Comparative calcium metabolism

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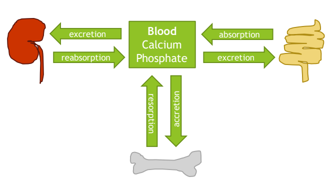
Calcium – a very short introduction

- Functions: skeleton, muscle contraction, nerve conduction, cellular signalling, blood clotting,…
- Absorption
  - Active
  - Passive
- Sources in animal feed: dairy products, limestone, bones, eggshells, Ca-salts, plants like alfalfa, herbs,…
- Ca homeostasis closely linked to P status

Calcium – homeostatic pathways



Comparative

Fish

- Skeleton and scales for Ca deposition
- Acellular bone – limited part in Ca homeostasis
  - Demineralisation only in prolonged, extreme Ca deficiency
- Regulation PTH-independent
  - Stanniocalcin = hypocalcaemic hormone → prevents Ca influx from water into gill cells

Fleming 1967; Flik & Verbost 1993; Dato-Cajegas & Yakupitiyage 1996; NRC 1993

Fish

Fleming 1967

CALCIUM METABOLISM OF TELEOSTS

TABLE 2. *Relative amounts of calcium from water and from a liver diet, stored during growth by brook trout. Each number is the average of a 25-fish sample.* (Data from McCay, *et al.*, 1936)

Initial Calcium	Final Calcium (12 weeks)	Calcium Stored	Calcium Fed	Calcium Taken from Water
360.3	495.5	135.2	27.9 <<	107.3
337.1	491.3	154.2	25.3 <<	128.9
368.6	516.7	148.1	28.5 <<	119.6

Fish

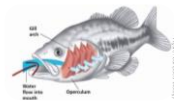


Figure: Campbell Biology

- Intestines: **passive transport** of Ca^{2+}
- **Ca uptake** from environment (water) possible in many fish via **gills**, oral epithelium and possibly fins
  - Water hardness
    - Seawater = high Ca content – no dietary Ca necessary in many species
      - No gastric HCl → low solubility of Ca
    - Freshwater = low Ca content – dietary Ca requirement + osmoregulation
      - Ca already in soluble form

Fleming 1967; Flik & Verbost 1993; Dato-Cajegas & Yakupitiyage 1996; NRC 2005, 2011

Reptiles

- High Ca requirement
  - Skeleton
  - In tortoises and turtles: carapace development – livelong growth!
  - Females: egg shell production
- Vitamin D-dependent Ca absorption
  - UV irradiation for vitamin D synthesis
    - Sunlight / UV-lamps, wavelength of irradiation 280/290-320nm ("UV-B")
    - Exposure time – self-regulated in panther chameleons
    - Cutaneous synthesis upregulated during low Ca, low vit D diet in veiled chameleons
    - Some lizard species may adapt UV sensitivity of their skin

Haxhiu et al. 2014; Hoby et al. 2012; Kamphues et al. 2014; Liesegang et al. 2001, 2007; Watson & Mitchell 2014

Reptiles

- Renal excretion of Ca → excess Ca intake may result in renal calcinosis
- Ca deficiency and/or vit D deficiency → metabolic bone disease

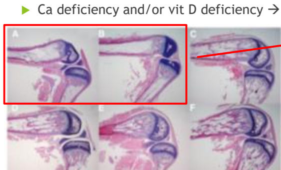


Figure from: Hoby et al. 2010

MBD in chameleons without Ca supplementation
→thin corticalis
→less mineralised osteoid
→lacking trabeculae

Haxhiu et al. 2014; Hoby et al. 2010; Kamphues et al. 2014;

Poultry – laying hens

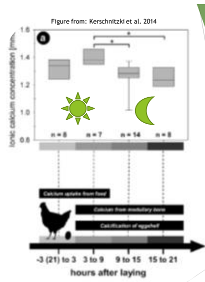
- **Eggshell** production = high Ca demand
- Strong genetic influence in layer lines
  - More efficient Ca utilisation in high performance lines
  - “general” upregulation of intestinal Ca transport – but not sufficient in low Ca diets
  - Age effect, possibly vit D-related
- “calcium appetite”
  - Offering Ca source separately from basal diet possible
- Recommended dietary Ca/P ratio ~ 5/1

Bar & Hurwitz 1987; Bues et al. 2019; Lieboldt et al. 2018; Packard & Packard 1984; Taher et al. 1984; Wilkinson et al. 2011

Poultry – laying hens

- Medullary bone as Ca pool → acute mobilisation of Ca for egg shells
  - Active bone resorption by osteoclasts
- Rhythm of Ca homeostasis
  - Blood Ca^{2+} at minimum levels ~16h before oviposition
  - Circadian changes of medullary bone Ca content
  - Changes of medullary bone architecture

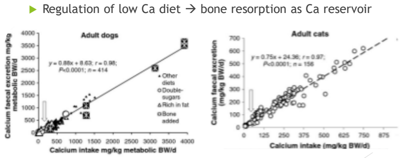
Figure from: Kerschnitzki et al. 2014



Parsons & Combs 1981; van der Velde et al. 1984; Etches 1987; Kirchgeßner 2004; Kerschnitzki et al. 2014

Dogs & cats

- Ca digestibility highly dependent on faecal DM excretion
- Not regulated by Ca intake level / requirement – linear function of intake
  - Basically independent of diet / Ca source
  - Regulation of low Ca diet → bone resorption as Ca reservoir



Böswald et al. 2018; Kienzle et al. 2017, 2019; Mack et al. 2015; Schmitt et al. 2018

Dogs & cats - ancestors

- Evolutionary adaptation to prey feeding

Mack et al. 2015

Dogs & cats

- Susceptible to Ca deficiency
- During growth and in adult maintenance
- Increased markers of bone resorption, less bone accretion

Puppy with Ca deficiency
Kölle et al. 2006

kitten fed meat only
Böswald unpublished

osteopenia (Ca, P, vit D $\downarrow$)
Dodd et al. 2019

Becker et al. 2012; Kölle et al. 2006; Liesegang et al. 1999; Schmitt et al. 2018

Omnivores

- Regulation of intestinal Ca absorption
  - Passive paracellular absorption
  - Active transcellular absorption – stimulated by vit D
- Low Ca intake – upregulation of aD(Ca)
- High fat diets decrease aD(Ca) in rodents

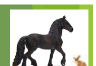
Favus et al. 1988; Frommelt et al. 2014; Schröder & Breves 2007; Song et a. 2003

Hindgut fermenters

- High Ca digestibility
  - Absorption in the small intestine
  - Renal excretion of excess Ca
  - →by-pass the large intestine so that P is available for microbial fermentation
- Renal excretion directly influenced by Ca intake ↔ constant plasma Ca

Schryver et al. 1970; Cheeke & Amberg 1973; Clauss & Hummel 2008; Böswald et al. 2018

Hindgut fermenters



Example: horse

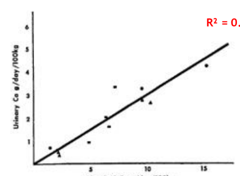


Fig. 3 Relationship of absorbed calcium to the renal excretion of calcium: $v_u = 0.291\ v_a + 0.057$. – ● – trial 1, – ▲ – trial 2, – ■ – trial 3. Correlation coefficient $r = 0.909$.

Schryver et al. 1970

Cattle

- Absorption begins in the forestomaches
  - High ruminal Ca absorption → less intestinal Ca absorption and vice versa
  - Potential link to transepithelial SCFA-transport
- Passive absorption dominates in maintenance – active absorption in times of higher demand

Boda & Cole 1956, Braithwaite 1976; Schröder & Breves 2007; Liesegang et al. 2008

Cattle

- Ca digestibility
  - There are reports of increasing aD(Ca) with increasing Ca demand
    - but not as an immediate response
    - only after depletion of body storage (skeleton!)
  - Phytate and oxalate do not decrease aD(Ca) – microbial degradation of complexes in the foregut
- Renal excretion relatively low and constant, independent of vit D, FGF-23

Boda & Cole 1956, Braithwaite 1976; Schröder & Breves 2007; Liesegang et al. 2008

Cattle

- Skeletal pool used during high Ca demand – loss of bone
  - Risk of milk fever at onset of lactation
    - Regulation disorder, relative Ca deficiency
  - Older animals are less able to replete the stores – risk higher > 3. lact.
    - Amount of vit D receptors ↓
    - t ½ of vit D ↓ due to higher degradation?!
    - Less resorptive surface on bone
    - PTH receptor insensitivity
  - Pre-calving high Ca diets
  - High P diets also increase risk – increase of vit D degradation
  - Low protein diets – aD(Ca) ↓, vit D activation ↓
  - DCAD
  - ….

Braithwaite 1976; DeGaris & Lean 2008; Firmenich et al. 2019; Wilkens 2019

Small ruminants

<u>Sheep</u>

= grazers

- Low dietary Ca alone does not stimulate Ca absorption
- Low Ca + calcitriol → aD(Ca) ↑
- Absolute Ca def. during late gestation (≠ cattle)

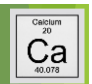
<u>Goats</u>

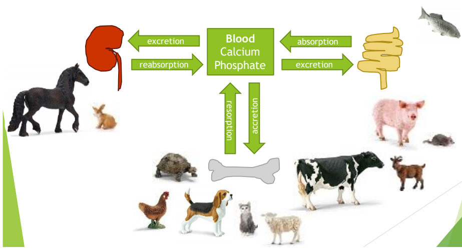
= intermediate feeders

- Adaptation to low Ca supply
  - Increased intestinal Ca absorption
  - esp. in jejunum
  - Vit D mediated
- Higher bone turnover rate than sheep

Hofmann 1989; Herm et al. 2015; Liesegang et al. 2003; Schröder & Breves 2007; Wilkens et al. 2011, 2012

Calcium – homeostatic pathways





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