Comparative calcium metabolism

Linda Böswald
Chair of Animal Nutrition and Dietetics
Ludwig-Maximilians-Universität München, Germany
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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

Calcium Metabolism of Teleosts

<table>
<thead>
<tr>
<th>Initial Calcium (mg/L)</th>
<th>Pooled Calcium (mg/L)</th>
<th>Calcium Secreted</th>
<th>Calcium Feed</th>
<th>Calcium Taken from Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>880</td>
<td>491.1</td>
<td>35.7</td>
<td>35.3</td>
<td>186.2</td>
</tr>
<tr>
<td>580</td>
<td>148.7</td>
<td>34.3</td>
<td>36.7</td>
<td>26.9</td>
</tr>
<tr>
<td>380</td>
<td>108.3</td>
<td>35.3</td>
<td>36.7</td>
<td>26.9</td>
</tr>
</tbody>
</table>
Fish

- Intestines: passive transport of Ca
- 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
  - Freshwater = low Ca content - dietary Ca requirement + osmoregulation
  - Ca already in solubil form

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

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


MBD in chameleons without Ca supplementation
  - Thin corticalis
  - Bone mineralised osteoid
  - Hacking trabeculae

**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

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

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**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 Ca²⁺ at minimum levels ~16h before oviposition
  - Circadian changes of medullary bone Ca content
  - Changes of medullary bone architecture


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**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

Ref: Stillwell et al. 2016; Stange et al. 2017, 2019; Hack et al. 2015; Schmitt et al. 2018
Dogs & cats - ancestors

- Evolutionary adaptation to prey feeding

Puppy with Ca deficiency
Kölle et al. 2006

Kitten fed meat only
Böswald unpublished

Osteopenia (Ca, P, vit D)
Dodd et al. 2019

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
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Osteopenia (Ca, P, vit D)
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; Frommel et al. 2014; Schröder & Breves 2007; Song et al. 2003
Hindgut fermenters

- High Ca digestibility
  - Absorption in the small intestine
  - Renal excretion of excess Ca
  - Bypass 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; Claus & Hummel 2008; Böswald et al. 2018

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

Cattle

- **Ca digestibility**
  - There are reports of increasing $\Delta$D(Ca) with increasing Ca demand
  - but not as an immediate response
  - only after depletion of body storage (skeleton!)
  - Phytate and oxalate do not decrease $\Delta$D(Ca) - microbial degradation of complexes in the foregut

- **Renal excretion relatively low and constant, independent of vit D, FGF-23**

Buda & Cole 1956, Braithwaite 1974; Schröder & Breves 2007; Liesegang et al. 2008

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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 ↓
  - 1 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 - $\Delta$D(Ca) ↓, vit D activation ↓
  - DCAD

Braithwaite 1974, DeGaris & Lene 2008; Finnerich et al. 2019; Wilkens 2019

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Small ruminants

**Sheep** = grazers

- Low dietary Ca alone does not stimulate Ca absorption
- Low Ca + calcitriol $\rightarrow$ $\Delta$D(Ca) ↓
- Absolute Ca def. during late gestation (= cattle)

Hofmann 1999a, den Otter et al. 2003; Liesegang et al. 2007; Schröder & Breves 2007; Wilkens et al. 2011; 2012

**Goats** = intermediate feeders

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

References I/III

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