



VITAMIN D

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Outline

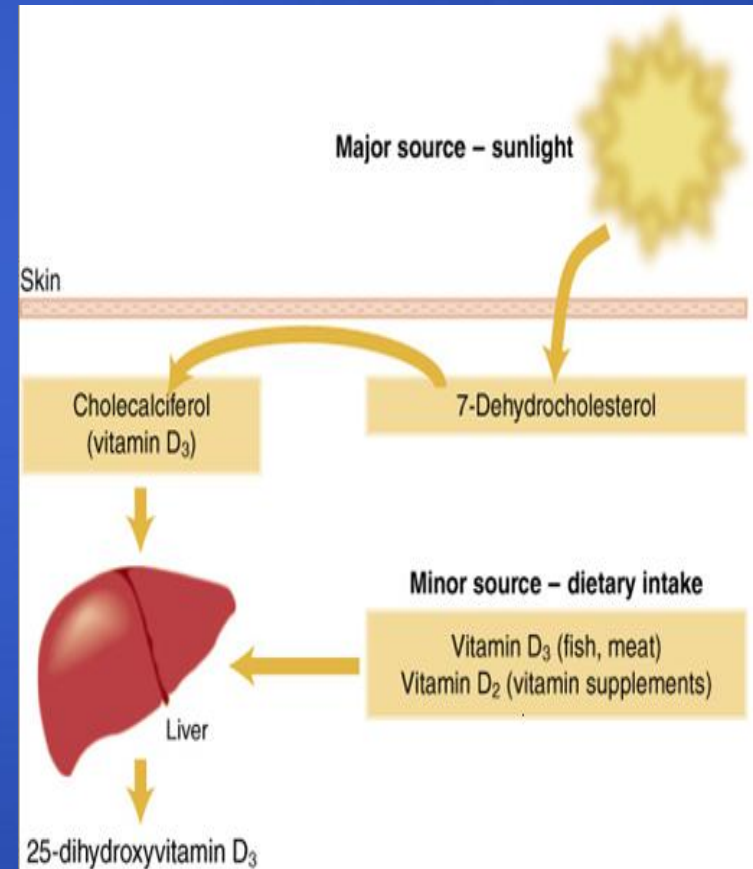
- Vitamin D sources and metabolism
- Benefits of Vitamin D
- Vitamin D deficiency and toxicity
- Optimal levels
- Available preparations

Types of Vitamin D

1. Cholecalciferol
2. Ergocalciferol
3. Calcitriol

Cholecalciferol

- Vitamin D₃
- Formed by action of UVB radiation on 7-dehydrocholesterol in skin
- Major form of supplemental Vit D in Aust
- Biologically inert
- Converted in liver to 25-hydroxyvitamin D



Ergocalciferol

- Vitamin D₂
- Produced by UVB irradiation of the plant sterol ergosterol
- Found in some supplements
- Biologically inert
- Same conversion as cholecalciferol
- Not as potent – 60%

Calcitriol

- 1,25-dihydroxyvitamin D
- Biologically active form
- 1000 x more active than D₃

Sources of Vitamin D

1. Cutaneous synthesis (sunlight)
2. Diet
 - ◆ Natural food sources
 - Egg yolks, fatty fish and fish liver oils
 - ◆ Artificial
 - Some low fat milk, margarine, cereals
 - Mushrooms exposed to UV radiation
 - ◆ Adults – 5-10% vitamin D from dietary source

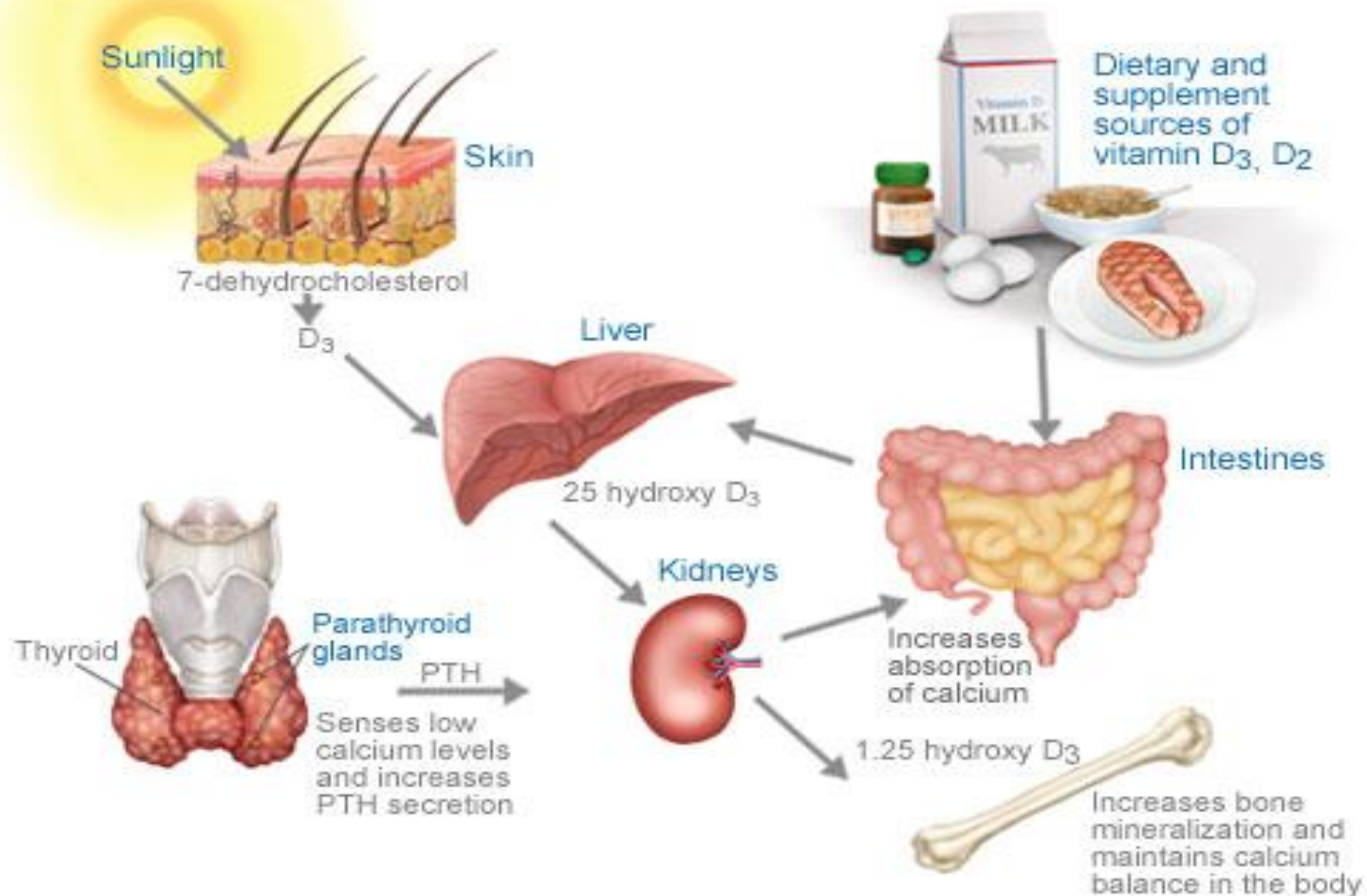
Sunlight

- Main source of Vit D for most people ? What is the minimal exposure required to prevent deficiency?
- Minimal erythema dose (MED)
 - Amount of UVB radiation exposure that causes faint redness
 - May be used as a vitamin D index
 - Factors affecting: season, sunscreen, lack of skin exposure, skin pigmentation
 - UVA can also cause erythema ? usefulness of MED

Sunlight

- 15% body surface (e.g. arms & hand) for $\frac{1}{3}$ of MED \rightarrow 1000 IU Vitamin D
- Short UV exposure may be more efficient than prolonged (sterol production)
- $\frac{1}{3}$ MED in Sydney
 - Summer (outside hrs 10am – 2pm) \rightarrow 6 to 8 minutes
 - Winter (12 pm): 16 to 28 minutes

Vitamin D Metabolism



Benefits of Vitamin D: Bone and extra-skeletal

Benefits of vitamin D - bone

- Deficiency → osteomalacia and insufficiency fractures
- Level I evidence: Vitamin D AND calcium supplementation reduce the risk of falls and fractures
- IOM report 2011:
 - “bone health is the only outcome that satisfied criteria for use as an indicator whereby causality was established”

Extra-Skeletal Benefits of Vitamin D

- Low levels associated with:
 - Autoimmune disease
 - Cardiovascular disease and metabolic disease
 - Some cancers
 - Neurological and mental health conditions
 - Respiratory disease and active TB
 - All cause mortality

Dr. Volker Spitzer / Nicole Spitzer

 vital

Super-Vitamin D

*Rundumschutz vor den
Krankheiten unserer Zeit:
Krebs, Diabetes, Herzkrankheiten,
Osteoporose u.v.a.m.*

Extra-Skeletal Benefits of Vitamin D

- ? Proposed level 75-80 nmol/L
- Limitations:
 - Observational studies
 - Not adjusted for confounders
 - Few randomised controlled trials
- IOM 2011:
 - “evidence deemed to be inconsistent, inconclusive as to causality, and insufficient to serve as a basis for DRI development”

Vitamin D inadequacy, toxicity and optimal levels

Vitamin D inadequacy

- Hypovitaminosis D
- Estimated 31% Australian adults have inadequate vitamin D status (25OHD < 50 nmol/L)
- Likely increased during winter and for those living in at latitudes further from the equator

	Serum 25(OH)D (nmol/L)	Potential Clinical Consequence
Vitamin D Deficiency	< 20 – 25	Clinical, biochemical, radiological & bone histological changes of osteomalacia
Vitamin D Insufficiency	25 – 75	2° hyperparathyroidism, Increased bone turnover Bone loss Fracture

Groups at risk of vitamin D inadequacy

- Lack of sunlight exposure
- Darker skinned people
- Obese people
- Less efficient synthesis of vitamin D in the skin
- Certain medications: e.g. cytochrome P₄₅₀ enzyme inducers

Toxicity

- Main concerns are hypercalciuria and hypercalcaemia
- Generally not seen until 25OHD levels reach 220 nmol/L
- No evidence of toxicity (i.e. hyper Ca) with doses up to 5000 IU/day or 50,000 IU per month
- HOWEVER...

Toxicity

- Large RCT, Sander *et al.* JAMA 2010
- Single annual oral dose 500,000 IU vitamin D₃ for 3-5 yrs in older women
- 15% increased risk of falls
- 26% increase in fractures
- Most pronounced 3 month post-dose (when levels highest)

So what is the optimal level?



What is the optimal level?

- Conflicting opinions
- IOS 2011:
 - Levels 50 nmol/L met the needs of 97.5% of the US population
 - Challenging the “more is better” concept
- Level II evidence: optimal mineral metabolism, bone density and muscle function at 25OHD 50-60 nmol/L

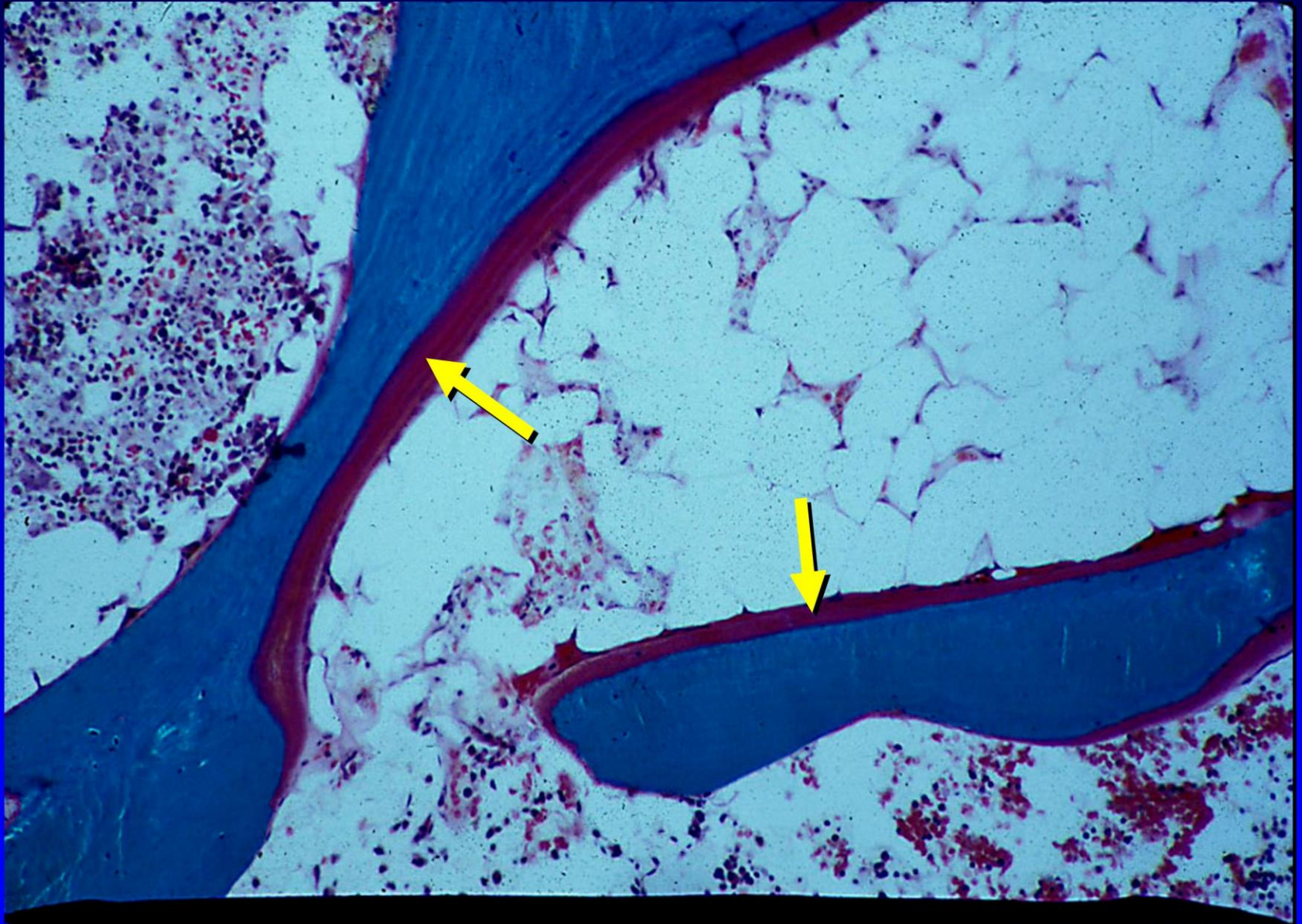
What is the optimal level?

- Deficiency = independent risk factor for falls and is associated with muscle weakness and impaired balance
- German study: increased osteoid in some patient's with level < 75 nmol/L
- BMJ Meta-analysis:
 - Minimum level 60 nmol/L required reduce falls

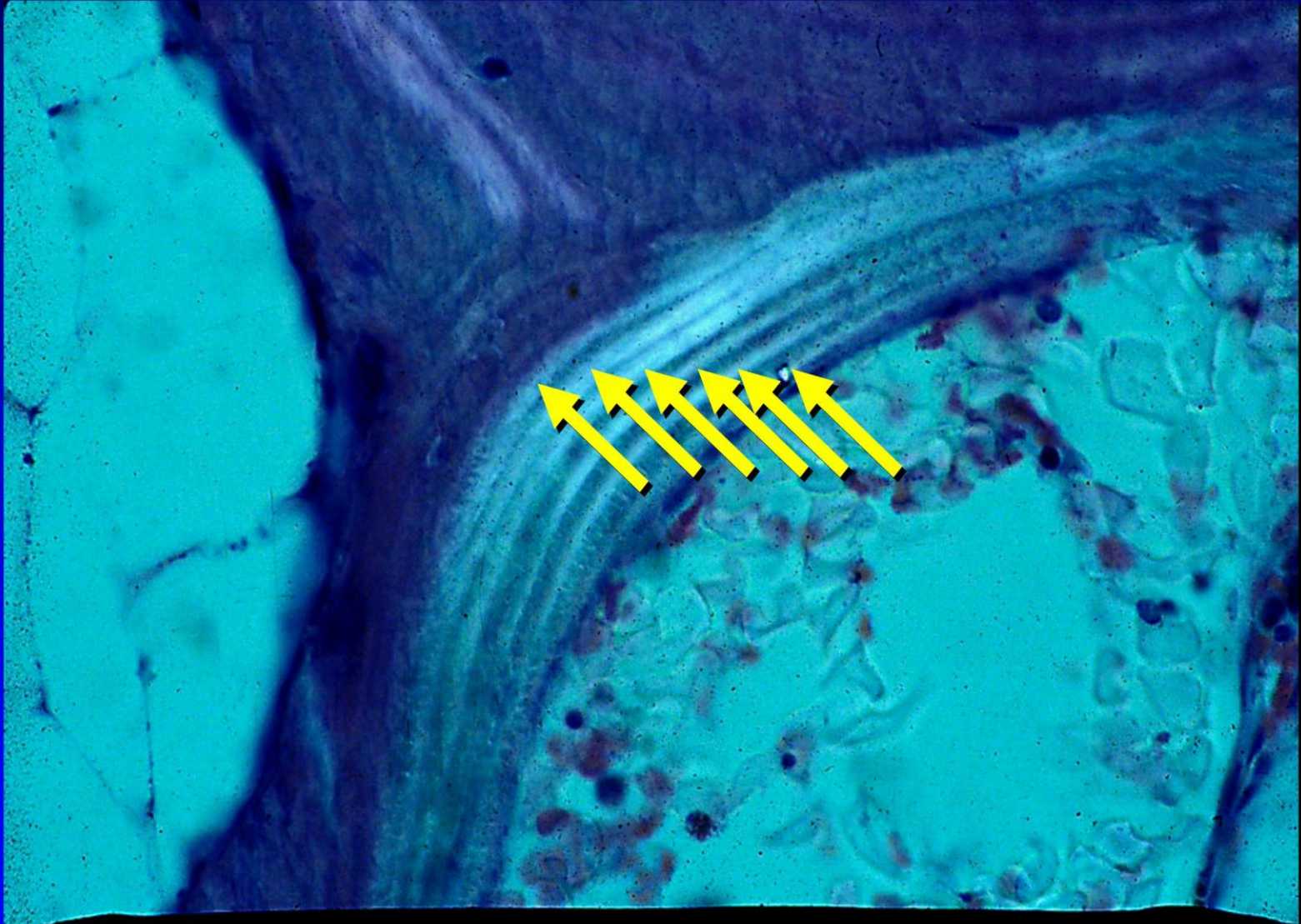
Prinel M et al. JBMR 2010

Bischoff-Ferrari et al. BMJ 2009

Excess amount of unmineralized matrix (osteoid)



Increased number of osteoid seams (viewed with polarized light)



What is the daily requirement?

- Requirements need to be assessed on an individual basis, but generally 600 to 1000 IU per day
- More will be required in patient is deficient
 - e.g. 25OHD 15–25 nmol/L, oral supplementation with 3000–5000 IU daily for 6–12 weeks can be used to replete stores followed by a maintenance dose
- Monitor 3-4 monthly until ideal dose is reached

Preparations available

- Oral capsules and tablet – generally 1000 IU
- Combined with calcium or multivitamin – generally have less (200-800 IU)
- Liquid drops – higher concentration, 1 mL = 5000 IU
- Compounded vitamin D – ? variable potency
- Intramuscular cholecalciferol

Summary

- Nearly 1/3 of the Australian population are vitamin D insufficient
- Sunlight is the major source of natural vitamin D in Australia
- Optimal level is controversial, probably somewhere between 50 and 75 nmol/L
- Supplementation in addition to calcium reduces fracture and falls risk
- ?extra-skeletal benefits
- Toxicity is generally a low risk
- Annual mega-dose vitamin D is not recommended

References

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