calcitriol (?PL placental lactogen, GH)
- ↓PTH demonstrates +ve ca balance

Renal calcium handling

- ↑Hypercalciuria (absorptive - ↑24 hr not spot fasting ca/cr)
- Pre-eclampsia assoc with hypocalciuria and ↓calcitriol
?altered renal handling, 25-OHD no effect, Ca suppl if ↓dietary ca

Skeletal and mineral metabolism

- +ve ca balance by mid preg
- ↑Bone turnover esp 3rd trimester with ↑bone resorption
- Small (or no) loss in BMD - large cohorts only
- In general no adverse effect of parity on bone health

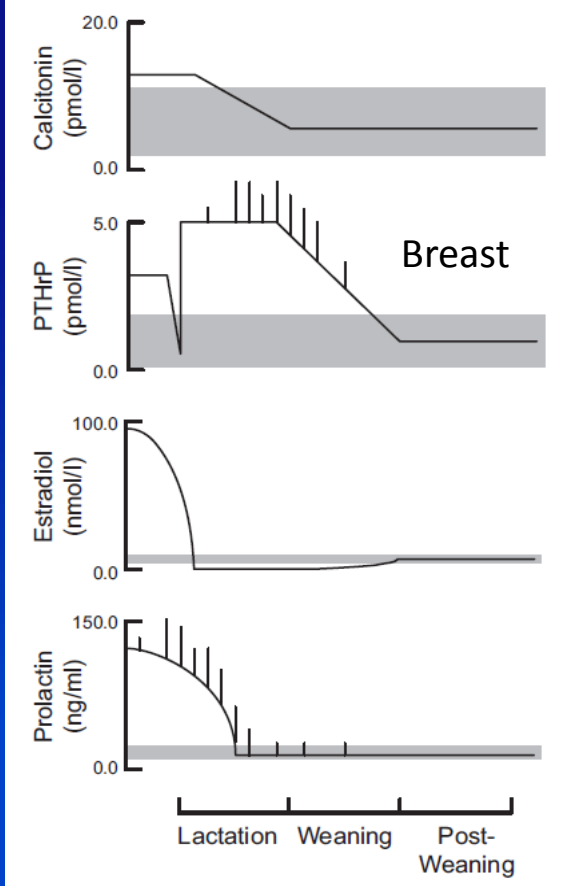
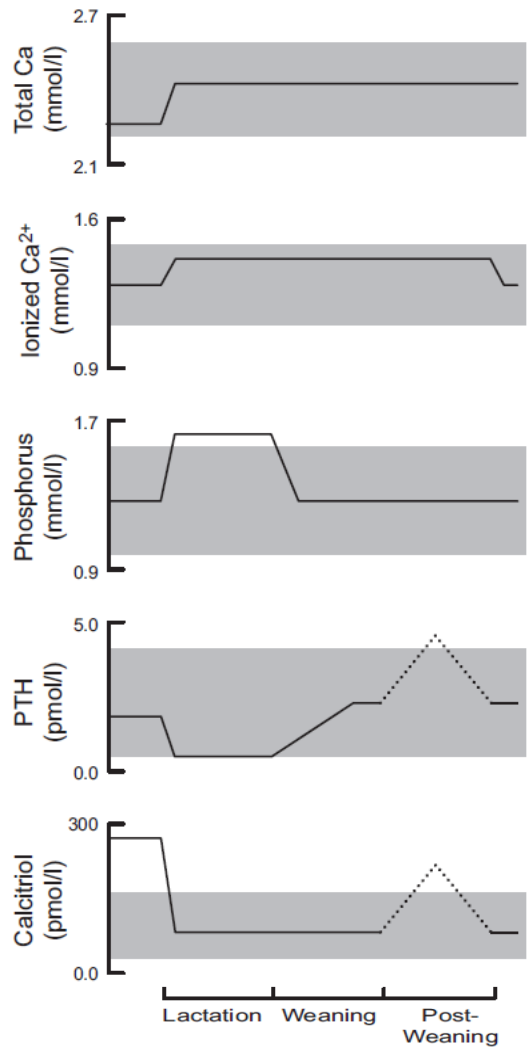
Low dietary ca during pregnancy

- ↑PTH, bone loss and risk of pregnancy assoc OP
- Maternal hypocalcemia → fetal hyperparathyroidism, OP and fracture
- Lowest quintile ↑risk pre eclampsia, ameliorated with ca suppl

Skeletal physiology during lactation

- Average ca loss \approx 200 mg/d (0-6 mths)
- \downarrow Intestinal ca absorption to normal
- \uparrow Renal ca reabsorption (PTHrP)
- Majority ca mobilised from bone
 - osteoclast-mediated bone resorption
 - osteocytic osteolysis
- PTHrP and low E2 regulate bone resorption

Changes during lactation



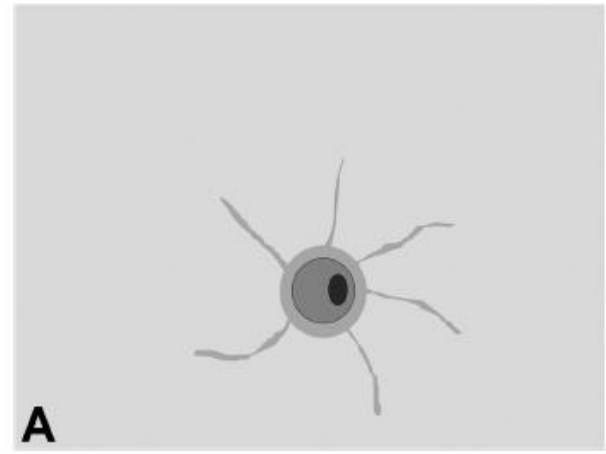
Skeleton and lactation

- Bone turnover markers increase
- ↓ BMD 5-10% LS (up to 20%), 3-4% hips
- ↑ bone loss with longer lactation
- Ca supplementation does not reduce bone loss
- Resumption of menses does not stop ongoing bone loss

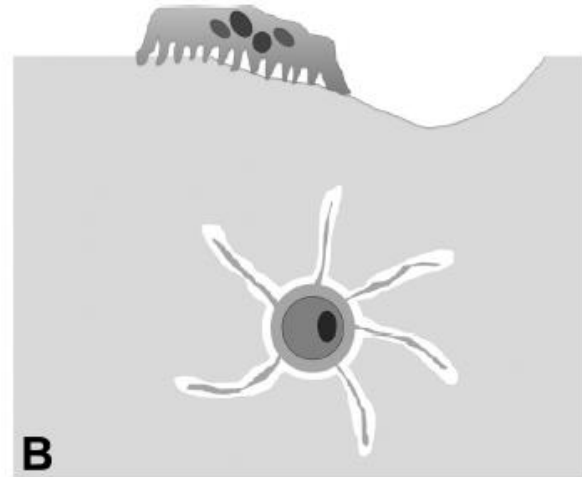
- Osteoclast bone resorption mainly trabecular bone
- Osteocytic osteolysis cortical and trabecular bone

- 6 mths GnRH → E2 def ↓LS BMD 2-4%, ↔hip BMD, ↑ Ca/Cr suggests low E2 permissive role, PTHrP major player

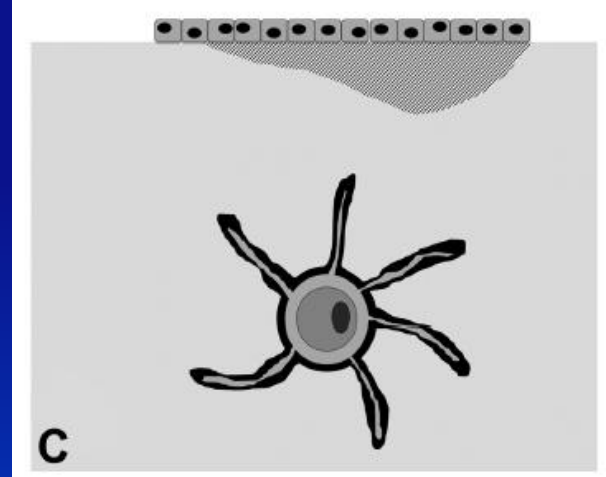
Bone resorption and osteocytic osteolysis



Quiescent



Lactation with bone resorption & osteocytic osteolysis



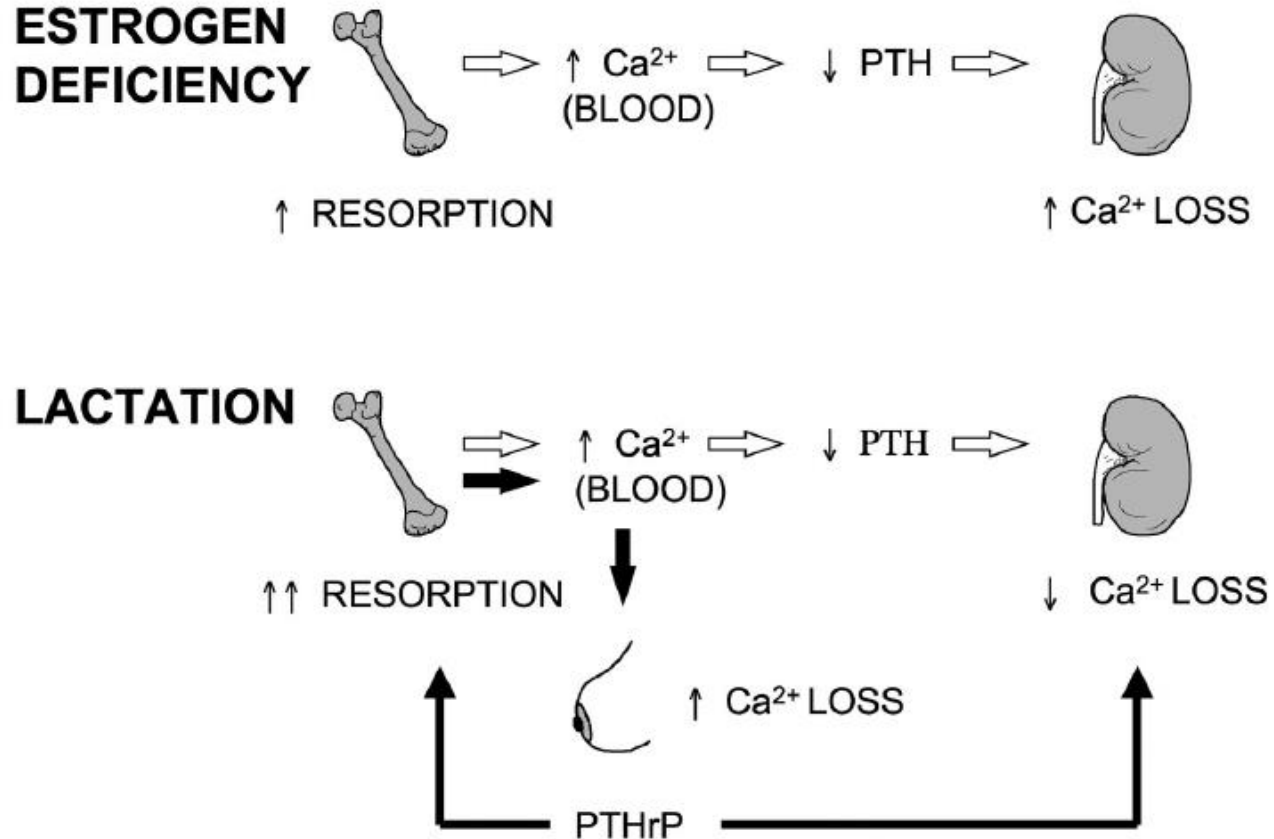
Post weaning with restoration of bone

Evidence for osteocytic osteolysis mainly from animal models

Lactation and bone physiology

E2 def only

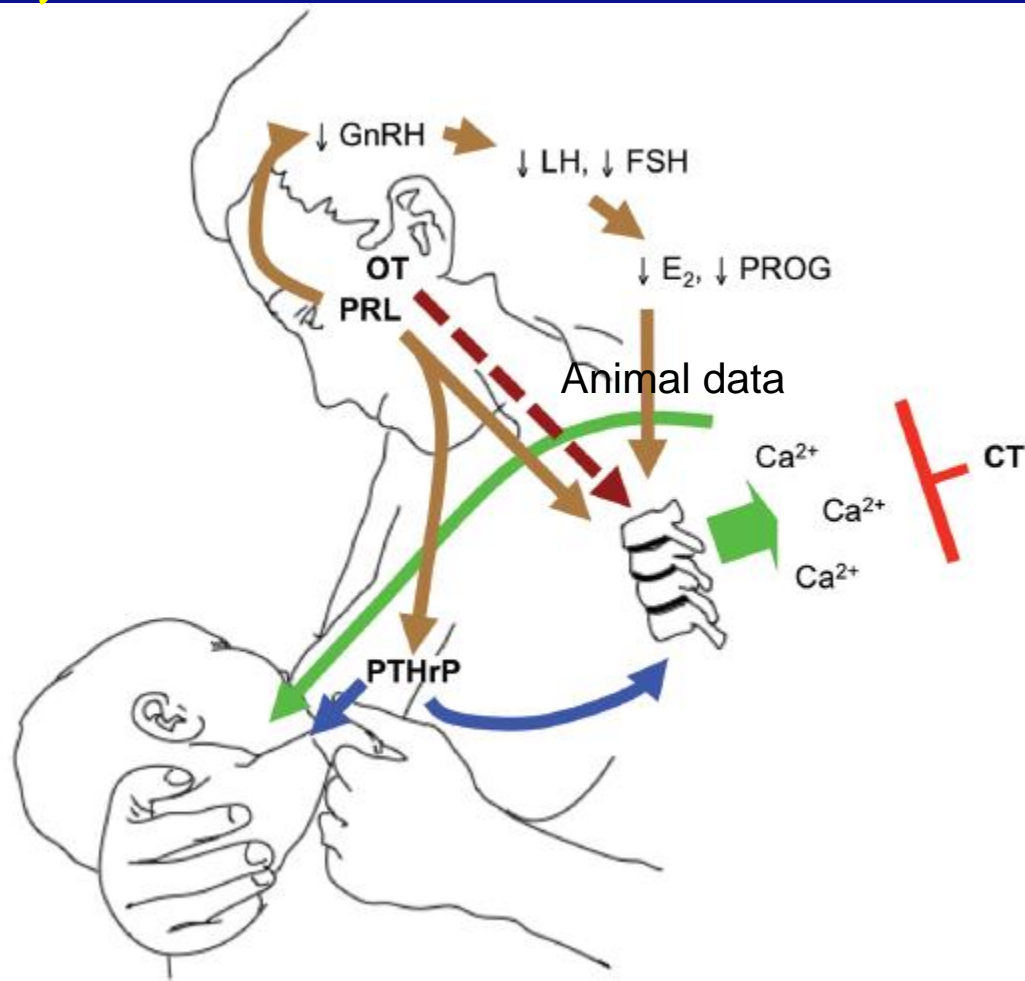
- ↓ bone loss
- ↑ renal ca exc
- Ongoing bone loss despite menses return



Breast, brain, bone and lactation

Suckling & PL
inhib GnRH → ↓E₂, prog
→ PTHrP from breast
↓E₂ and PTHrP
→ bone loss
Ca actively pumped into
breast milk

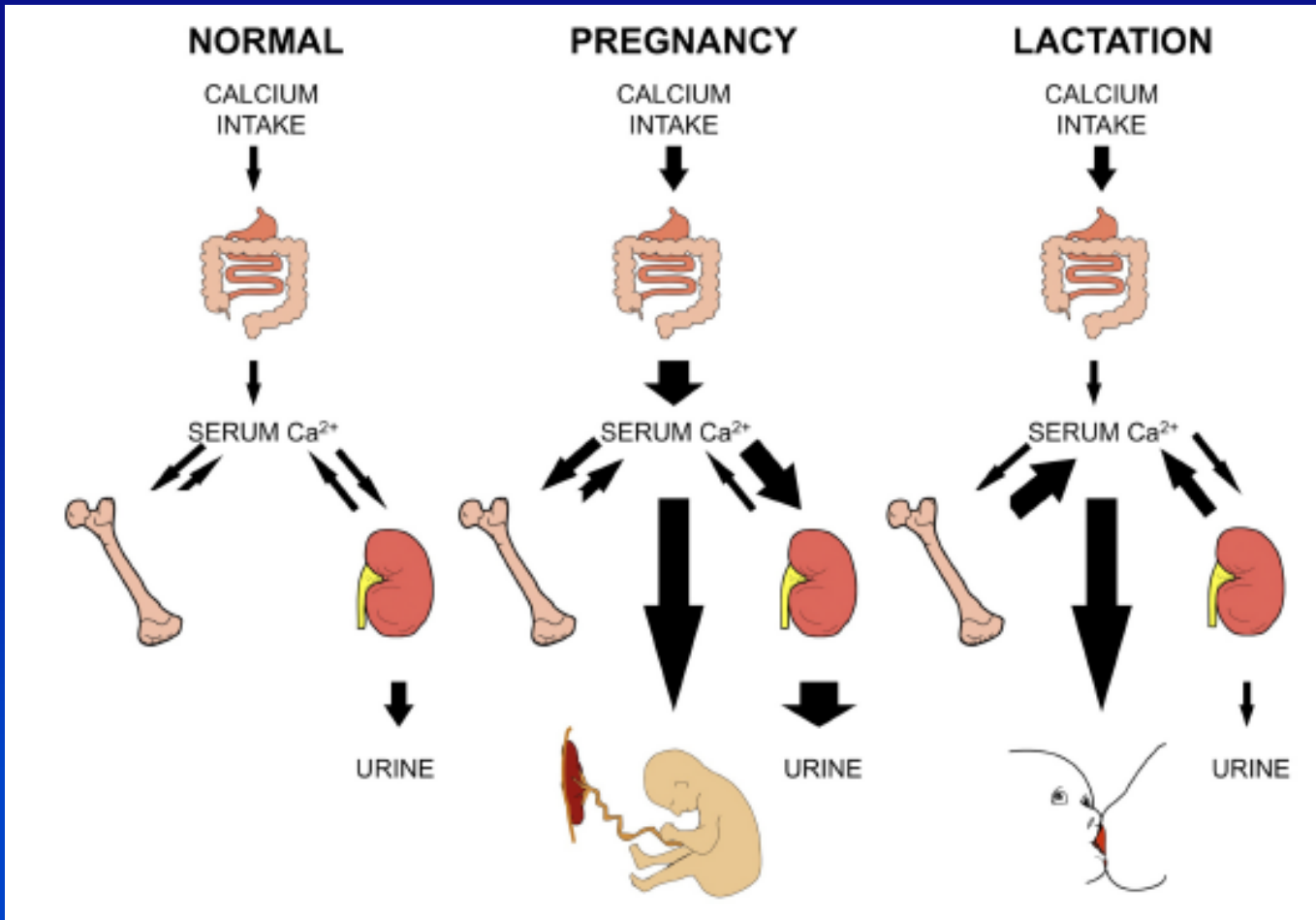
??oxytocin, calcitonin



Post weaning and bone recovery

- ↑bone turnover - formation > resorption
- Bone mass generally returns to normal by 12 mths (DXA)
- HR-pQCT - recovery of microarchitecture, ? deficits with longer lactation (limited data)
- ? increased cross-sectional femur diameter
- Neutral effect on BMD and fracture risk - epidemiological studies
- Adolescent preg no adverse impact
- Recovery time relates to lactation time
- ↑ ca intake and wt bearing exercise may enhance BMD

Calcium and bone homeostasis



Osteoporosis in Pregnancy

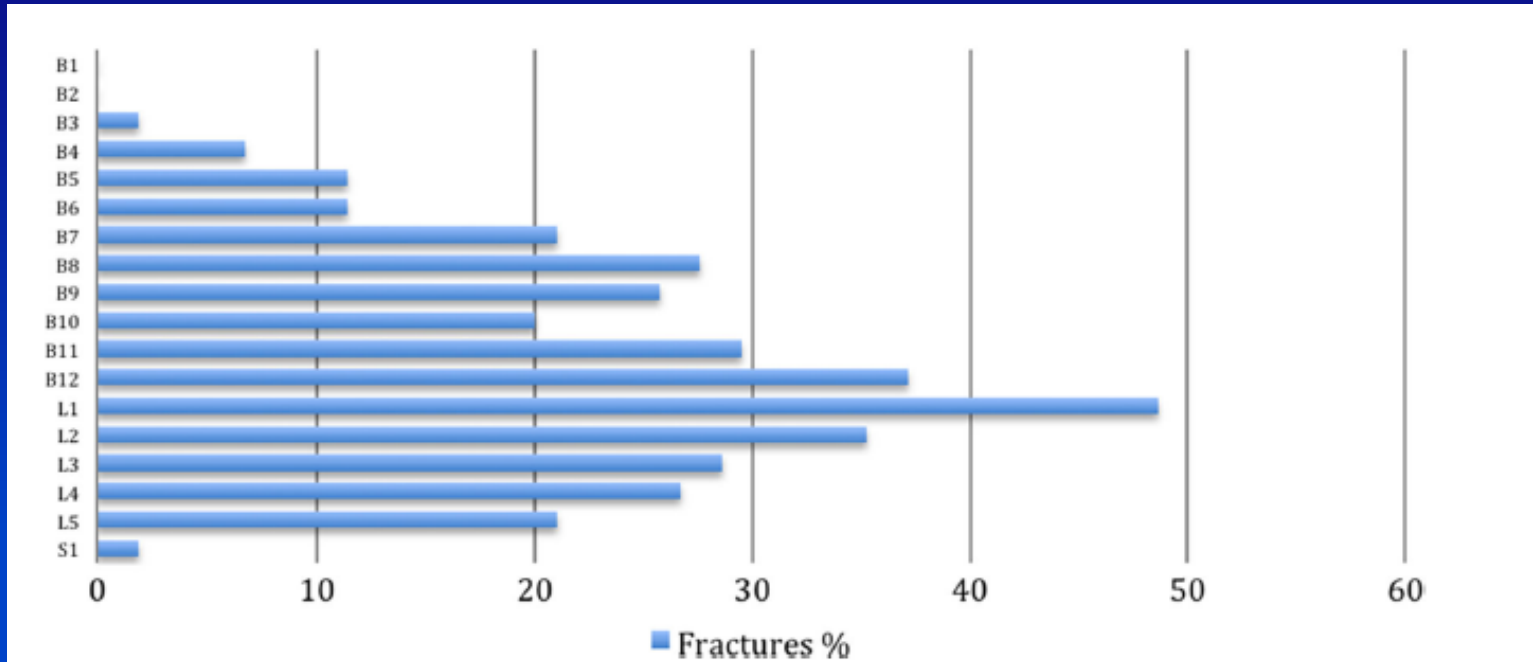
- 4-8/1,000,000 pregnancies
- Vertebral fractures most common – 3rd trimester
- Gen 1st preg, mostly does not recur ?underlying abn treated
- Causes
 - Pre-existing skeletal fragility
 - ↑ skeletal resorption 3rd trimester if ↓Ca transferred to fetus
(↓dietary ca abs – ↓intake, malabs, ↓vit D)
 - Additional factors- ↑ wt bearing, lordosis, anorexia, genetic low bone mass, renal ca leak, POI etc

Pregnancy associated osteoporosis

102 PAO matched case-control study, German ref centre

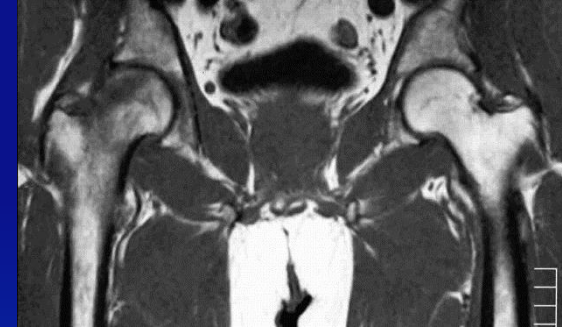
88% fractures, mean 3.3, commonest T/L spine

↑childhood dental problems, ↑2x severe diseases in preg with immobilisation, ↓sport



Transient Osteoporosis of the Hip

- 3rd trimester
- Pain, limp or # hip
- Can be bilateral
- Also in men (men>women 28:3)
- Fem head/neck radiolucent, low BMD ?artifact
- MRI bone marrow oedema
- Resolves in months
- Aetiology unclear
 - ? femoral venous stasis, fetal pressure on obturator nerve, relative immobility
- Not systemic bone resorption
- Any pregnancy
- Other hip during pregnancy or non pregnancy

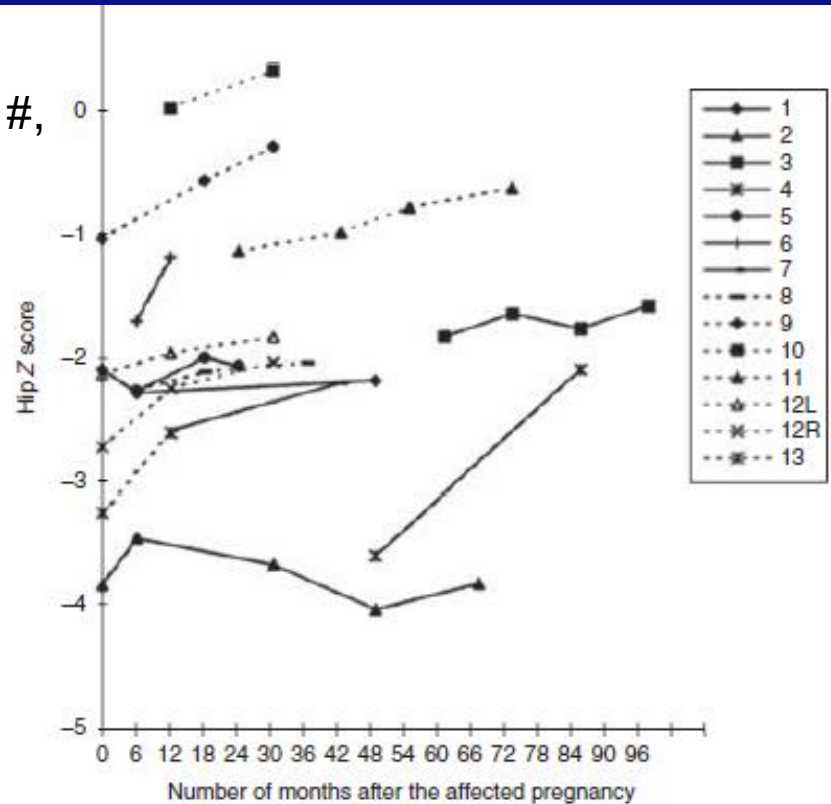
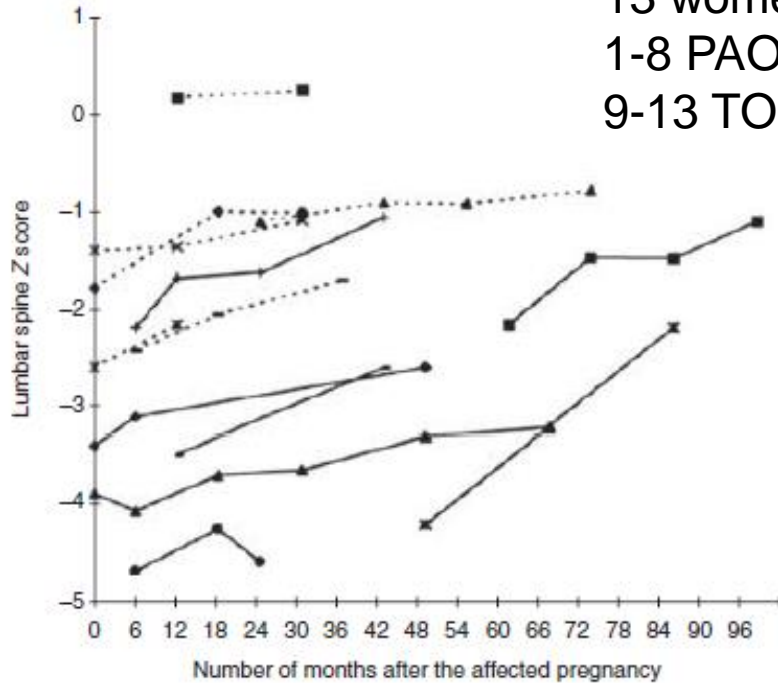


Management of fracture in pregnancy/lactation

- Limited evidence
- ? underlying cause
- Optimise calcium (1200mg/d) and vitamin D
- Wt bearing/resistance exercise for mobility, avoid heavy lifting
- Vertebral # generally don't recur in subsequent pregnancies
- ↑Bone density/strength post weaning to pre-pregnancy level
- Wean early
- Pharmacological therapy only judiciously, gen not
- BP and Dmab cross placenta
- RV of 78 BP prior to/during preg, 7 pre/during lactation¹
 - no serious fetal adverse effect
 - transient hypoca (high dose), ↓gestational age, ↓birth wt

BMD and pregnancy associated osteoporosis

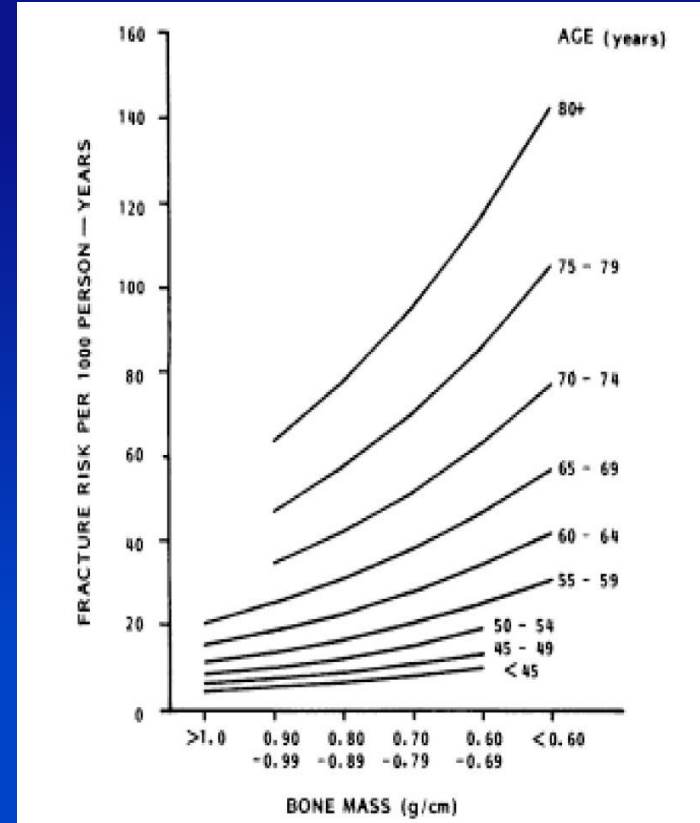
13 women
1-8 PAO spine #,
9-13 TOH



Premenopause and osteoporosis

BMD testing

- Z-scores <2.0, “Below expected for age”
- Avoid “osteopenia” in otherwise healthy
- Most cross-sectional studies
- ↓↓ fracture risk
- No longitudinal data on short term # risk
- Risks/benefits of Rx unclear
- # premenop → ↑risk post menop #
RR1.7¹
40-90% assoc with secondary cause



Idiopathic Osteoporosis in Premenopause

- Low trauma fracture with no secondary cause
- FHx common
- Heterogenous
- Bone biopsy and hormonal data suggest low and high bone remodeling
 - Low bone turnover - ↑microarchitectural deficits, ↑IGF-1
 - High bone turnover - idiopathic hypercalciuria

Bone architecture - IOP and low BMD

104 women - 45 IOP with #, 19 ILBMD, 40 controls

Subjects - ↓wt, ↓BMI, similar BTM, E2, IGF-1, vit D, ↑PTH, ↑TRAP5b

HR-pQCT – microarchitecture disruption, ↓stiffness distal radius, tibia

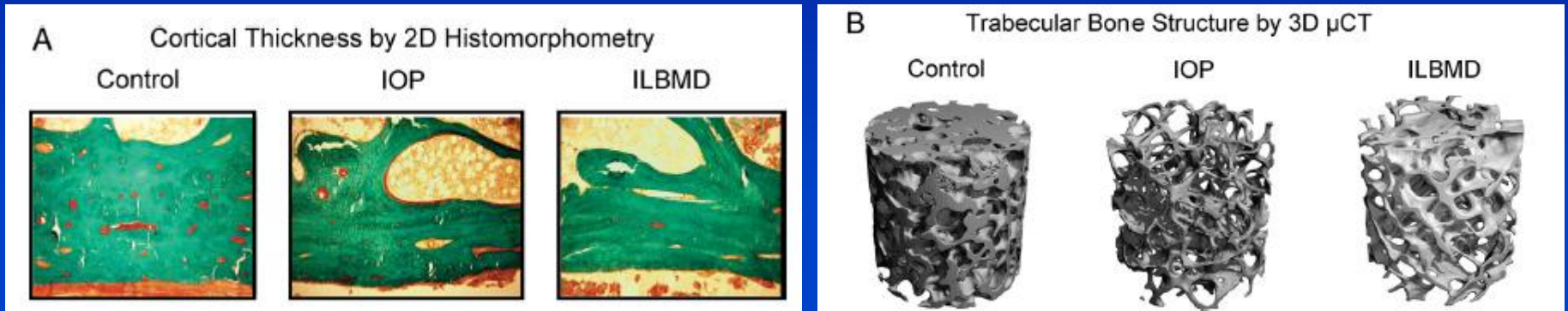
IOP and ILBMD indistinguishable

Iliac crest biopsy - ↓bone vol, trab thickness and connectivity, cortical width

Lowest tertile of bone formation (BFR/BV) worse parameters, ↑IGF-1

?osteoblast dysfunction with IGF-1 resistance

Highest bone turnover trend to ↑1,25-(OH)₂ D, urinary ca, PTH



Management of premenopausal OP

- Low BMD with no fracture and no underlying cause
- Lifestyle and observe
- Rpt BMD 1-2 yrs to ensure stability

- Known secondary cause
- Rx cause if possible
- If ongoing secondary cause, fractures, bone loss, consider antiresorptives
- E2 replacement if E2 deficient (ineffective in AN)
- BP, TPDT on a case-by-case basis

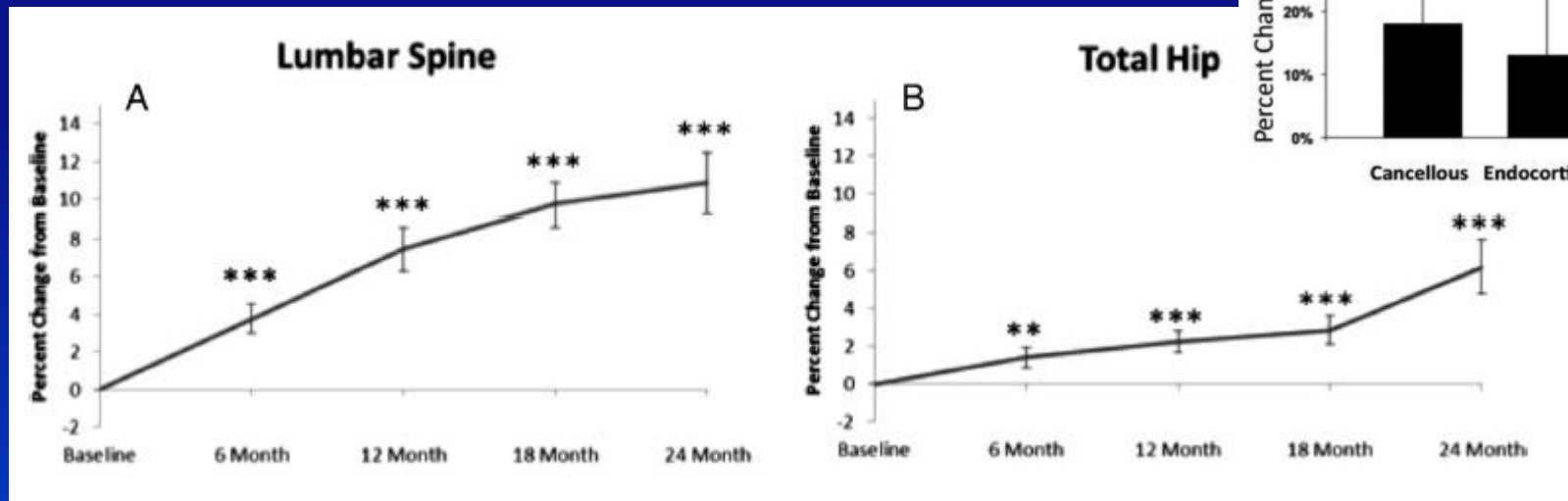
OCP and HT in premenopause

	Healthy premenopausal	Oligo/amenorrhoeic premenopausal	Anorexic premenopausal	Perimenopausal
Positive effect	–	2 RCTs	–	1 RCT
	3 Cohort	5 Cohort	–	4 Cohort
	7 X-sectional	–	2 X-sectional	3 X-sectional
Subtotal	10	7	2	8
No effect	4 RCTs	1 RCT	3 RCTs	–
	9 Cohort	1 Cohort	1 Cohort	–
	15 X-sectional	–	–	2 X-sectional
	1 Case series	–	1 Case series	1 Case series
Subtotal	29	2	5	3
Negative effect	–	–	–	–
	4 Cohort	–	1 Cohort	–
	3 X-sectional	–	–	–
	–	1 Case report	–	–
Subtotal	7	1	1	0
Total	46	10	8	11

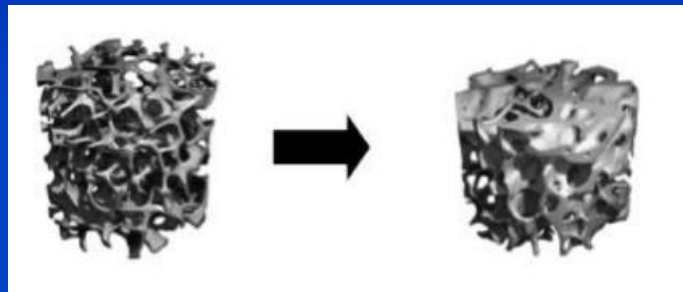
RCT, Randomised controlled trial; X-sectional, cross sectional.

Teriparatide in IOP

21 women with # or low BMD



4/21 min BMD↑
Lowest bone turnover
Biopsy parameters ↑



Bone change after TPDT cessation

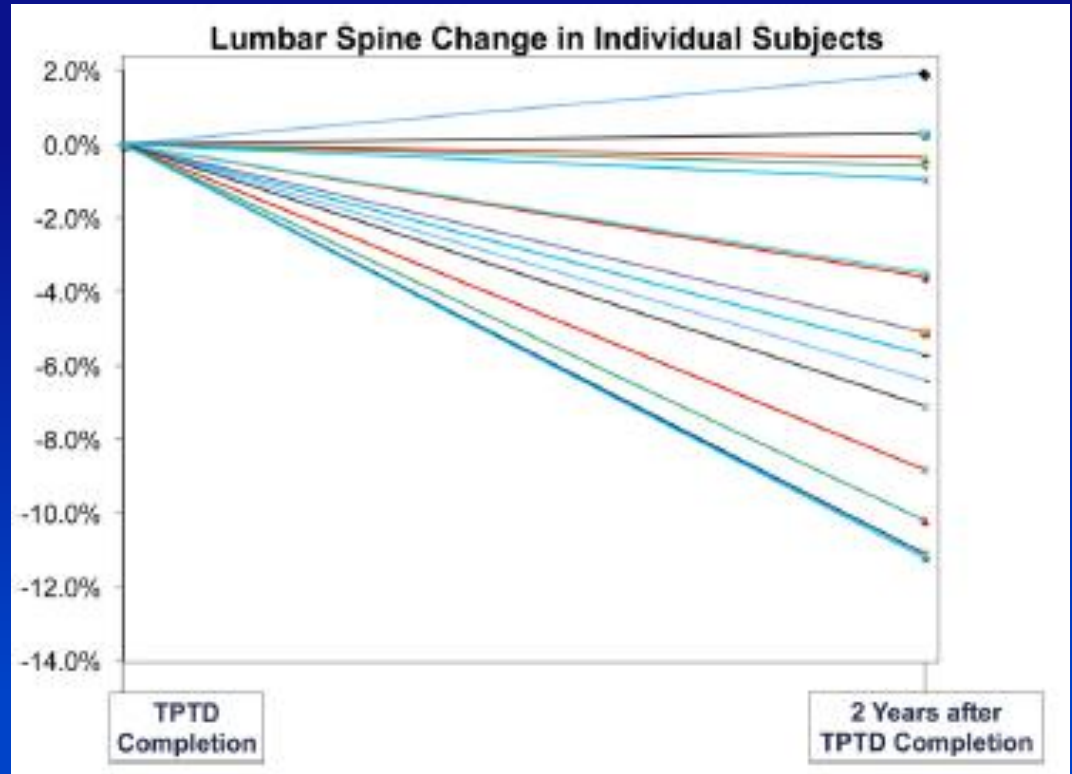
39 ± 6 yrs

10/15 women >3% loss LS

Incl 3/5 women on OCP

Age > 40yrs

Greatest ↑ in BMD



Premenopause, Pregnancy and Bone Health

- Pregnancy not detrimental for bone health
- Adequate calcium intake important due to high fetal demands
 - ↑calcium absorption during pregnancy
 - ↑bone resorption during lactation
 - recovery post weaning
- Pregnancy associated osteoporosis rare, doesn't recur
- Osteoporosis in premenopause
 - exclude secondary cause
 - unless ongoing fracture, antiresorptive treatment rarely required