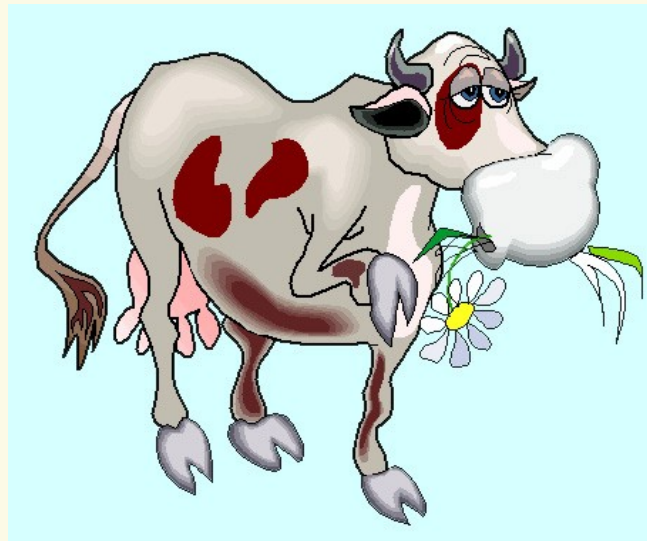


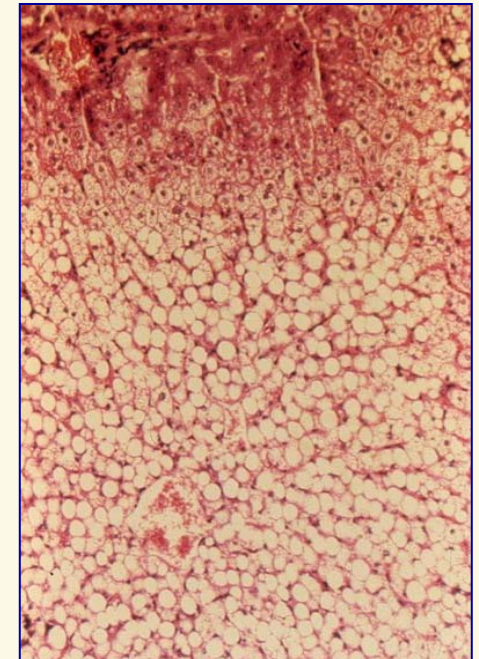
Nutritional aspects of the fatty liver syndrome in dairy cows



Concetta Amato
European College of Veterinary and Comparative Nutrition
Residency class 2015
September 15th- 16th
Toulouse

Fatty liver syndrome (1)

- Fatty liver syndrome is metabolic disorder that result from **intense fat mobilization** during hormonal changes and negative energy balance associated with the **transition period**.
- The **liver is an important metabolic organ**. It plays a central role in controlling energy metabolism, hormonal status, detoxification of harmful compounds, immune responsiveness and reproductive function. Livers can become engorged with fat when **there is an increase in the uptake of fatty acids from blood**.

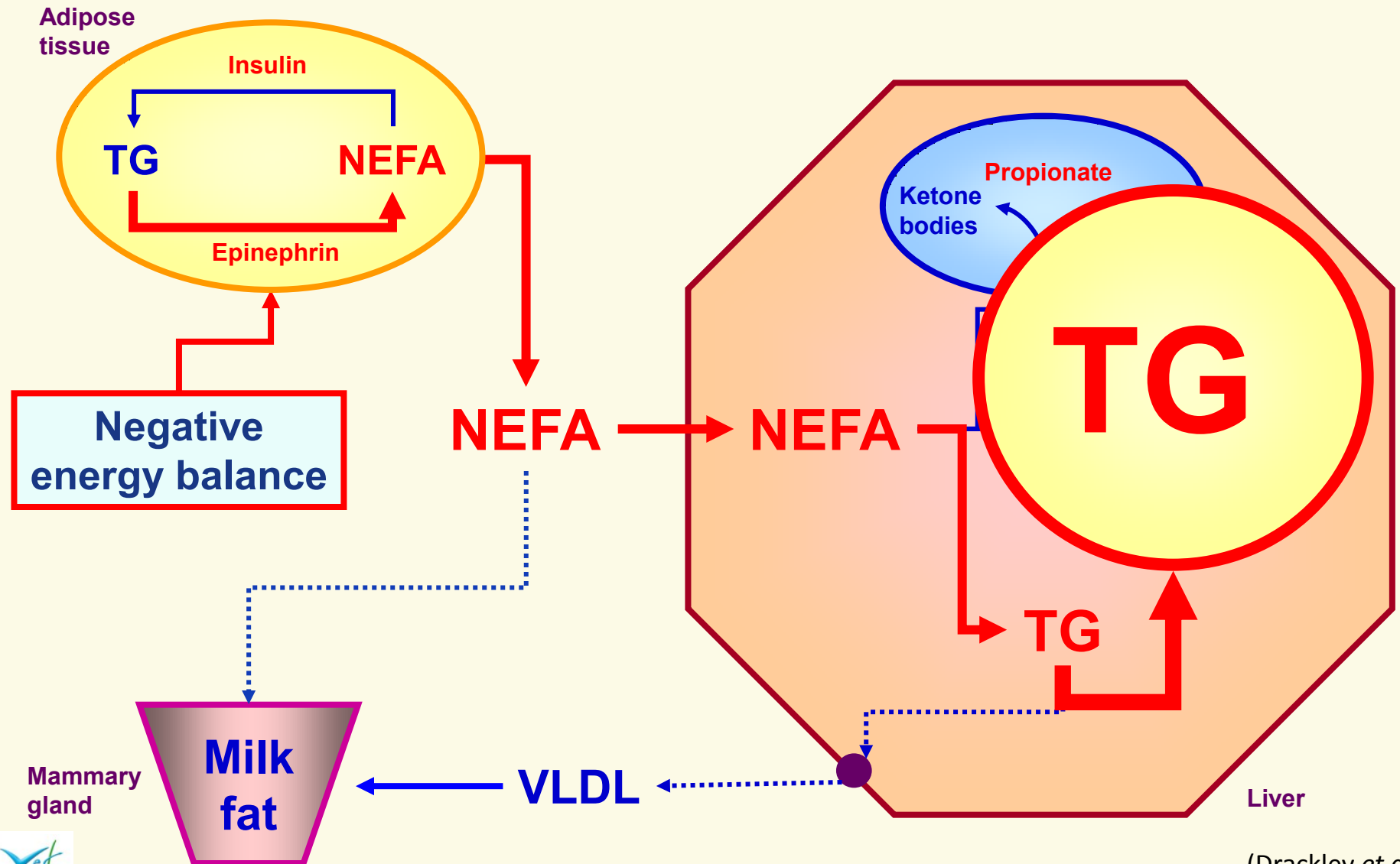


Fatty liver syndrome (2)

- Meeting the **nutritional and metabolic needs** of the dairy cow **during the transition to lactation** is a great challenge for optimal health and lactation performance.
- Fatty liver arises in response to various nutritional, hormonal, or toxic effects, but has mainly been reported as **a physiological or pathological situation resulting from an excessive mobilization of fat**.
- Fat infiltration occurs prior to and mainly during calving.
- More than **50% of multiparous dairy cows** would experience fatty liver at calving.
- An excessive infiltration has been associated **with increased incidence of mastitis, displaced abomasum, retained placenta, metritis, poor reproductive performance, and immune suppression**.
- Cows with fatty liver are also more prone to develop **ketosis and suffer production losses**.

(Veenhuizen *et al.*, 1991; Bobe *et al.*, 2004; Gonzalez *et al.*, 2011; Zom, *et al.* 2011; Goselink *et al.* 2012; Grummer, 2013)

Relationships among lipid metabolism in adipose tissue, liver, and mammary gland



(Drackley et al. 1999)

Main physiological hormone changes occurring in early lactation

↓ insulin

↑ prolactin

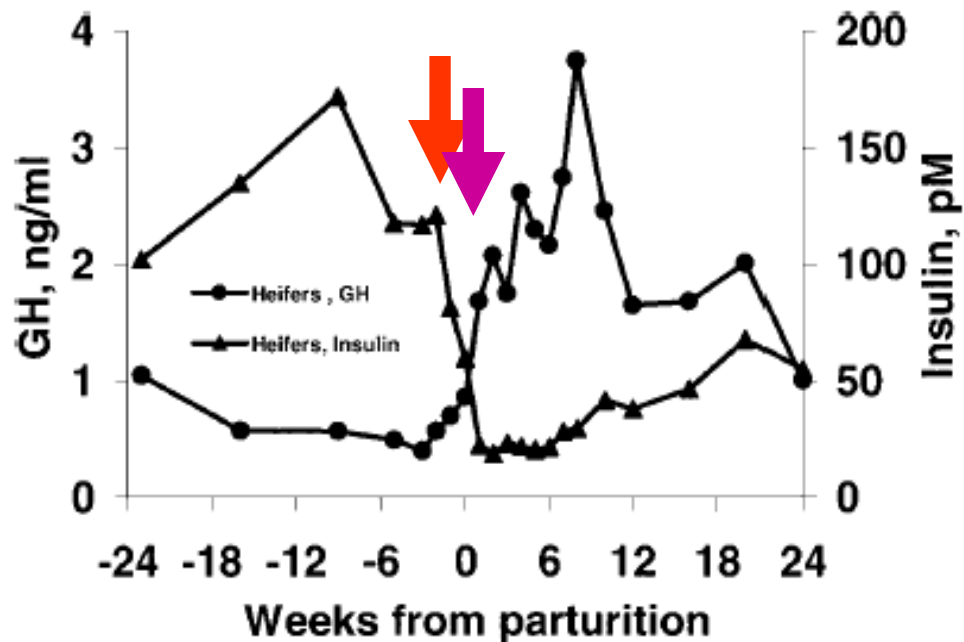
↑ somatotropin

↑ glucocorticoids

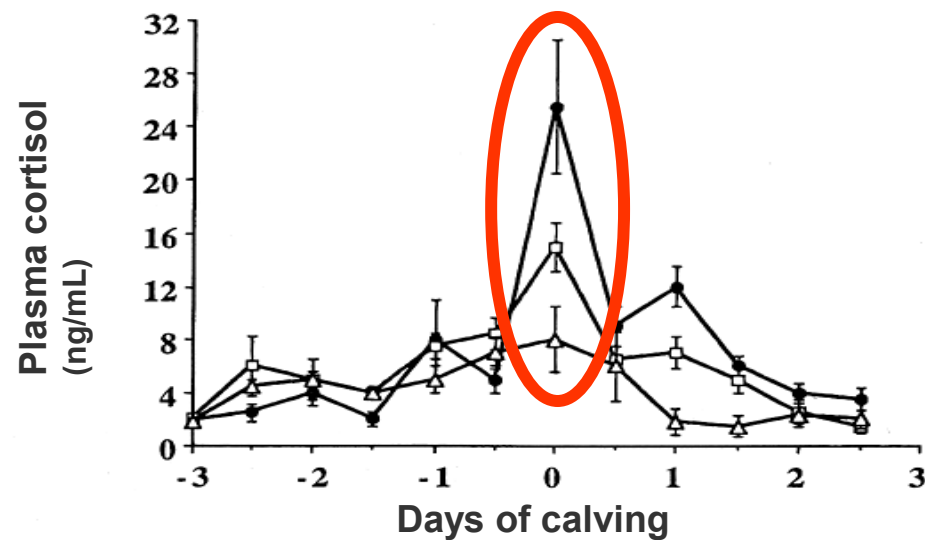
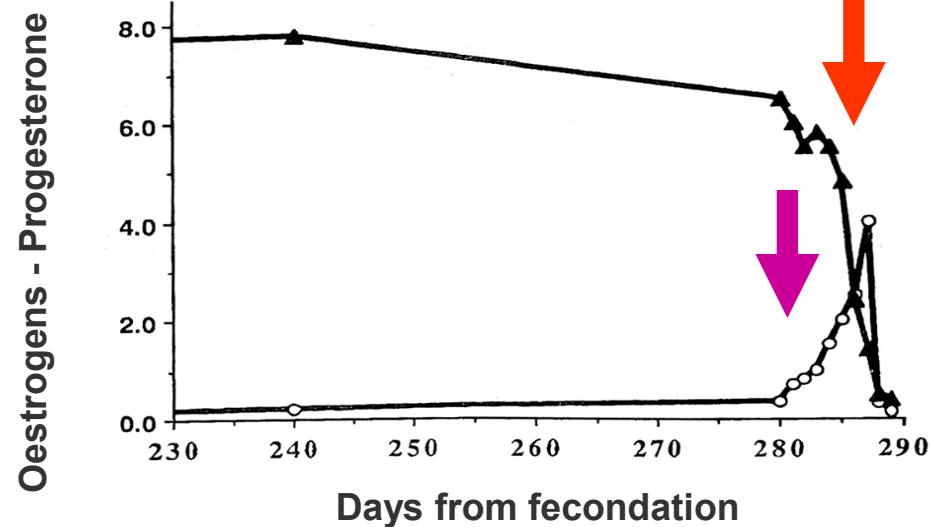
↓ IGF-I

↓ thyroid hormones

- ✓ All these changes are related to the new metabolic status of the cow.
- ✓ At the same time
 - the mammary tissue develops,
 - and food intake increases as well as food utilization.



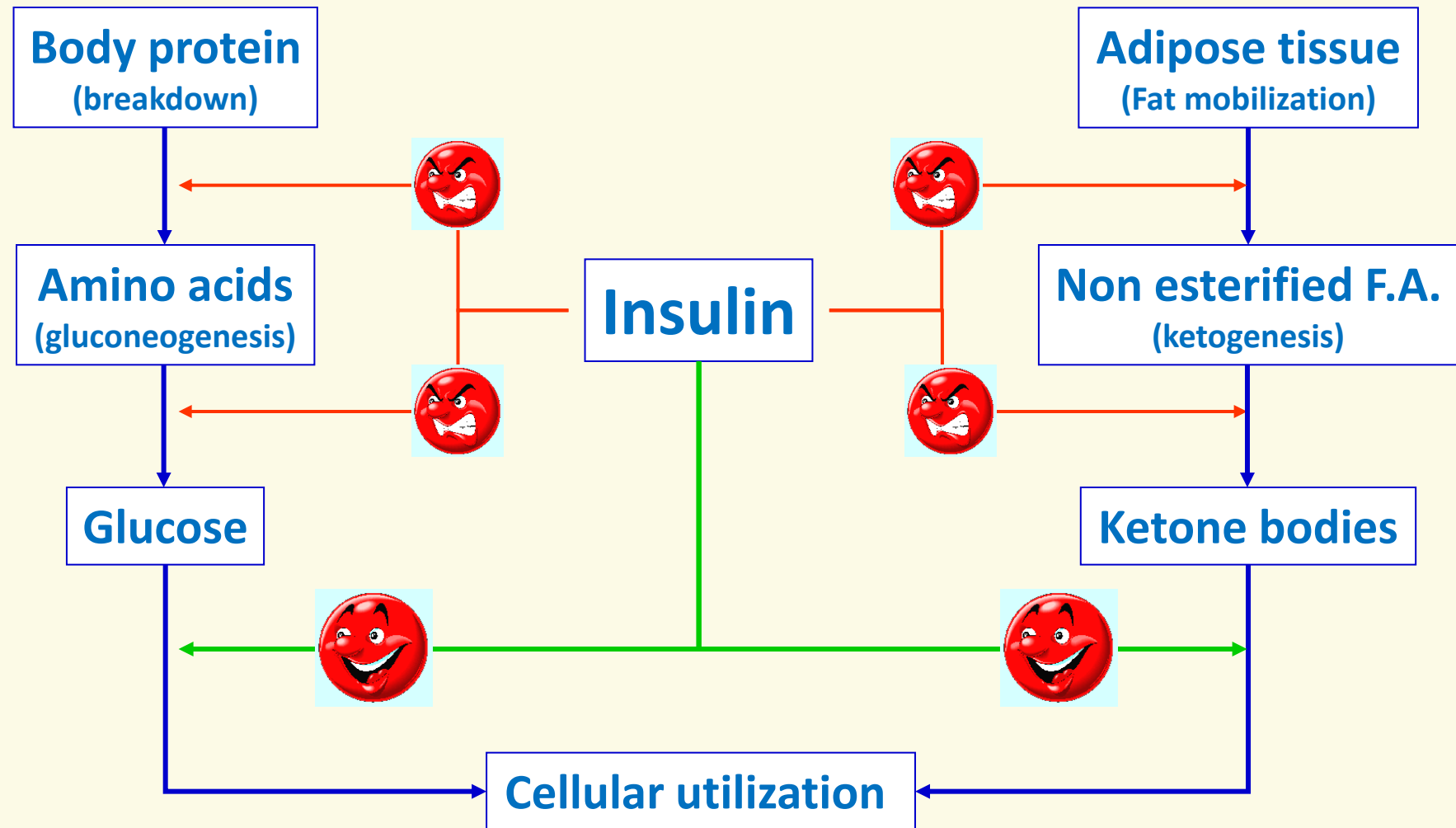
(Ingvarsen and Andersen 2000)



(Horst and Jorgensen 1982)

Cortisol & calcemia in paretic, non paretic, and borderline dairy cows

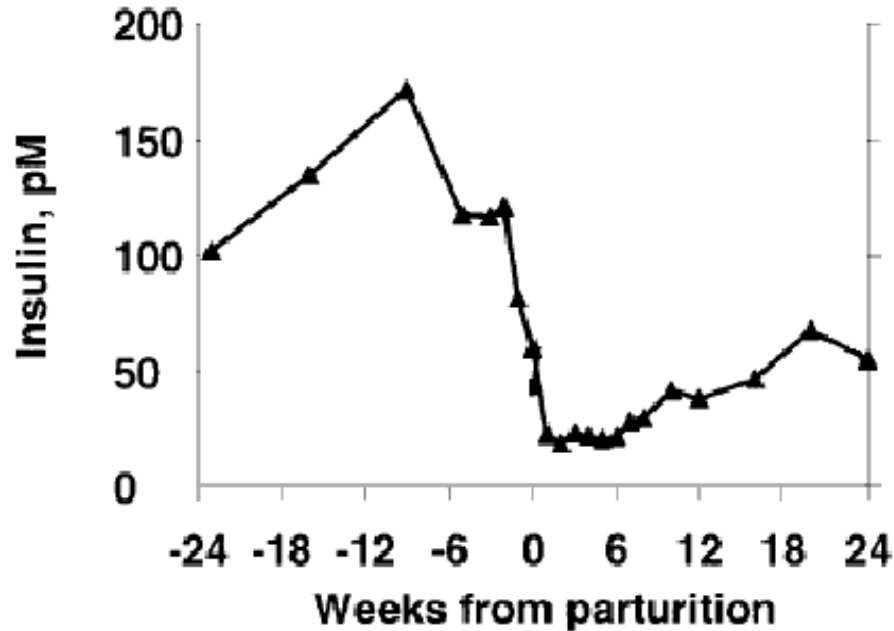
Insulin : main regulatory functions on nutrient utilization



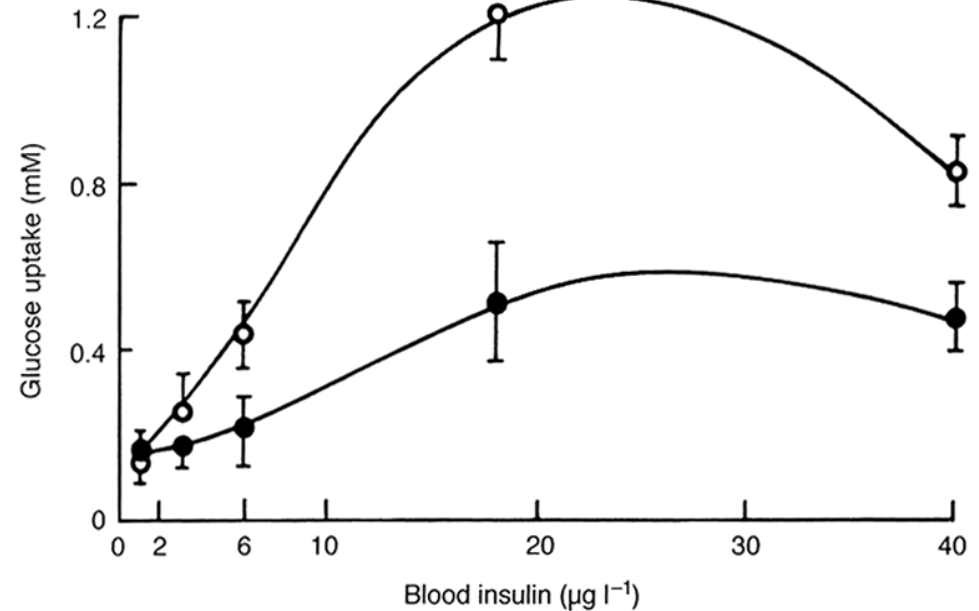
Temporarily, all anabolic and anti catabolic effects of insulin are suppressed

This leads to a major reduction in triglyceride synthesis, and predisposes to lipolysis through attenuation of the antilipolytic effect of insulin.

Plasma insulin - Insulin sensitivity - Consequences



Serum concentration of insulin during the periparturient period in heifers
(Ingvarsen and Andersen 2000)



Effect of insulin on the arterio-venous difference for glucose across the hindlimb of non-lactating (○) and lactating sheep (●)
(Vernon *et al.*, 1990)

Main physiological adaptations occurring in early lactation (Bauman 2000)

Increased output

- Mammary tissue**
- ↑ number of secretory cells
 - ↑ supply of blood
 - ↑ nutrient use

Increased input

- Food intake**
- ↑ quantity
- Digestive tract**
- ↑ size
 - ↑ absorptive capacity
 - ↑ rates of nutrient absorption

Main physiological adaptations occurring in early lactation (Bauman 2000)

Increased synthesis and redistribution of nutrients

Liver

Anabolic activity dramatically increases

- ↑ gluconeogenesis
- ↑ glycogen mobilization
- ↑ protein synthesis

Adipose tissue

- ↑ lipolysis
- ↓ fatty acid uptake and synthesis

Skeletal muscle

- ↓ glucose utilization
- protein → degradation ↑ synthesis ↓

Bone

- ↑ mobilization of Ca and P

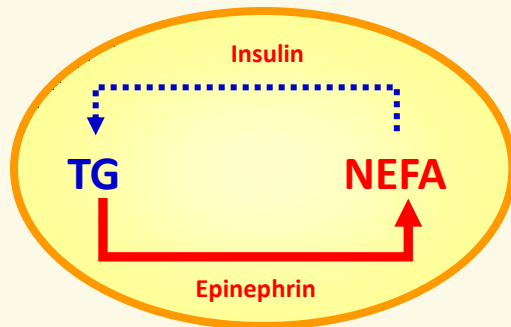
Oriented
nutrient
release

All these changes contribute to sustain mammary function and export

Body condition at calving

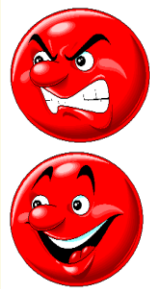
↑ BC → ↑ Fat stores

↑ Stores → ↑ Mobilization



↑ Energy intake

↑ Protein intake



■ An excessive **body condition** at calving is a predisposing factor to fat release and fatty liver.

■ The more the **fat cow** has lipid stores the more it releases fatty acids when nutritional and hormonal conditions favor lipolysis.

■ **High energy level** in diets given prior to calving induce a more important weight gain and then weight loss, higher plasma non-esterified fatty acid levels, and higher hepatic lipid infiltration in early lactation.

■ The effect of energy intake prior to calving can be modulated by **protein availability**.

Increasing the protein level by 15 % (that is from 14 to 16 % in the diet) allowed to a decrease in fat infiltration by up to two-thirds.

Body condition at calving

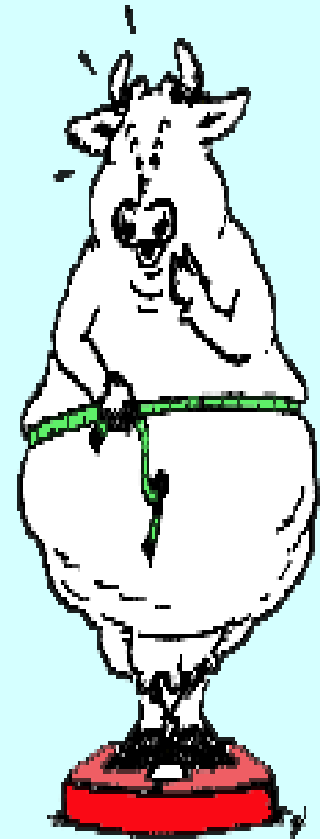
Excess body condition and important weight loss predispose strongly to fatty liver



Too fat → risk of diseases ↑



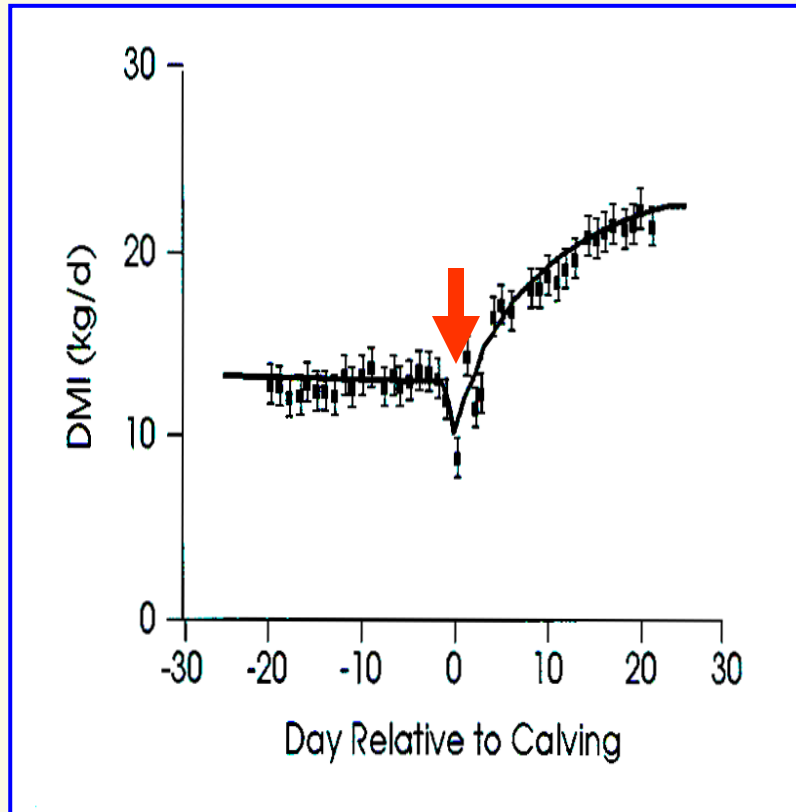
liver



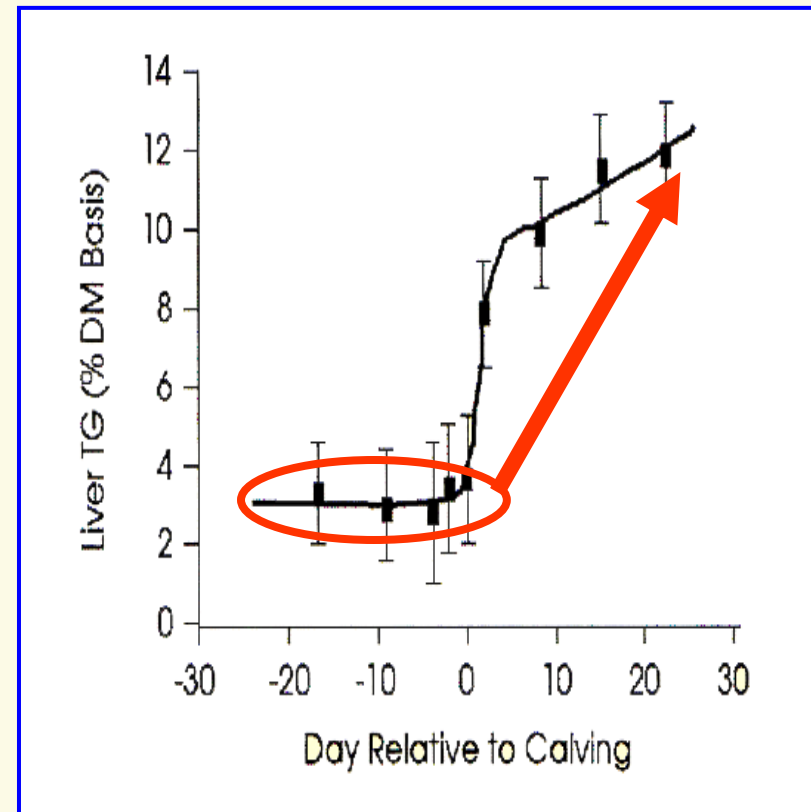
Too lean → production ↓



Food intake and hepatic infiltration



Dry matter intake around parturition in dairy cows
(Vasquez-Anon *et al.* 1994)



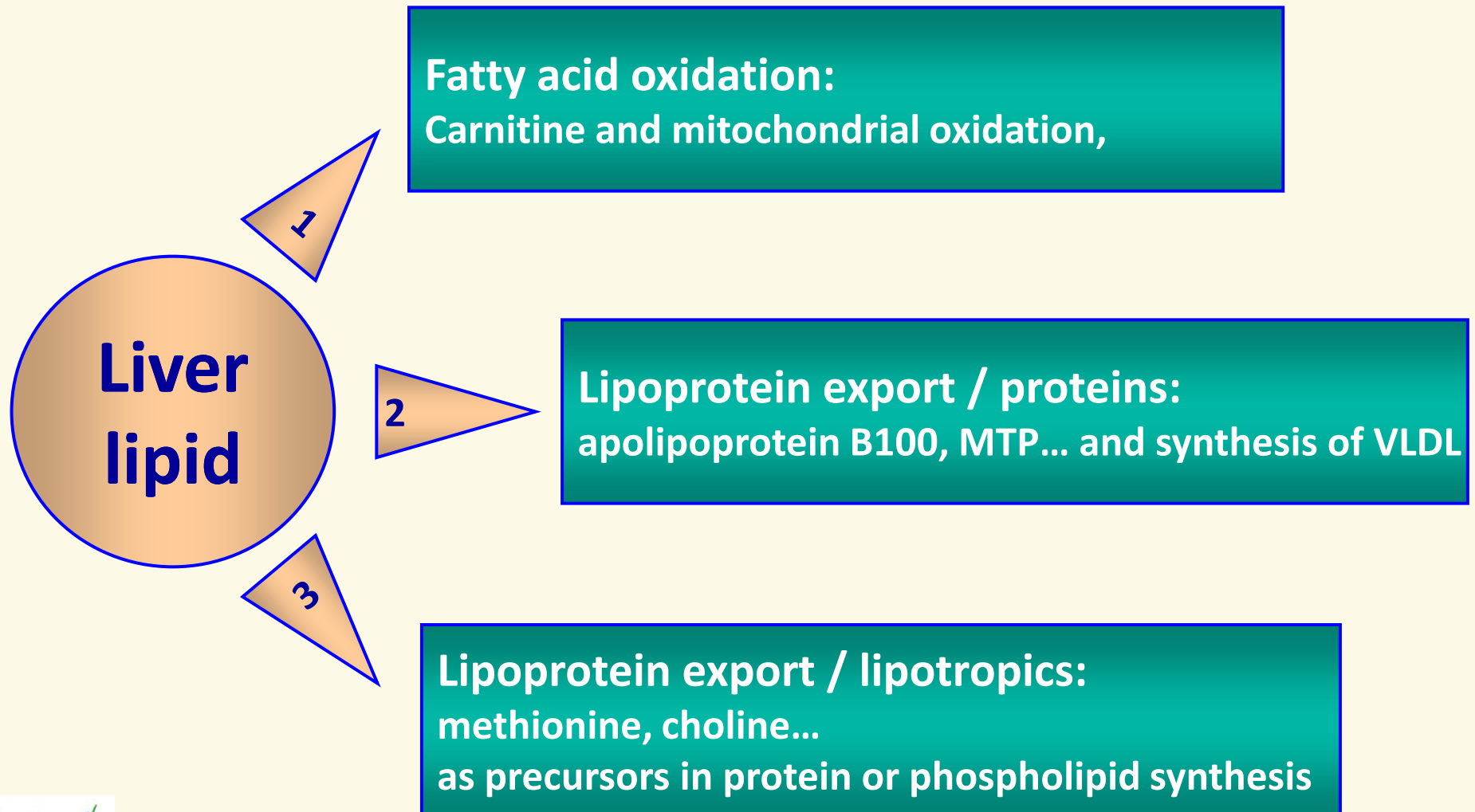
Changes in liver T.G. around parturition in dairy cows
(Vasquez-Anon *et al.* 1994)

Intake level decrease by 30% within the 2 last weeks prior to calving, which is responsible for fat mobilization.

Two weeks before calving, hepatic lipid level is approximately 5%. The day after calving, it reaches up to 10 to 15% in 3 cows out of 4.

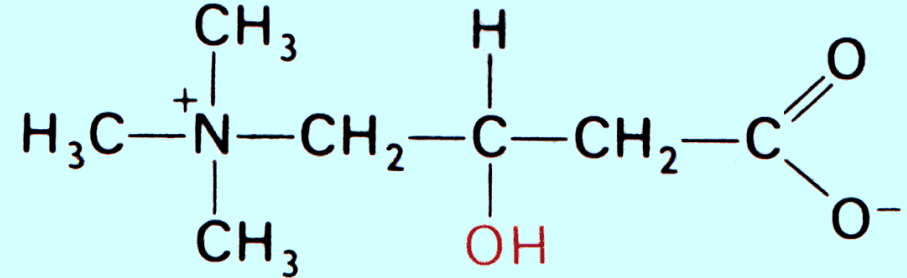
(Zom, *et al.* 2011; Grummer, 2013)

Hepatic lipid metabolism: main ways



Carnitine and mitochondrial oxidation

- Carnitine is an important key factor in liver fatty acid oxidation
- Carnitine is able to **modulate the intracellular concentrations of free- and acyl-Coenzyme A.**



Carnitine

Carnitine is bio-synthetized from lysine and méthionine

Carnitine is a required cofactor for carnitine palmitoyltransferase-I , **which condenses**

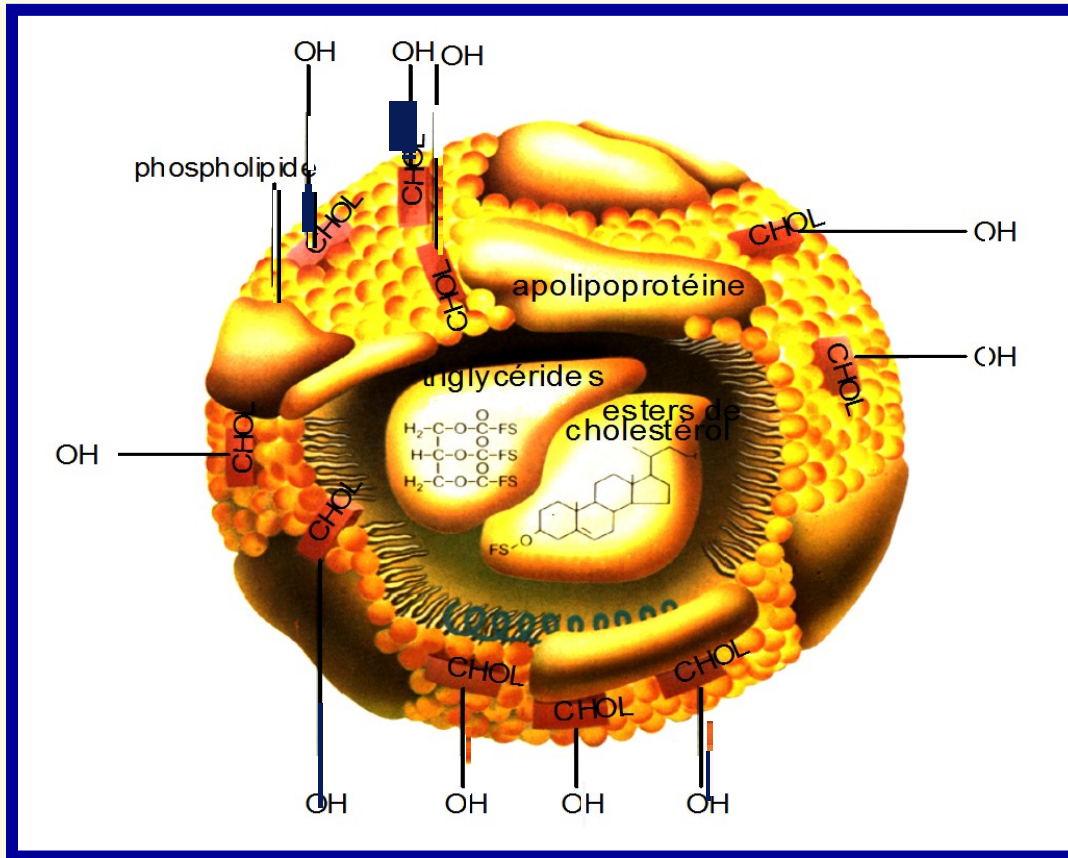
Carnitine with activated long-chain fatty acids (LCFA) **for transport from cytosol into mitochondria;**

therefore, carnitine is essential **for mitochondrial β -oxidation of LCFA (lower in ruminants compared to non-ruminants.**

Hepatic β -oxidation of LCFA is stimulated by exogenous carnitine in several

(Owen *et al.*, 2001; Spaniol *et al.*, 2003; Carlson *et al.*, 2007; Goselink *et al.*, 2012)

Triglyceride export : Very low density lipoprotein (VLDL)



VLDL
size, structure and composition

300-800 Å

Apo B100, C-III, C-II, E

50-60 % Triglycerides

14-22 % Cholesterol

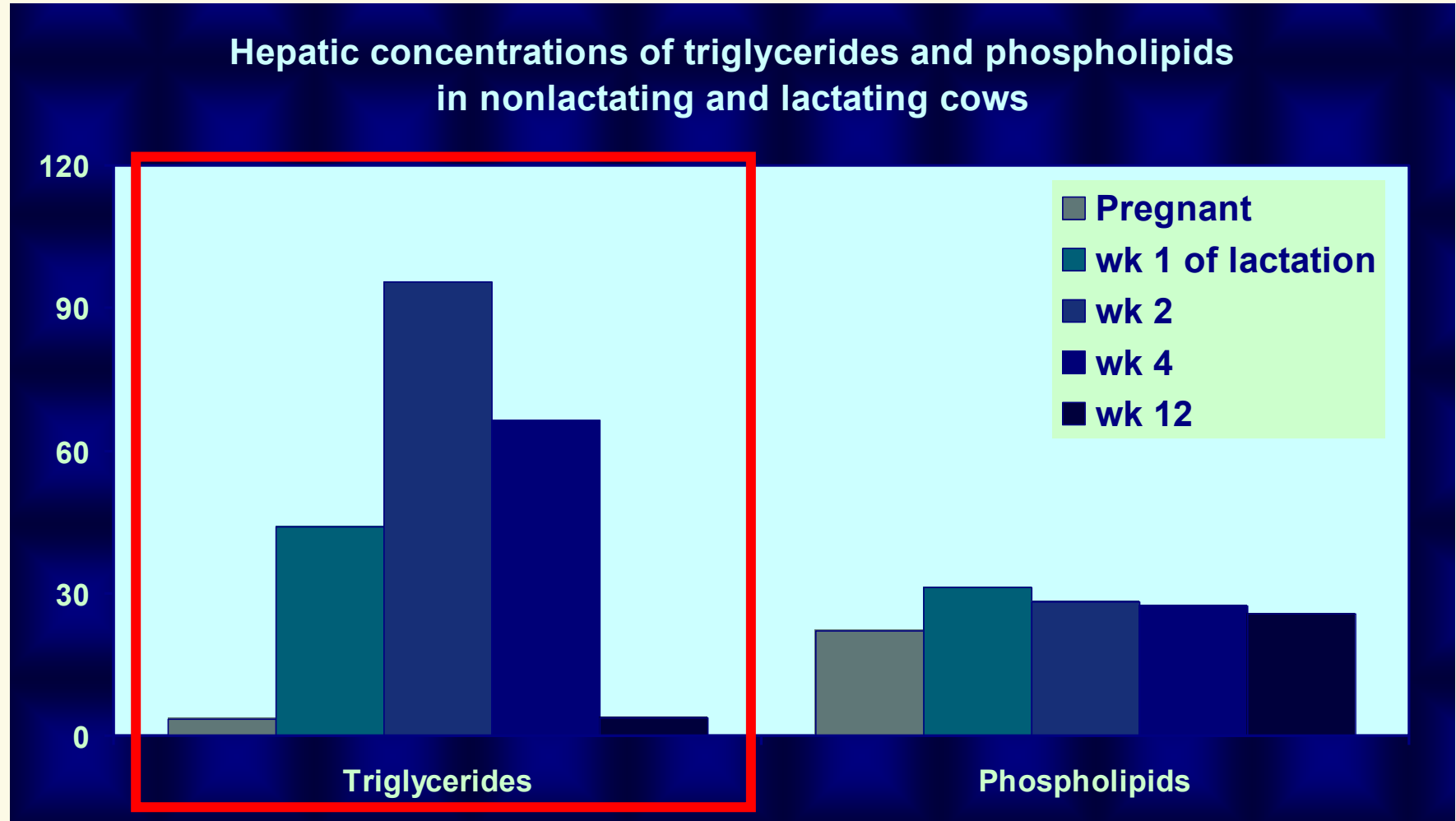
12-20 % Phospholipids

• **Low ability of ruminant liver to export triglycerides as part of VLDL : contribute to fatty liver**

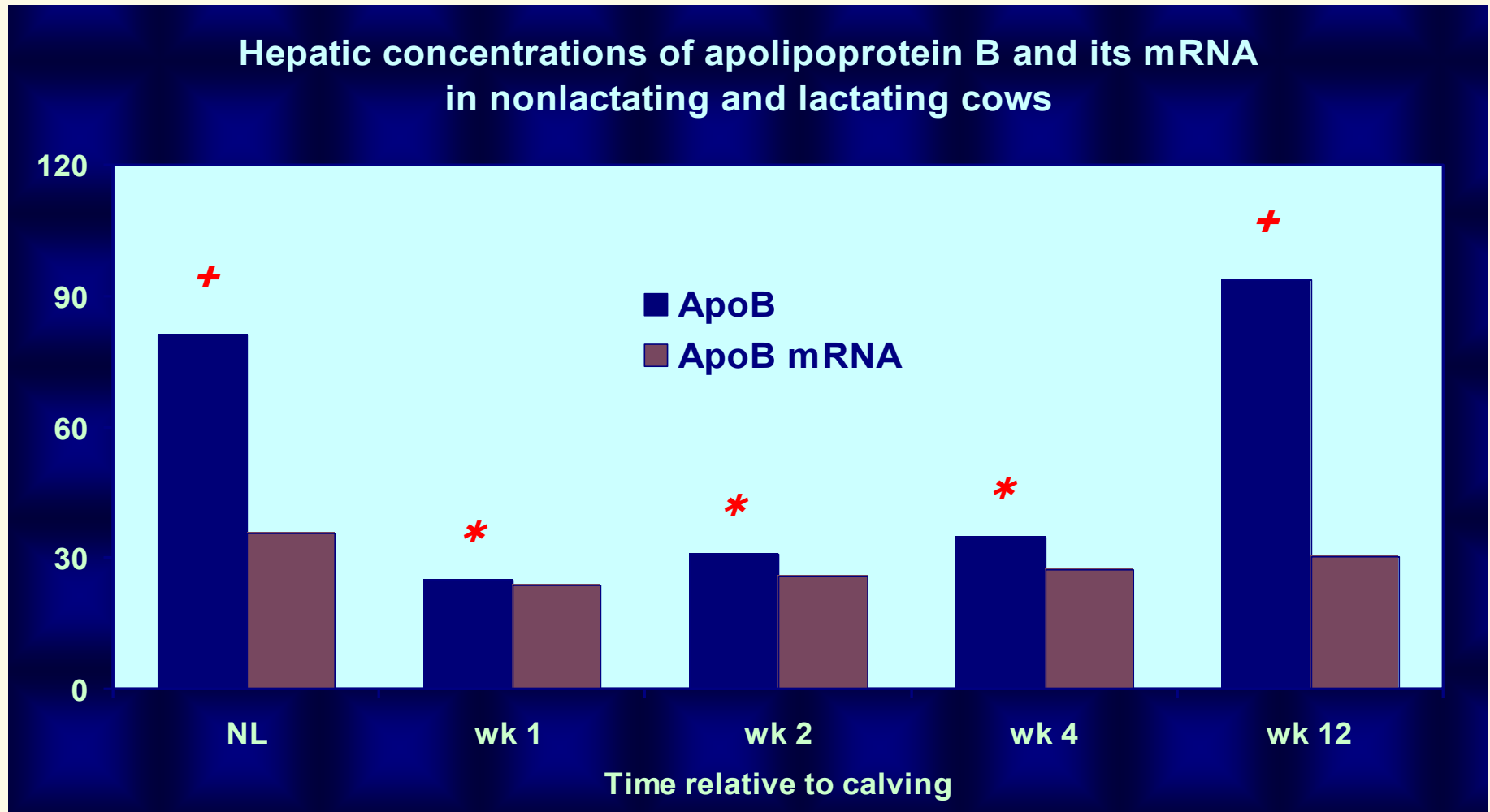
• **Two proteins play a major role in VLDL synthesis:**

- **apolipoprotein B100 that is its main constitutive protein**
- **and microsomal triglyceride transfer protein, which is needed for its assembly.**

Liver apolipoprotein B100 in early lactation (Gruffat et al. 1997)



Liver apolipoprotein B100 in early lactation (Gruffat et al. 1997)

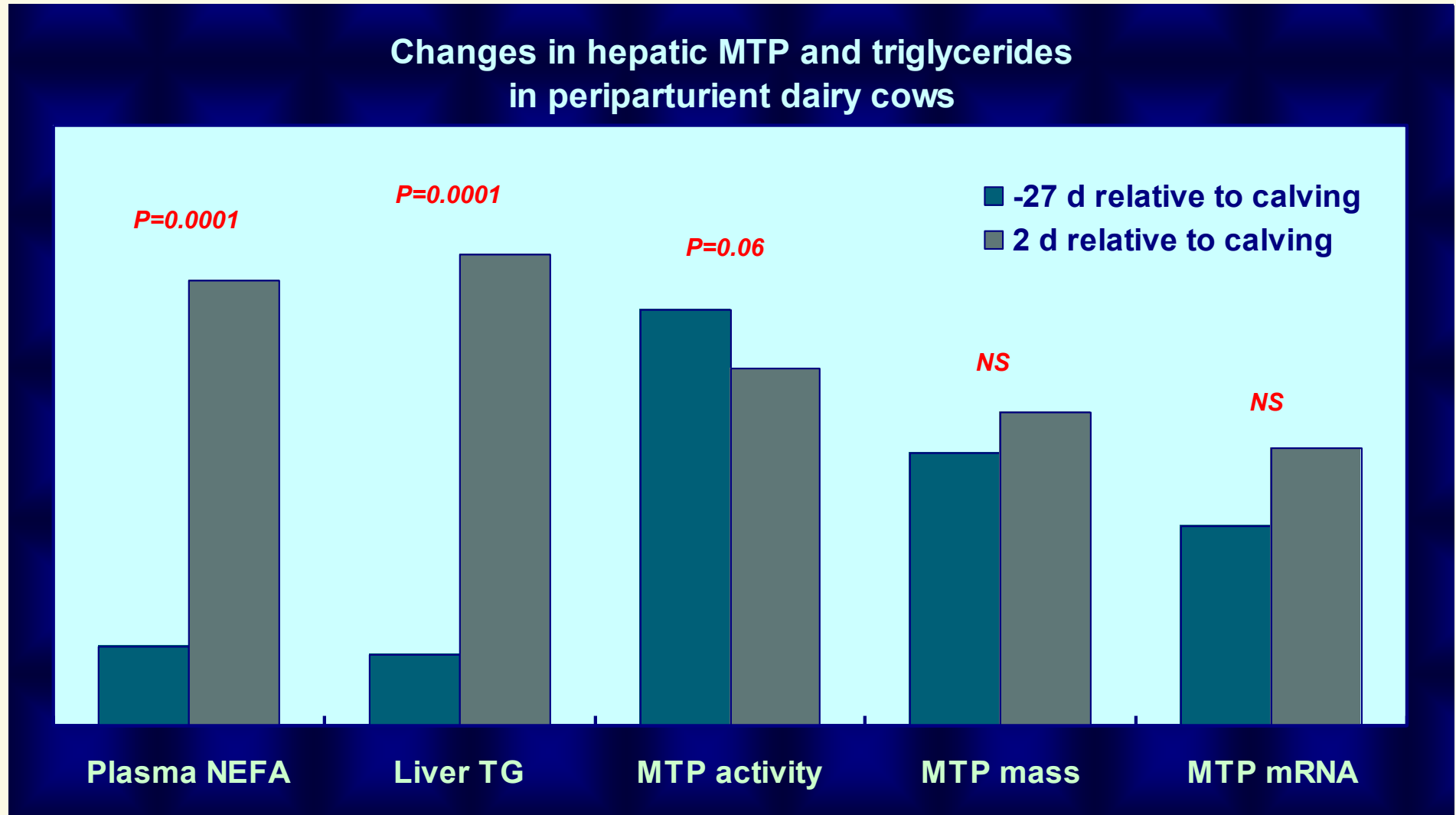


Microsomal triglyceride transfer protein inhibitors

- **MTP inhibitors have been tested for their potential role in the treatment of cardiovascular diseases**
 - ✓ Block hepatic secretion of very low density lipoproteins (VLDL) and intestinal secretion of chylomicrons.
 - ✓ Lower low density lipoprotein (LDL) cholesterol and reduce postprandial lipemia.
 - ➔ Benefit in the treatment of atherosclerosis and consequent cardiovascular disease.
- **Main adverse effect:**

The blockage of hepatic lipid secretion leads to fatty liver

Changes in hepatic microsomal triglyceride transfer protein and triglycerides in periparturient dairy cows (Bremmer et al. 2000)



(Bremmer et al. 2000; Goselink et al. 2012)

DL-methionine

Among amino acids methionine plays a major role.

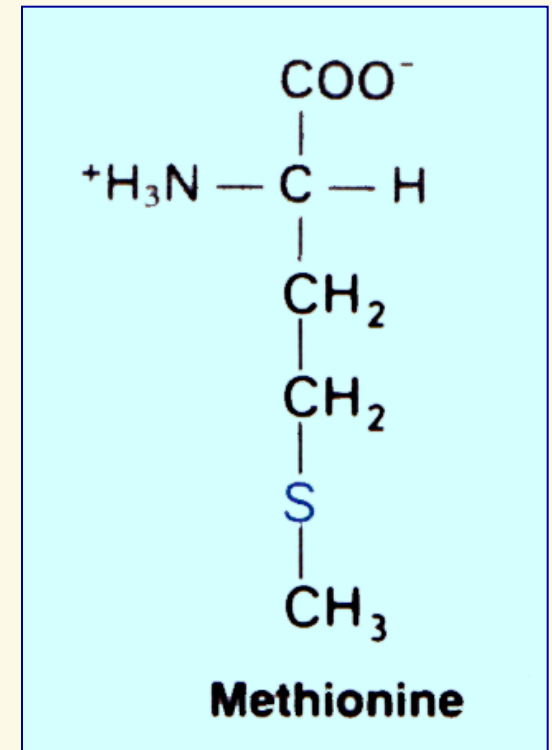
✓ The limiting factor of **protein synthesis** in most dietary situations.

It could therefore limit

- protein synthesis (apolipoproteins...)
- carnitine synthesis (Met + Lys)

✓ Its specific role as **lipotropic factor** has also been suggested:

- as other methyl group donor,
- it contributes to synthesis of phospholipids that are needed for VLDL assembly



Homocysteine → Methionine → Homocysteine / Vitamin B12, Folates

L-methionine infusion – DL-methionine oral administration

- Intravenous infusions of L-methionine

- ↓ ketone body formation

- ↑ hepatic gluconeogenesis

- ↑ secretion of VLDL

- ↓ fatty acid infiltration

- Dietary supplements of DL-methionine

- ➡ same effects

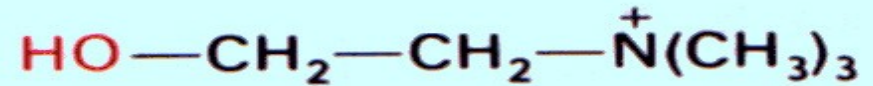
(Shibano et Kawamura, 2006)

Choline

Choline is crucial for normal function of all cells. ...

Lipotropic effect : It is a precursor of phospholipids

Phospholipids (PC), are components of all cell membranes and lipoproteins that function to transport lipids through the circulatory system.



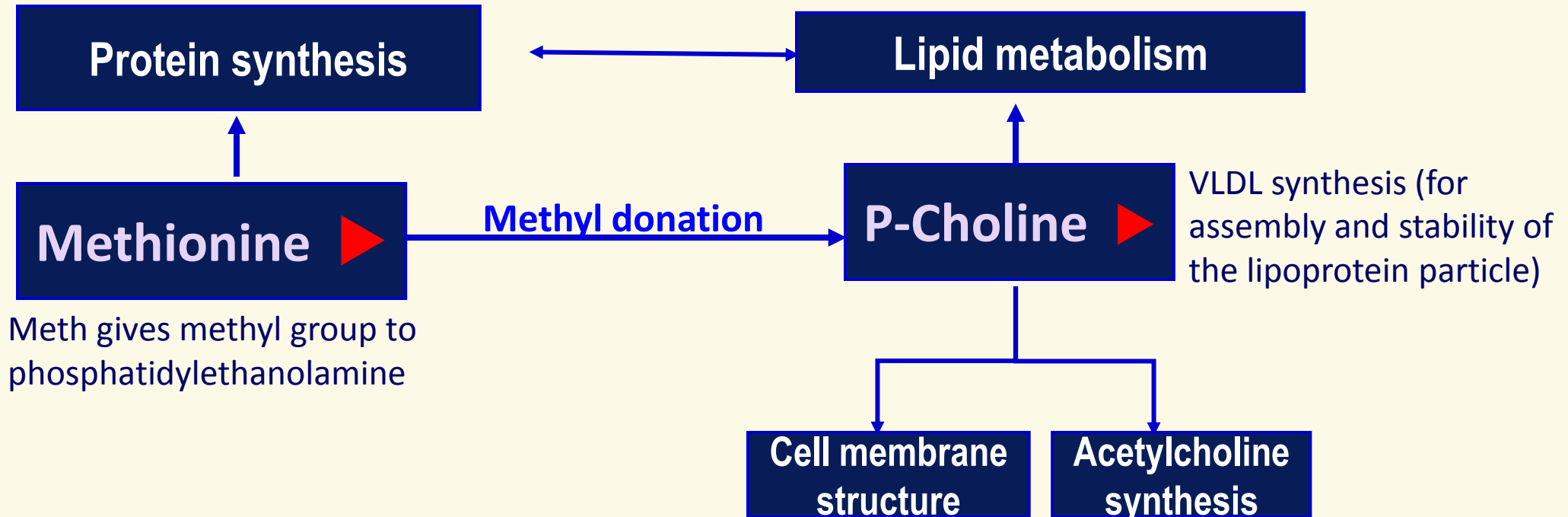
Choline

Produced in the body by methylation ethanolamine

- ✓ Choline is a **source of methyl groups**, therefore, it can spare methionine and have interactions with other nutrients involved in one-carbon metabolism (e.g. folate).
- ✓ Choline is also a **component of acetylcholine**, an important neurotransmitter.
- ✓ **Choline deficiency** induces hepatic steatosis: in animals, as well as calves.
- ✓ **Rumen-protect choline supplementation** during the transition period improves hepatic fat export in periparturient dairy cows and this may potentially decrease the risk for metabolic disorders in the periparturient dairy

Interrelationships between methionine and choline in liver metabolism

Choline metabolism highly depends on methyl transfers, and therefore on methionine



- ✓ This indicates:
- Choline biosynthesis is an important outcome of methionine,
 - and that **choline and methionine** play therefore central roles in hepatic lipid metabolism.
- **Choline** has an additional specific role in neurotransmitter synthesis and cell membrane structure as phosphatidylcholine,
and **methionine** has a specific role in protein synthesis.

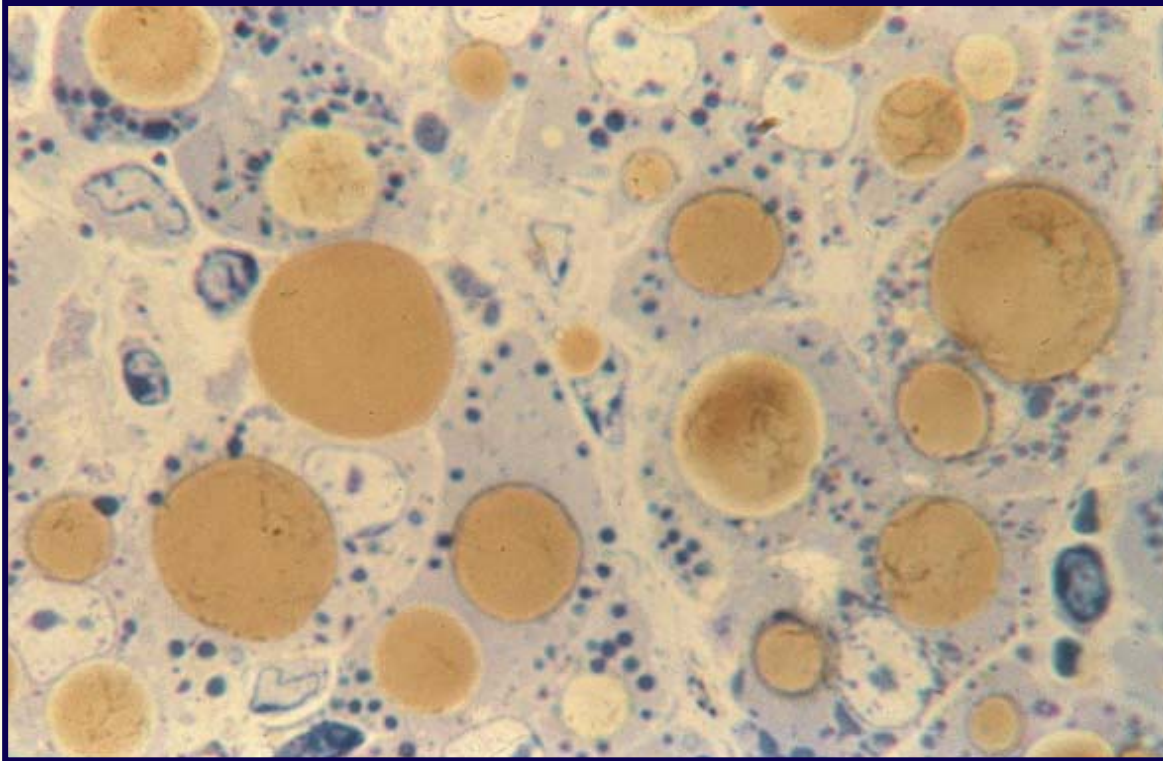
Other nutritional factors (hepatoprotectors...)

- ☞ Sorbitol **Choleretic agent**
 - ☞ Betaine
 - ☞ Inositol
 - ☞ Glutathione
 - ☞ Orotic acid
- } **Cholagogues: lipotropic factors**
- ☞ B vitamin, especially vitamin B12 and niacin
 - ☞ Propylene glycol

➤ No experiment has been definitely conclusive regarding a lowering effect on incidence or severity of fatty liver.

➤ They are more or less known as factors improving the overall hepatic function. Especially,
• daily drenching with half to one liter propylene glycol **increases glycemia and lowers plasma non esterified fatty acids.**

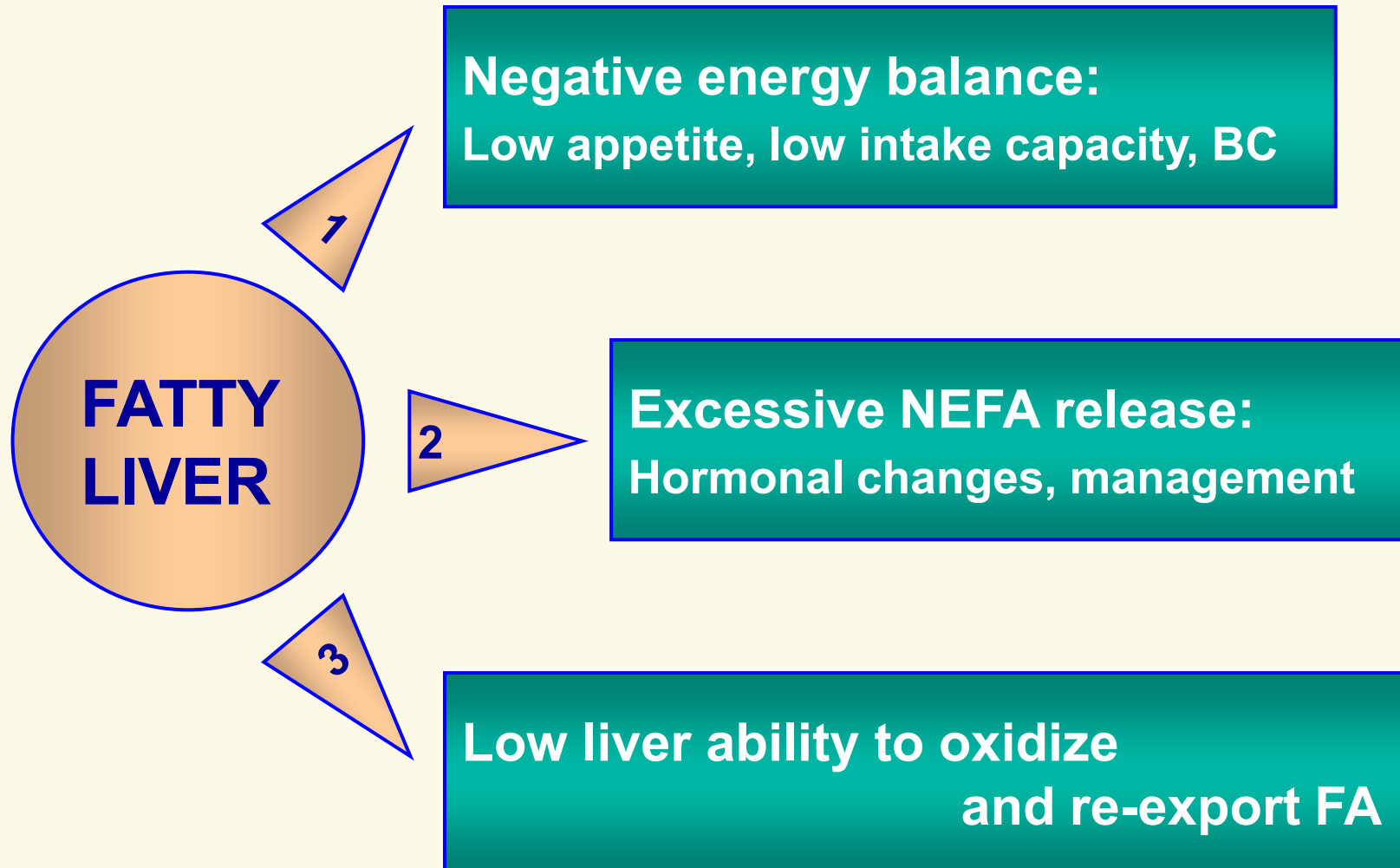
Conclusion



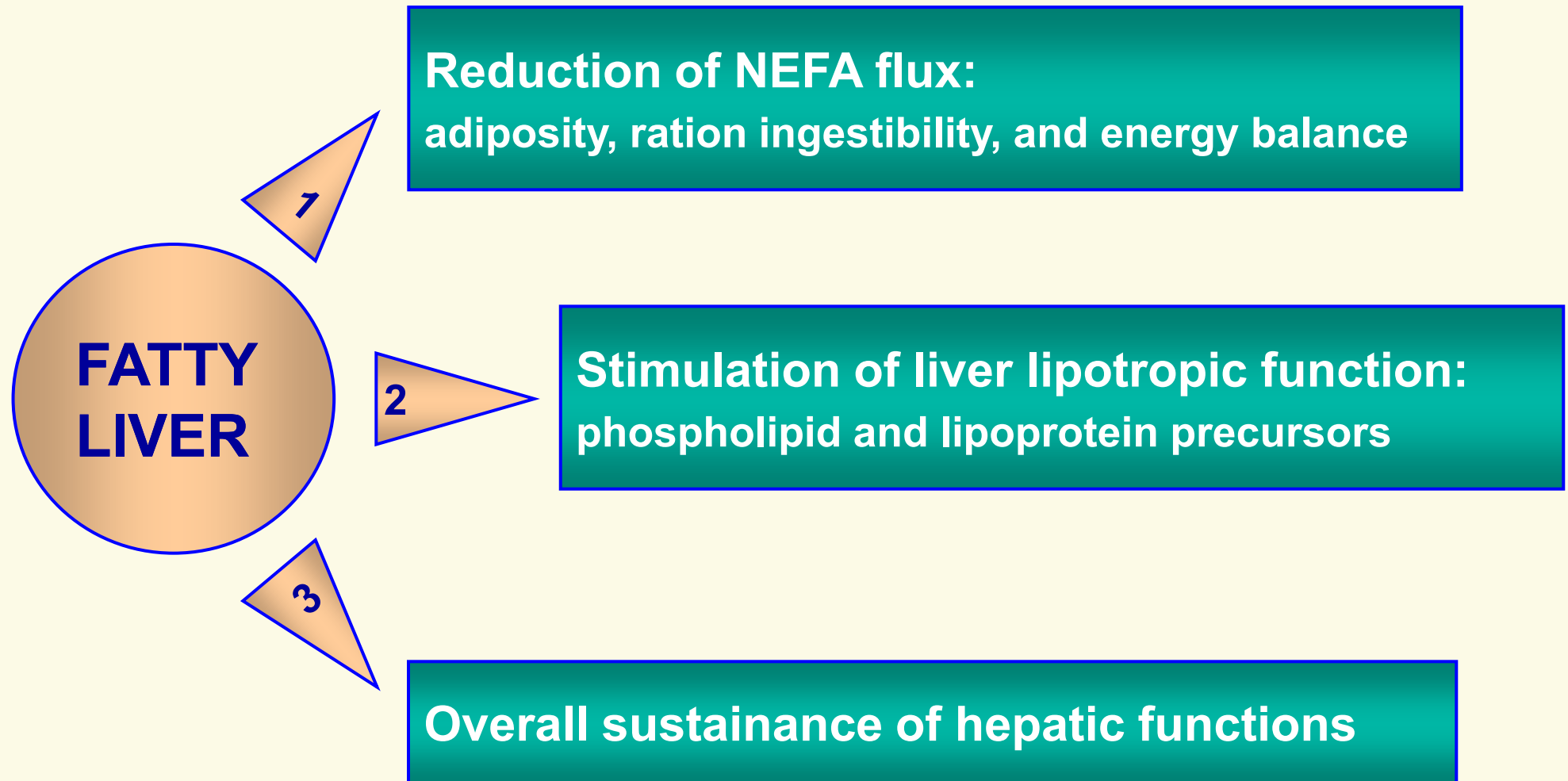
Causes

Solutions

Fatty liver : main causes



Fatty liver : main solutions



**Thank you
for your
attention!**



References

- Veenhuizen, J. J., J. K. Drackley, M. J. Richard, T. P. Sanderson, L. D. Miller, and J. W. Young. 1991. Metabolic changes in blood and liver during development and early treatment of experimental fatty liver and ketosis in cows. *J. Dairy Sci.* 74:4238-4253.
- Bobe, G., J. W. Young, and D. C. Beitz. 2004. Invited review: Pathology, etiology, prevention, and treatment of fatty liver in dairy cows. *J. Dairy Sci.* 87:3105–3124.
- González, F. D., R. Muiño, V. Pereira, R. Campos, and J. L. Benedito. 2011. Relationship among blood indicators of lipomobilization and hepatic function during early lactation in high-yielding dairy cows. *J. Vet. Sci.* 12:251-255.
- Collier, R. J., L. H. Baumgard, A. L. Lock and D. E. Bauman. 2005. Physiological limitations, nutrient partitioning. In *Yields of farmed species. Constraints and opportunities in the 21st century* (ed. R Sylvester-Bradley and J Wiseman), pp. 351–377. Nottingham University Press, Nottingham, UK.
- Grummer, R. R. 2008. Nutritional and management strategies for the prevention of fatty liver in dairy cattle. *The Veterinary Journal* 76 , 10–20.
- Drackley, J. K. 1999. Biology of dairy cows during the transition period: The final frontier? *J. Dairy Sci.* 82:2259–2273.
- Ingvarsen, K. L. and J. B. Andersen. 2000. Integration of metabolism and intake regulation: A review focusing on periparturient animals. *J. Dairy Sci.* 83:1573–1597.
- Horst, R. L. and N. A. Jorgensen. 1982. Elevated plasma cortisol during induced and spontaneous hypocalcemia in ruminants. *J. Dairy Sci.* 65:2332–2337.
- Vernon, R. G., A. Faulkner, W. W. Hay, D. T. Calvert, D. J. Flint. 1990. Insulin resistance of hind-limb tissues in vivo in lactating sheep. *Biochem J.* Sep 15; 270(3):783-6.
- Gruffat, D., D. Durand, Y. Chilliard, P. Williams, D. Bauchart. 1997. Hepatic gene expression of apolipoprotein B100 during early lactation in underfed, high producing dairy cows. *J. Dairy Sci.* 80, 657-666
- Bremmer, D. R., S. J. Bertics, S. A. Besong and R. R. Grummer. 2000. Changes in hepatic microsomal triglyceride transfer protein and triglyceride in periparturient dairy cattle. *J. Dairy Sci.* 83:2252–2260
- Vazquez-Añon, M., J. Bertics, M. Luck and R. R. Grummer. 1994. Peripartum liver triglycerides and plasma metabolites in dairy cows. *Journal of Dairy Sciences* 77 1521–1528.
- Shibano, K. and S. Kawamura. 2006. Serum free amino acid concentration in hepatic lipidosis of dairy cows in the periparturient period. *The Journal of Veterinary Medical Science*, 68, 393–396.
- Grummer, R. R. 2013. Choline: A Limiting Nutrient for Transition Dairy Cows. *Proceedings of the Florida Ruminant Nutrition Conference*, p.22-29.
- Zom, R. L. G, J. van Baal, R. M. A. Goselink, J. A. Bakker, M. J. de Veth, A. M. van Vuuren. 2011. Effect of rumen-protected choline on performance, blood metabolites, and hepatic triacylglycerols of periparturient dairy cattle. *J. Dairy Sci.* 94:4016-4027.
- Goselink, R., J. van Baal, A. Widaja, R. Dekker, R. Zom., M. J. de Veth, A. van Vuuren. 2012. Regulation of hepatic triacylglycerol level in dairy cattle by rumen-protected choline supplementation during the transition period. *J. Dairy Sci.* 96: 1102-1116.

CLINICAL ASSESSMENT AND TREATMENT OF AN OBESE CAT

Nutrition and Endocrinology Unit

ONIRIS - National College of Veterinary Medicine, Food Science and Engineering, Nantes (France)

Obesity in companion animals

Obesity = accumulation of excessive amounts of adipose tissue



excessive dietary intake

Inadequate energy utilization

↑ Risk of several chronic diseases :

- Osteoarthritis
- Diabetes mellitus
- Hepatic lipidosis
- Respiratory distress
- Decreased heat tolerance
- Cardiac failure
- Kidney disease
- Skin disorders

Risk factors :

- ✓ Breed
- ✓ Age (middleage)
- ✓ Gender & Neutering
- ✓ Sedentary lifestyle & lack of exercise
- ✓ Endocrine diseases
- ✓ Drugs
- ✓ Feeding dietary factor
- ✓ Sociological factors
- ✓ Number of animals

(German,2006)

Clinical assessment

- 1) **Patient assessement** : review the medical record for associated concurrent health issue (hystory and physical examination)
- 2) **Feeding assessment** : food intake, physical activity
- 3) **BCS:** determine the degree to which the patient is overweight or obese



Essential goals to develop a feeding plan for weight loss management



1) Patient assessment

AXOUE:

❖ 10 years old

❖ neutered female

❖ domestic shorthair cat

She was presented for routine geriatric health maintenance at Oniris veterinary teaching hospital.

History and physical examination

- ❖ Normal vital signs
- ❖ Dull hair coat
- ❖ BW 7.7 kg
- ❖ BCS 8/9
- ❖ MCS normal muscle mass
- ❖ Recurrent episodes of feline idiopathic cystitis
- ❖ Low-intensity activity
- ❖ No other animals in the household

2) Feeding method assessment

Assessment is based on estimate of the Maintenance Energy Requirement (MER) that is the amount of energy needed to maintain animal at its current weight.



The prediction of MER is useful to make adjustment to the daily energy intake (DEI) for the weight loss plan.

Dietary history

The dietary history has as objectives to:

- obtain an accurate accounting of all of food fed on a typical day
- evaluate all the ways that the food is involved in interaction between the pet and the other members of the household
- reveal potential obstacles in advance and allow the weight loss plan to be tailored to the patient improving chances of successful outcomes.

(Fascetti, 2012)

Dietary history

Axoue was fed :

- a dry specialty adult cat food
free choice ED= 3.6 kcal ME/g

→ 70 g/day (2 meals/day)

+

- moist grocery store cat food
ED= 0.7 kcal ME/g

→ 15 g once a day

**Maintenance
energy
requirement =**

255 kcal ME/day

3) Assessment of body condition

The Axoue BCS was assessed as 8/9 corresponding to 40% body fat.

Ideal body weight = current weight x (100 – percent body fat) /0.8

Axoue ideal BW → 5,8 kg



Feeding plan for weight loss

➤ Calculation based on current food intake:

requires knowledge of the number of calories patient is currently eating based on information obtained from his diet history.

➤ Calculation based on estimated ideal BW:

the use of resting energy requirement for optimal weight as an initial estimate of calories required for appropriate weight loss.

Treatment

- ☐ Choosing a calorie restriction food with an increased nutrient-to-calorie ratio should be considered to avoid excessive restriction of essential nutrients and to compensate the decreased bioavailability of these nutrients when fiber content is increased.
- ☐ Increasing feeding frequency and feeding with canned foods which are higher in moisture to improve satiety.
- ☐ Incorporating in the WL plan 10% daily energy intake in treats.
- ☐ Increasing exercise.
- ☐ Sensitizing the owner about importance of regulary nutritional assessments and respect of indications for success of diet planning.

(Laflamme,2012; Fascetti 2012)

WL feeding plan for Axoue

- 20 % DEI



Nutritional assessment after
3-4 weeks



Weight loss expected
1%-2% per week

<1% → 10% reduction of DEI

>2% → 10% increase of DEI



Axoue diet assessment

DAILY ALLOWANCE ENERGY : 255 kcal/d



20 % reduction

DEI 205 kcal ME/d



- 60 g of a **reduced calorie food**: 200 kcal ME (3.4 kcal ME/g)
- 15 g of moist grocery store food: 10 kcal ME (0.7 kcal ME/g <10% of DEI as treat)

The 2nd Axoue diet assessment

4 weeks after...

BW 7,7 kg

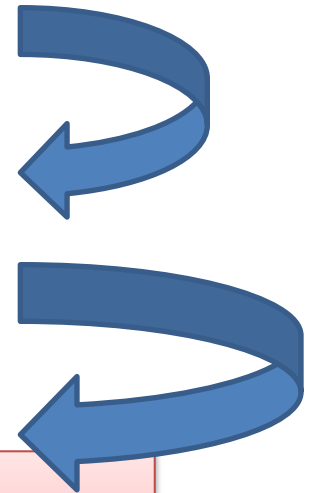
BCS 8/9

BW stable

10% reduction of DEI

DEI = 175 kcal ME/d

- 50 g of reduced calorie food: 170 kcal ME/d
- 15 g moist grocery store brand food: 10 kcal ME/d



The 3rd Axoue diet assessment

4 weeks after...

BW 7.2 kg → 1.6 % BW loss per week

BCS 8/9

MCS normal

The weight loss expected per week has been reached but owner reported that Axoue changed behaviour:

- increased mewing to require food
- stole food

→ We decided to increase amount and change into a moist reduced calorie food to improve satiety

DEI = 175 kcal ME/d

- 80 g /day of reduced calorie moist food canned (ED 0.85 kcal ME/g)
- 30 g of reduced calorie dry food/day

4th diet assessement

4 weeks after...

BW 6.9 kg → 1 % BW loss per week

BCS 7/9

✓ MCS mild muscle wasting

✓ Axoue didn't like new canned food prescribed



4th diet assesement

Current FOOD 1	For 100 kcal ME
CP	11 g
CF	3.8 g
ENA	8.4 g
CFib	2.7 g
ED	3.4 kcal ME/g



FOOD 2	For 100 kcal ME
CP	11.6
CF	3.3 g
ENA	9 g
CFib	4.1 g
ED	3.2 kcal ME/g

DEI = 175 kcal ME/d

- 80g /day of reduced calorie moist food canned (ED 0.8 kcal ME/g)
- 35 g of reduced calorie dry food/day (ED 3.2 kcalME/g)

Discussion

After 4 months of diet Axoue has lost 10% of BW and she switched from BCS 8/9 to 7/9.

In three patient reassessments we adjusted feeding plan:

- ➔ applying **10% reduction to DEI** to achieve 1%- 2% body weight loss per week considering change in BCS
- ➔ introducing **moist food** in small and **multiple meals** to improve satiety and acceptability
- ➔ switching from a first reduced calorie food to a second reduced calorie **food higher in crude protein g/ 100 kcal ME** to avoid loss of lean body mass.

Conclusion

Many overweight or obese cats are at risk of impaired health and reduced longevity

Efficacy of weight loss program in clinical setting can be a challenge...

Successful feeding program begins with a thoroughly conducted diet history.

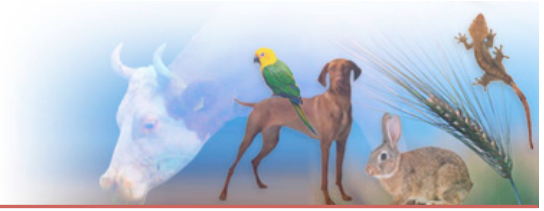
Follow-up rechecks are essential for monitoring and adjusting the plan to ensuring the success of the program.

Thank you for your attention



University of
Zurich^{UZH}

Institute of Animal Nutrition



Effect of nutrition on the intestinal health of pigs – focus on microbiota Review

ACCREDITED BY EAAC/EFMD

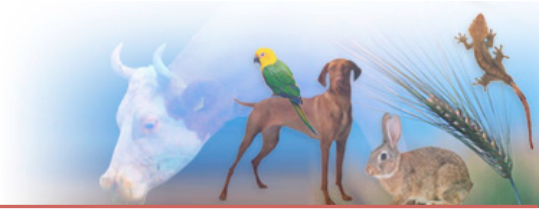
University of Bern | University of Zurich
vetsuisse-faculty



Residency class 2015

Dr. med. vet. Kerstin Gerstner

Prof. Dr. med. vet. Annette Liesegang (supervisor)



GI-Physiology

Critical points of nutrition in pigs

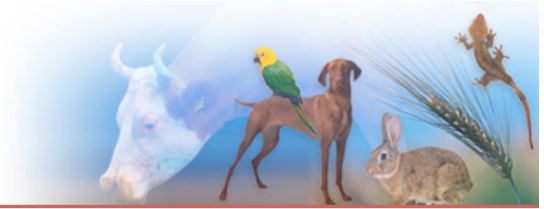
Factors affecting intestinal health – topics of actual interest

Summary & Conclusion





GI - physiology

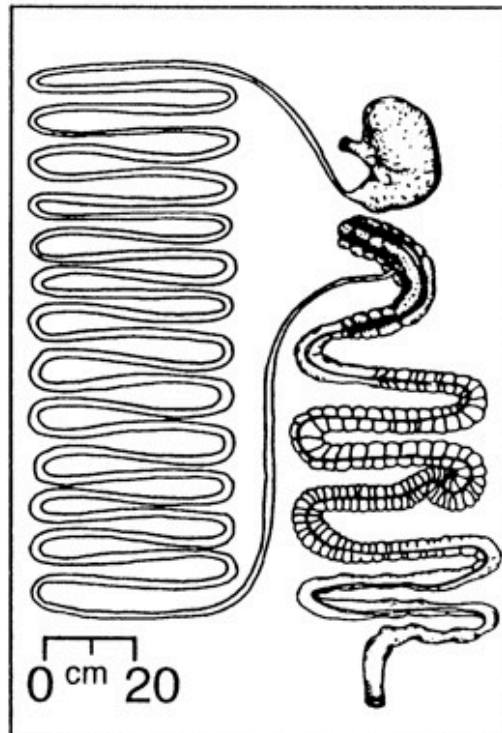


Monogastric & omnivorous

Efficient enzymatic digestion of starch, sugar, proteins, fat in the small intestine (praecaecally)

Gastric acid → deactivating bacteria in the diet

Partial digestion of plant fibre by microbiota in the large intestine



Pig

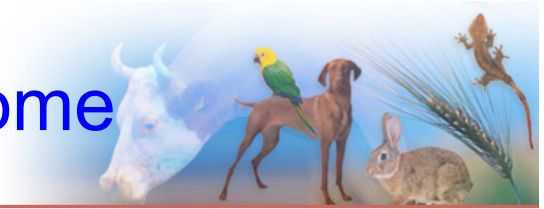
(*Sus scrofa*)

Body length: 125 cm

C. E. Stevens, I. D. Hume; Contributions of Microbes in Vertebrate Gastrointestinal Tract to Production and Conservation of Nutrients
Physiological Reviews 1998



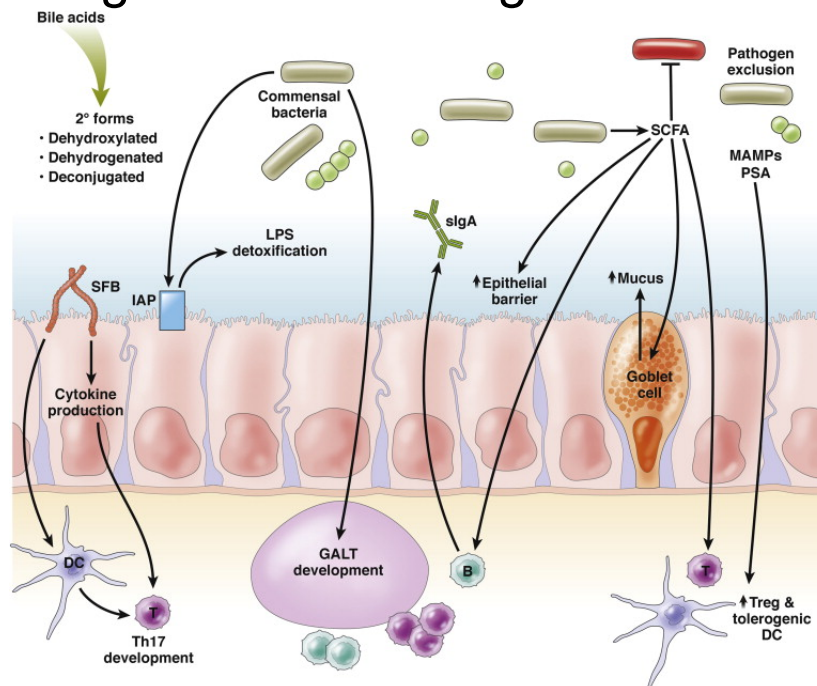
Influence of intestinal microbiome



Microbial fermentation particularly in the colon, to a lesser extent also in stomach & small intestine (SCFA detection)

Hindgut SCFA absorption → 15-24% of maintenance energy for growing & finishing pigs (Yen et al 1991, Mc Burney et al 1993)

SCFA might contribute to gastric ulcer formation (Argenzio et al 1996)



Ohland C.L., Jobin C.; *Cellular and Molecular Gastroenterology and Hepatology* 2015 1, 28-40 DOI: (10.1016/j.jcmgh.2014.11.004)

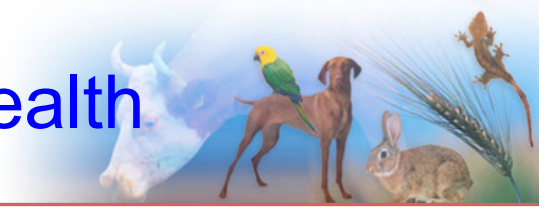
Argenzio RA, Eisemann J. Mechanisms of acid injury in porcine gastroesophageal mucosa. *Am J Vet Res.* 1996

Yen, JT; Nienaber, JA; Hill, DA; Potential Contribution Of Absorbed Volatile Fatty-Acids To Whole-Animal Energy Requirement In Conscious Swine; *Journal Of Animal Science* 1991





Critical points for nutrition & health



Nutrition of

the pregnant & lactating sow

(overfeeding or negative energy balance), MMA

weanling piglets

decreased FI followed by compensatory increased intake

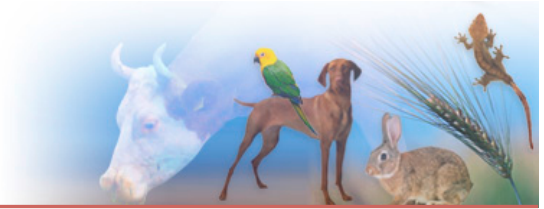
→ predisposition of diarrhoea

(fattening pigs in the early phases)





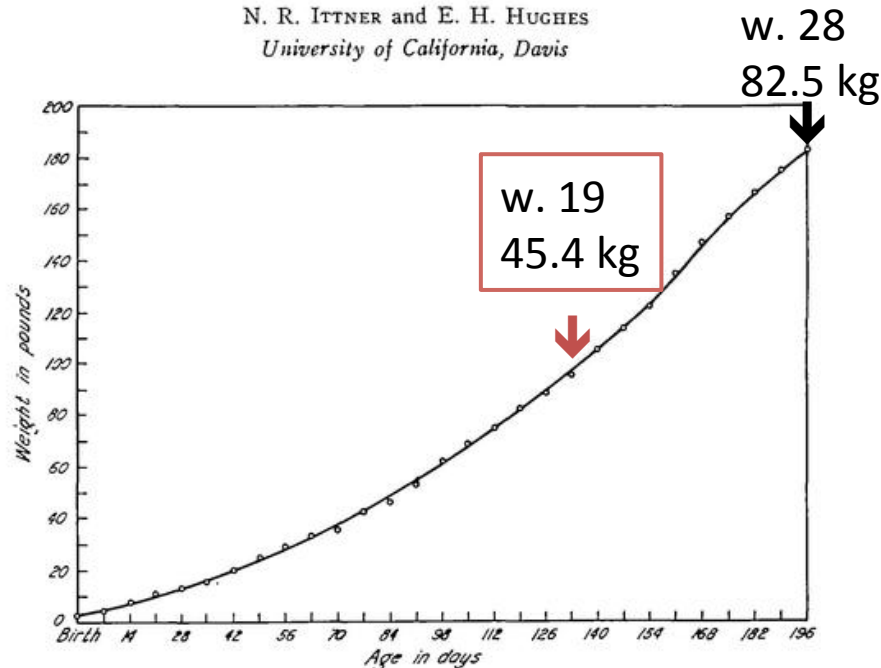
Production in general



Goal: low costs, high performance, low pollution

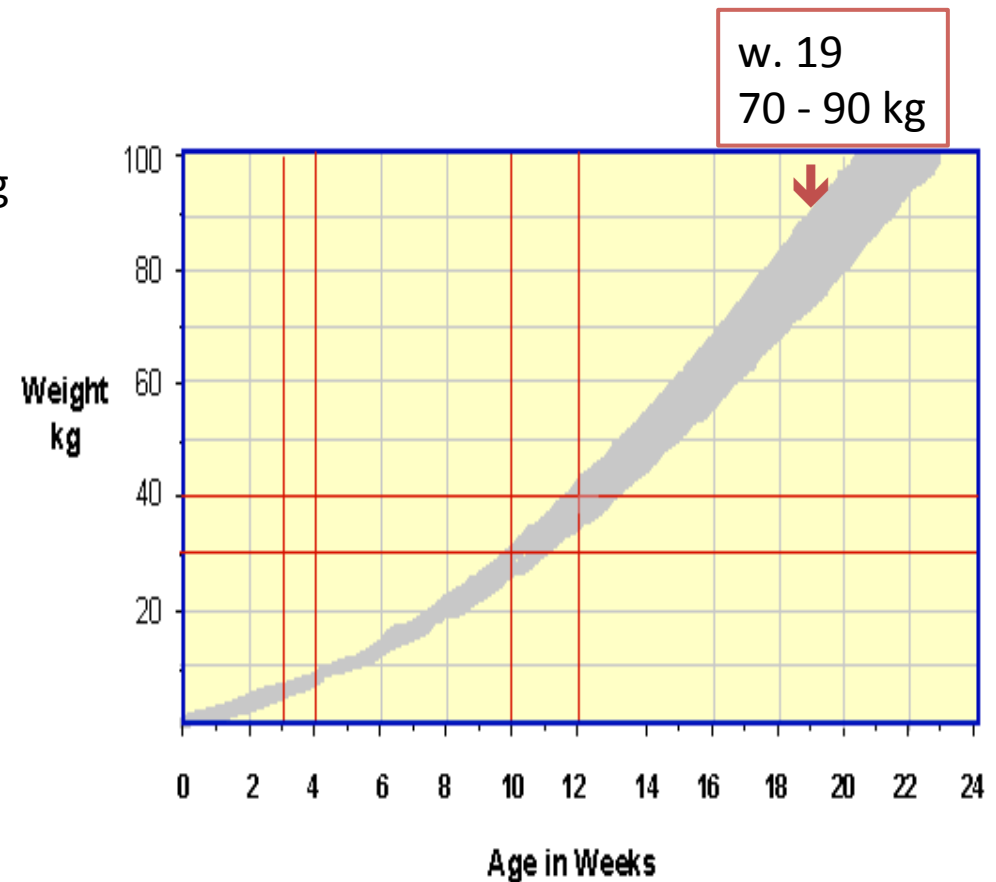
A NORMAL GROWTH CURVE FOR SWINE

N. R. ITTNER and E. H. HUGHES
University of California, Davis



Average growth rate of 457 pigs, from birth to 196 days of age, in the University of California herd. The maximum rate of gain was at an age of about six months, after which the weekly gains began to decrease.

J Hered (1938) 29 (10): 385-386

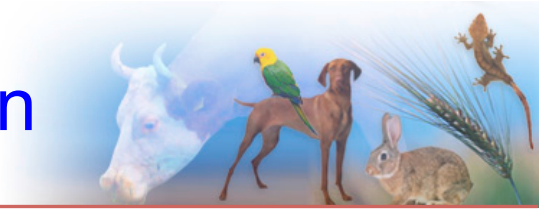


Book: Garth Pig Stockmanship Standards; Dr. John Carr; 1998





Critical points of swine nutrition



Sows in reproduction

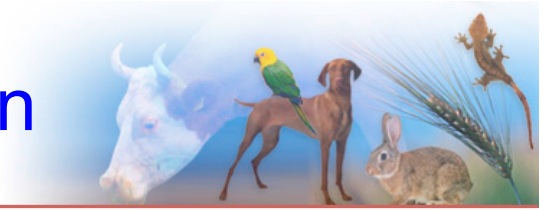
Goals: ≥ 13 piglets (≈ 1.5 kg birth weight)
fast birth without complications
loss of piglets until weaning $< 12\%$
service 4-5 d after weaning

Difficulties: overfeeding during gestation \rightarrow birth complications, MMA
negative energy balance during lactation
 \rightarrow bodyweight \downarrow , reproductive performance \downarrow





Critical points of swine nutrition



Sows in reproduction

MMA – prevention: feed restriction 1-2 days before birth

laxatives (wheat bran, Glauber's salt)

acidifying substances (acidification of urine,
anion-cation-gap)

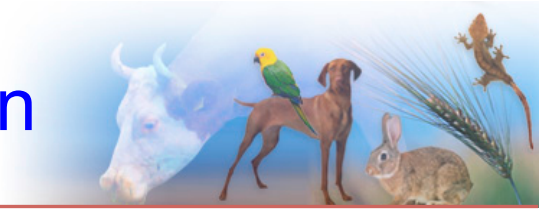
prebiotics

water!





Critical points of swine nutrition



Weaning

> d 21 (\approx d 25 – d 28)

supplementary feed > d 10 of age

stimulation of enzyme production & gastric acid secretion

changes in intestinal anatomy → increase crypt depth, villus length

adaption of intestinal microbiota

Lalles, J.P., Bosi, P., Smidt, H., and Stokes, C.R. (2007) Nutritional management of gut health in pigs around weaning. *Proc Nutr Soc*

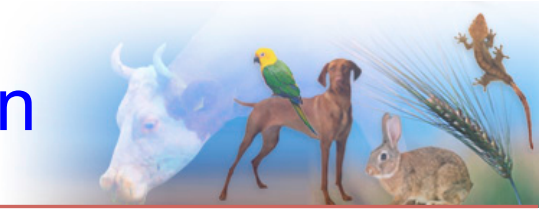
Supplemente zur Tierernährung für Studium und Praxis, 12. überarbeitete Auflage

Nutrient Requirements of Swine, NRC 2006





Critical points of swine nutrition



After weaning – feeding recommendations:

feed restriction, small portions (avoid overeating)

restricted protein content (guarantee amino acid intake!)

fibre content ↑ ((>3%, <7%) ↑ passage rate of feces, acidify feces)

hygienic quality of the feed ↑

add organic acids (↓ pathogens in the feed)

prebiotics

Lalles, J.P., Bosi, P., Smidt, H., and Stokes, C.R. (2007) Nutritional management of gut health in pigs around weaning. *Proc Nutr Soc*

Supplemente zur Tierernährung für Studium und Praxis, 12. überarbeitete Auflage

Nutrient Requirements of Swine, NRC 2006





Immune system maturation & microbiome



Birth of piglets: little/ no passive immunity → need of antibodies (colostrum)
fecal flora similar to the fecal flora of the sow
fecal flora: mainly Firmicutes & Bacteroidetes

During 1st 14 d: mucosal immune system develops (e.g. Peyer's patches)
differentiation of fecal flora from the fecal flora of the sow,
but still similar between littermates

≈ 28 d CD8+ T-cells infiltrate the intestine

≈ 6 w IgA production starts

Thompson CL, Wang B, Holmes AJ; The immediate environment during postnatal development has long-term impact on gut community structure in pigs; The ISME Journal, 2008

Metabolic fingerprinting and fermentative capacity of the intestinal flora of pigs during pre- and post-weaning periods. Katouli M, Lund A, Wallgren P, Kühn I, Söderlind O, Möllby R; Journal of applied microbiology ; 1997.

Kim HB¹, Borewicz K, White BA, Singer RS, Sreevatsan S, Tu ZJ, Isaacson RE. Longitudinal investigation of the age-related bacterial diversity in the feces of commercial pigs. Vet Microbiol. 2011





Immune system maturation & microbiome



„cohabitation“ effect – similar fecal flora in cohoused pigs (not in siblings)

Fecal flora: unstable phases after weaning & moving to a fattening stable

Adults: Firmicutes & Spirochaetes

Fermentative capacity of fecal flora ↑ before weaning
 ↓ after dietary change (milk to solid
 feed to fattening diet)

Thompson CL, Wang B, Holmes AJ; The immediate environment during postnatal development has long-term impact on gut community structure in pigs; *The ISME Journal*; 2008

Katouli M, Lund A, Wallgren P, Kühn I, Söderlind O, Möllby R; Metabolic fingerprinting and fermentative capacity of the intestinal flora of pigs during pre- and post-weaning periods. *Journal of applied microbiology* ; 1997.

Kim HB¹, Borewicz K, White BA, Singer RS, Sreevatsan S, Tu ZJ, Isaacson RE. Longitudinal investigation of the age-related bacterial diversity in the feces of commercial pigs. *Vet Microbiol*. 2011

Konstantinov, S.R., Awati, A.A., Williams, B.A., Miller, B.G., Jones, P., Stokes, C.R., *et al.* (2006) Post-natal development of the porcine microbiota composition and activities. *Environ Microbiol*





Immune system maturation & microbiome



Microbiota detected around weaning:

Bacteroidetes and *Firmicutes*: predominant phyla present at **each age**

Microbiota of **suckling piglets**: *Bacteroides*, *Oscillibacter*, *Escherichia/Shigella*, *Lactobacillus*, unclassified *Ruminococcaceae* genera

Microbiota of **weaned piglets**: increase of *Acetivibrio*, *Dialister*, *Oribacterium*, *Succinivibrio* and *Prevotella* genera

Lactobacillus fermentum: vertical transfer via breast milk or faeces

Prevotella: positively correlated with luminal secretory IgA concentrations and body weight

Mach N, Berri M, Estelle J, Levenez F, Lemonnier G, Denis C, Leplat JJ, Chevalleyre C, Billon Y, Dore J, Rogel-Gaillard C, Lepage P; Early-life establishment of the swine gut microbiome and impact on host phenotypes; Environmental Microbiology Reports (2015)





Affecting intestinal health – mother's milk



Similar “core microbial metatranscriptome” in the distal intestine

differences in bacterial genus:

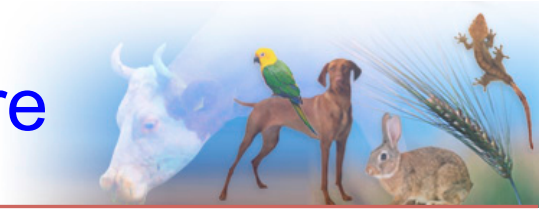
mother fed neonatal piglets: *Prevotella*

neonatal piglets fed with an artificial formula: *Bacteroides*





Affecting intestinal health - fibre



Soluble fibre increase number & activity of microflora in the large intestine
(Montagne et al 2003)

Increased total tract digestibility of fibre in pigs fed with chicory fibre (Liu et al 2013, Ivarsson et al 2012)

Increased total dietary fibre content → decreased apparent protein digestibility & gross energy (Ivarsson et al 2012)

Ivarsson, E., Liu, H.Y., Dicksved, J., Roos, S., and Lindberg, J.E. (2012) Impact of chicory inclusion in a cereal-based diet on digestibility, organ size and faecal microbiota in growing pigs. *Animal* **6**: 1077–1085.

Ivarsson E, Roos S, Liu HY, Lindberg JE. Fermentable non-starch polysaccharides increases the abundance of Bacteroides-Prevotella-Porphyromonas in ileal microbial community of growing pigs. *Animal*. 2014

Liu H, Ivarsson E, Lundh T, Lindberg J, Chicory (*Cichorium intybus* L. and cereals differently affect gut development in broiler chickens & young pigs *Journal of Animal Science and Biotechnology* 2013

L. Montagne, J.R. Pluske, D.J. Hampson; A review of interactions between dietary fibre and the intestinal mucosa, and their consequences on digestive health in young non-ruminant animals; *Animal Feed Science and Technology*





Affecting intestinal health – proteins



Low protein (14% CP) vs. normal protein (20% CP) diet:

- ↓ feed intake
- ↓ weight gain,
- ↓ metabolites of protein and carbohydrate fermentation (ammonia, branched chain fatty acids, acetate)
- ↓ microbial diversity

(Luo et al 2015)





Affecting intestinal health - minerals



Pigs supplemented with an increased amount of zinc: performance↑; No effect on number of excreted *E. Coli* and enterococci or on the functions of circulating neutrophils (Jensen-Waern et al 1998)

Study dose: 2500 mg/kg feed vs. legislation limit of 150 mg/ kg

Enterobacteriaceae, *Escherichia* group & *Lactobacillus* spp. ↓ in weaned pigs fed with high amounts of zinc, effect diminished for *Enterobacteria* with increasing age, permanent for *Lactobacillus* species (Pluske 2013, Starke et al 2014)

Study dose: 2425 mg/kg feed vs. legislation limit of 150 mg/ kg

Starke IC, Pieper R, Neumann K, Zentek J, Vahjen W. The impact of high dietary zinc oxide on the development of the intestinal microbiota in weaned piglets. FEMS Microbiol Ecol. 2014

Pluske JR Feed- and feed additives-related aspects of gut health and development in weanling pigs. J Anim Sci Biotechnol. 2013

Jensen-Waern, M., Melin, L., Lindberg, R., Johannisson, A., Petersson, L., and Wallgren, P. (1998) Dietary zinc oxide in weaned pigs – effects on performance, tissue concentrations, morphology, neutrophil functions and faecal microflora. Res Vet Sci





Affecting intestinal health - minerals



Increased diversity of *E. coli* clones and a significantly higher rate of multiresistant *E. coli* in pigs fed with a high dose of zinc compared to pigs fed zinc in an amount covering the needs (Bednorz et al 2013)

High diversity & species richness in mucosa associated bacteria also at pars non-glandularis of the stomach of weaned pigs & *Lactobacillus*↑ by a diet rich in Ca & P vs. moderate Ca & P (Mann et al 2014)

Bednorz C, Oelgeschläger K, Kinnemann B, Hartmann S, Neumann K, Pieper R, Bethe A, Semmler T, Tedin K, Schierack P, Wieler LH, Guenther S The broader context of antibiotic resistance: zinc feed supplementation of piglets increases the proportion of multi-resistant *Escherichia coli* in vivo. *Int J Med Microbiol.* 2013

Mann, E., Schmitz-Esser, S., Zebeli, Q., Wagner, M., Ritzmann, M., and Metzler-Zebeli, B.U. (2014) Mucosa- associated bacterial microbiome of the gastrointestinal tract of weaned pigs and dynamics linked to dietary calcium-phosphorus. *PLoS ONE*





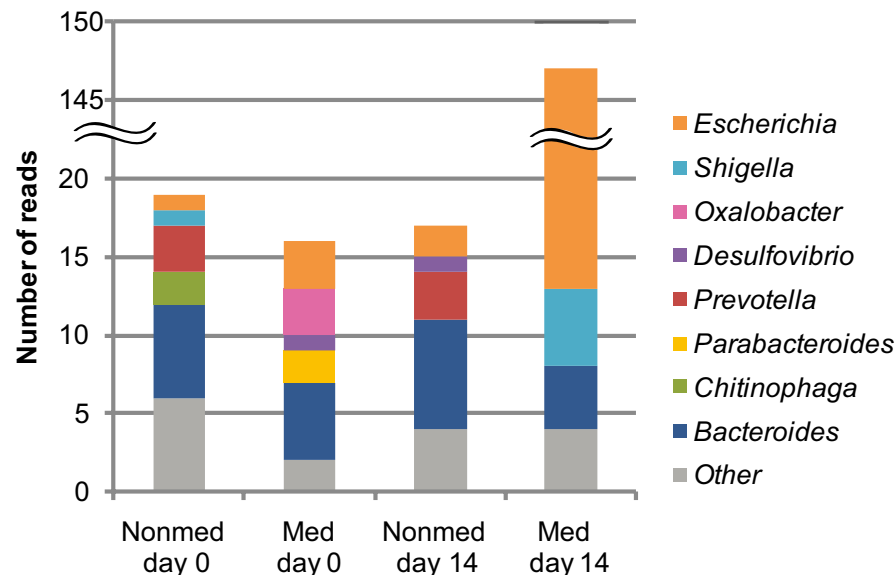
Affecting intestinal health - antibiotics



Antibiotics and to a lesser extent additional management procedures in early life affect composition & diversity of gut microbiota in piglets

(Schokker et al 2014)

Piglets raised in a highly controlled environment & subtherapeutic antibiotic treatment (Looft et al 2012):



Proteobacteria ↑ (driven by *E. coli*)

microbial functional genes related to energy production & conversion ↑

antibiotic resistance genes ↑

Schokker, D., Zhang, J., Zhang, L.L., Vastenhouw, S.A., Heilig, H.G., Smidt, H., *et al.* (2014) Early-life environmental variation affects intestinal microbiota and immune development in new-born piglets. *PLoS ONE*

Looft, T., Johnson, T.A., Allen, H.K., Bayles, D.O., Alt, D.P., Stedtfeld, R.D., *et al.* (2012) In-feed antibiotic effects on the swine intestinal microbiome. *Proc Natl Acad Sci USA*





Affecting intestinal health - environment



Significant similarity between stable communities developing in cohabiting pigs → the outcome of gut colonization in piglets might be influenced by the immediate environment (Thompson et al 2008)

Piglets housed in environments of excessive hygiene:

impaired progression & stabilisation of an adult-type gut microbiota, despite the acquisition of a highly diverse microbiota in early life.

Firmicutes ↓ in isolator-reared animals compared to outdoor-reared (Schmidt et al 2011)

Schmidt B, Mulder IE, Musk CC, Aminov RI, Lewis M, Stokes CR, Bailey M, Prosser JI, Gill BP, Pluske JR, Kelly D. Establishment of normal gut microbiota is compromised under excessive hygiene conditions. PLoS One. 2011

Thompson, C.L., Wang, B., and Holmes, A.J. (2008) The immediate environment during postnatal development has long-term impact on gut community structure in pigs. *ISME J*





Affecting intestinal health - probiotics



Weaning highly affects the gut microbiota (*Lactobacilli* ↓, lactic acid ↑ ammonia ↓ in weaned pigs; no effect on total VFA concentration)

(Konstantinov et al 2006)

Feeding *Enterococcus faecium* one month before birth of piglets led to an individually different increase of *Lactobacillus spp.* in sows and piglets

(Starke et al 2013)

Probiotic supplementation (*Lactobacillus*) has been shown to increase average daily gain, nutrient digestibility (e.g. protein) and improve immunity (by stimulating epithelial lymphocytes) (Yu et al 2008)

Konstantinov SR, Awati AA, Williams BA, Miller BG, Jones P, Stokes CR, Akkermans AD, Smidt H, de Vos WM; Post-natal development of the porcine microbiota composition and activities. *Environ Microbiol.* 2006

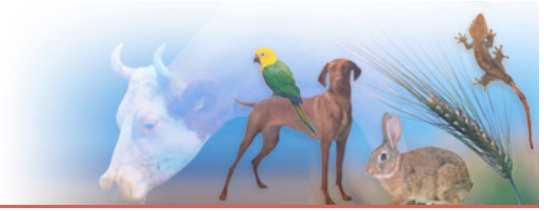
Starke IC, Pieper R, Neumann K, Zentek J, Vahjen W. Individual responses of mother sows to a probiotic *Enterococcus faecium* strain lead to different microbiota composition in their offspring. *Benef Microbes.* 2013

Yu, H.F., Wang, A.N., Li, X.J., and Qiao, S.Y. (2008) Effect of viable *Lactobacillus fermentum* on the growth performance, nutrient digestibility and immunity of weaned pigs. *J Anim Feed Sci*



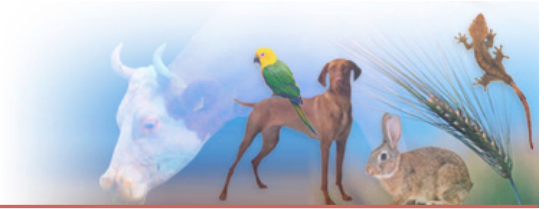


Summary & conclusion



- Early days of piglet's life are of utmost importance for the intestinal health of the pig's whole life
- Intestinal health could be supported by dietary supplements like probiotics or diet formulations containing increased amounts of particular nutrients (e.g. zinc)
 - legislation limits & side effects
- Intestinal health should be based on good management procedures for housing and feeding
- «The» ideal diet or supplement to compensate management failures does not exist





Argenzio RA1, Eisemann J. Mechanisms of acid injury in porcine gastroesophageal mucosa. *Am J Vet Res.* 1996 Apr;57(4):564-73.

Bednorz C, Oelgeschläger K, Kinnemann B, Hartmann S, Neumann K, Pieper R, Bethe A, Semmler T, Tedin K, Schierack P, Wieler LH, Guenther S The broader context of antibiotic resistance: zinc feed supplementation of piglets increases the proportion of multi-resistant *Escherichia coli* in vivo. *Int J Med Microbiol.* 2013 Aug;303(6-7):396-403. doi: 10.1016/j.ijmm.2013.06.004.

Clemens ET, Stevens CE, Southworth M. Sites of organic acid production and pattern of digesta movement in the gastrointestinal tract of swine. *J Nutr.* 1975 Jun;105(6):759-68

Inoue, R., Tsukahara, T., Nakanishi, N., and Ushida, K. (2005) Development of the intestinal microbiota in the piglet. *J Gen Appl Microbiol* 51: 257–265.

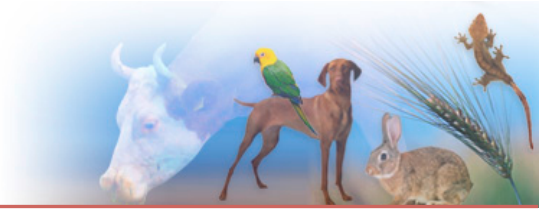
Ivarsson, E., Liu, H.Y., Dicksved, J., Roos, S., and Lindberg, J.E. (2012) Impact of chicory inclusion in a cereal-based diet on digestibility, organ size and faecal microbiota in growing pigs. *Animal* 6: 1077–1085.

Ivarsson E, Roos S, Liu HY, Lindberg JE. Fermentable non-starch polysaccharides increases the abundance of *Bacteroides-Prevotella-Porphyromonas* in ileal microbial community of growing pigs. *Animal.* 2014 Nov;8(11):1777-87. doi: 10.1017/S1751731114001827

Jensen-Waern, M., Melin, L., Lindberg, R., Johannisson, A., Petersson, L., and Wallgren, P. (1998) Dietary zinc oxide in weaned pigs – effects on performance, tissue concentrations, morphology, neutrophil functions and faecal microflora. *Res Vet Sci* 64: 225–231

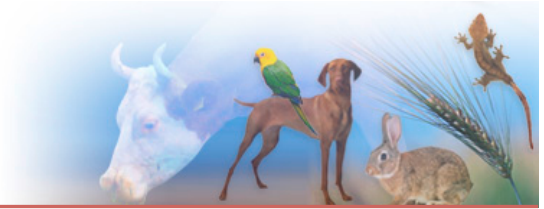
Katouli M, Lund A, Wallgren P, Kühn I, Söderlind O, Möllby R; Metabolic fingerprinting and fermentative capacity of the intestinal flora of pigs during pre- and post-weaning periods. *Journal of applied microbiology* ; 1997.





- Kim HB, Borewicz K, White BA, Singer RS, Sreevatsan S, Tu ZJ, Isaacson RE. Longitudinal investigation of the age-related bacterial diversity in the feces of commercial pigs. *Vet Microbiol.* 2011
- Konstantinov SR, Awati AA, Williams BA, Miller BG, Jones P, Stokes CR, Akkermans AD, Smidt H, de Vos WM; Post-natal development of the porcine microbiota composition and activities. *Environ Microbiol.* 2006 Jul;8(7):1191-9.
- Lalles, J.P., Bosi, P., Smidt, H., and Stokes, C.R. (2007) Nutritional management of gut health in pigs around weaning. *Proc Nutr Soc* 66: 260–268.a
- Liu H, Ivarsson E, Lundh T, Lindberg J, Chicory (*Cichorium intynus* L.) and cereals differently affect gut development in broiler chickens & young pigs *Journal of Animal Science and Biotechnology* 2013,
- Looft, T., Johnson, T.A., Allen, H.K., Bayles, D.O., Alt, D.P., Stedtfeld, R.D., *et al.* (2012) In-feed antibiotic effects on the swine intestinal microbiome. *Proc Natl Acad Sci USA* 109: 1691–1696.
- Luo Z, Li C, Cheng Y, Hang S, Zhu W. Effects of low dietary protein on the metabolites and microbial communities in the caecal digesta of piglets. *Arch Anim Nutr.* 2015;69(3):212-26. doi: 10.1080/1745039X.2015.1034521
- Mach N, Berri, M, Estelle J, Levenez F, Lemonnier G, Denis C, Leplat JJ, Chevaleyre C, Billon Y, Dore J, Rogel-Gaillard C, Lepage P; Early-life establishment of the swine gut microbiome and impact on host phenotypes; *Environmental Microbiology Reports* (2015)
- Mann, E., Schmitz-Esser, S., Zebeli, Q., Wagner, M., Ritzmann, M., Metzler-Zebeli, B.U. (2014) Mucosa-associated bacterial microbiome of the gastrointestinal tract of weaned pigs and dynamics linked to dietary calcium-phosphorus. *PLoS ONE* 9: e86950.
- McBurney MI, Sauer WC. Fiber and large bowel energy absorption: validation of the integrated ileostomy-fermentation model using pigs. *J Nutr.* 1993 Apr;123(4):721-7.





Montagne L, Pluske JR, Hampson DJ; A review of interactions between dietary fibre and the intestinal mucosa, and their consequences on digestive health in young non-ruminant animals; *Animal Feed Science and Technology* 108 (2003) 95–117

Pluske JR Feed- and feed additives-related aspects of gut health and development in weanling pigs. *J Anim Sci Biotechnol*. 2013 Jan 7;4(1):1. doi: 10.1186/2049-1891-4-1.

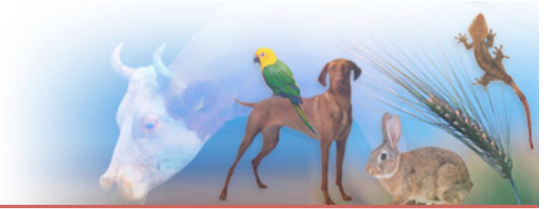
Poroyko, V., White, J.R., Wang, M., Donovan, S., Alverdy, J., Liu, D.C., and Morowitz, M.J. (2010) Gut microbial gene expression in mother-fed and formula-fed piglets. *PLoS ONE* 5: e12459.

Schmidt B, Mulder IE, Musk CC, Aminov RI, Lewis M, Stokes CR, Bailey M, Prosser JI, Gill BP, Pluske JR, Kelly D. Establishment of normal gut microbiota is compromised under excessive hygiene conditions. *PLoS One*. 2011;6(12):e28284. doi: 10.1371/journal.pone.0028284.

Schokker, D., Zhang, J., Zhang, L.L., Vastenhouw, S.A., Heilig, H.G., Smidt, H., *et al.* (2014) Early-life environmental variation affects intestinal microbiota and immune development in new-born piglets. *PLoS ONE* 9: e100040.

Spreeuwenberg, M.A., Verdonk, J.M., Gaskins, H.R., and Verstegen, M.W. (2001) Small intestine epithelial barrier function is compromised in pigs with low feed intake at weaning. *J Nutr*





Starke IC, Pieper R, Neumann K, Zentek J, Vahjen W. Individual responses of mother sows to a probiotic *Enterococcus faecium* strain lead to different microbiota composition in their offspring. *Benef Microbes*. 2013;4(4):345-56. doi: 10.3920/BM2013.0021

Stevens CE, Hume ID; Contributions of Microbes in Vertebrate Gastrointestinal Tract to Production and Conservation of Nutrients; *Physiological Reviews* 1998 Vol. 78 no. 2, 393-427 DOI

Thompson, C.L., Wang, B., and Holmes, A.J. (2008) The immediate environment during postnatal development has long-term impact on gut community structure in pigs. *ISME J* **2**: 739–748.

Yen, JT; Nienaber, JA; Hill, DA; Potential Contribution Of Absorbed Volatile Fatty-Acids To Whole-Animal Energy Requirement In Conscious Swine; *Journal Of Animal Science* Vol: 69 Iss: 5 P: 2001-2012

Yu, H.F., Wang, A.N., Li, X.J., and Qiao, S.Y. (2008) Effect of viable *Lactobacillus fermentum* on the growth performance, nutrient digestibility and immunity of weaned pigs. *J Anim Feed Sci* **17**: 61–69.

Books:

Supplemente zur Tierernährung für Studium und Praxis, 12. überarbeitete Auflage, 2014

Nutrient Requirements of Swine, NRC 2006





Dog with chronic renal failure and pancreatitis - a case report

Britta Kiefer-Hecker
LMU Munich, Germany

„Snoopy“



History

- Labrador Retriever
- Male, spayed
- 8 years old
- 34 kg bodyweight, BCS 2,5/5
- Multidog (3) household
- Owner is nurse in vet clinic

Diagnosis

- Chronic renal failure (CRF)
 - Pancreatitis
- **Dietary recommendation**

Blood chemistry

Serum parameter	Reference values	19.12.2014	
Urea mg/dl	9-29	97	↑
Crea mg/dl	<1.4	5.6	↑
P mmol/l	0.9-1.7	2.1	↑
Ca mmol/l	2.1-2.9	2.7	
Potassium mmol/l	3.9-5.8	4.9	
α-amylase U/l	< 1264	3176	↑
Lipase U/l	< 298	713	↑
cPLI* µg/l	> 200** & >400***	446	↑
Albumin g/dl	2.8-4.3	2.8	
Total protein g/dl	5.4-7.6	6.6	
*Canine pancreatic lipase, **questionable, ***suspected pancreatitis CRF: values out of reference only since 75% damage, Missing information of urine quality: Specific gravity, proteinuria?, protein-creatinine-ratior			

IRIS
Stage 4

Suspected
pancreatitis

Dietary recommendations

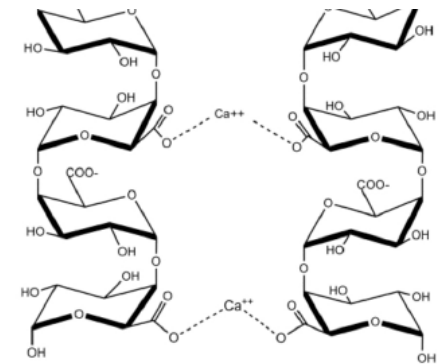
CRF

- Protein and Phosphorus ↓
(according to blood values)
- Protein quality ↑
- Fat and cereals ↑
- Sodium (↓), potassium (↑)
according to serum profile
- B vitamins ↑
- Additionally: pectin (soluble fiber)
- Avoid anorexia

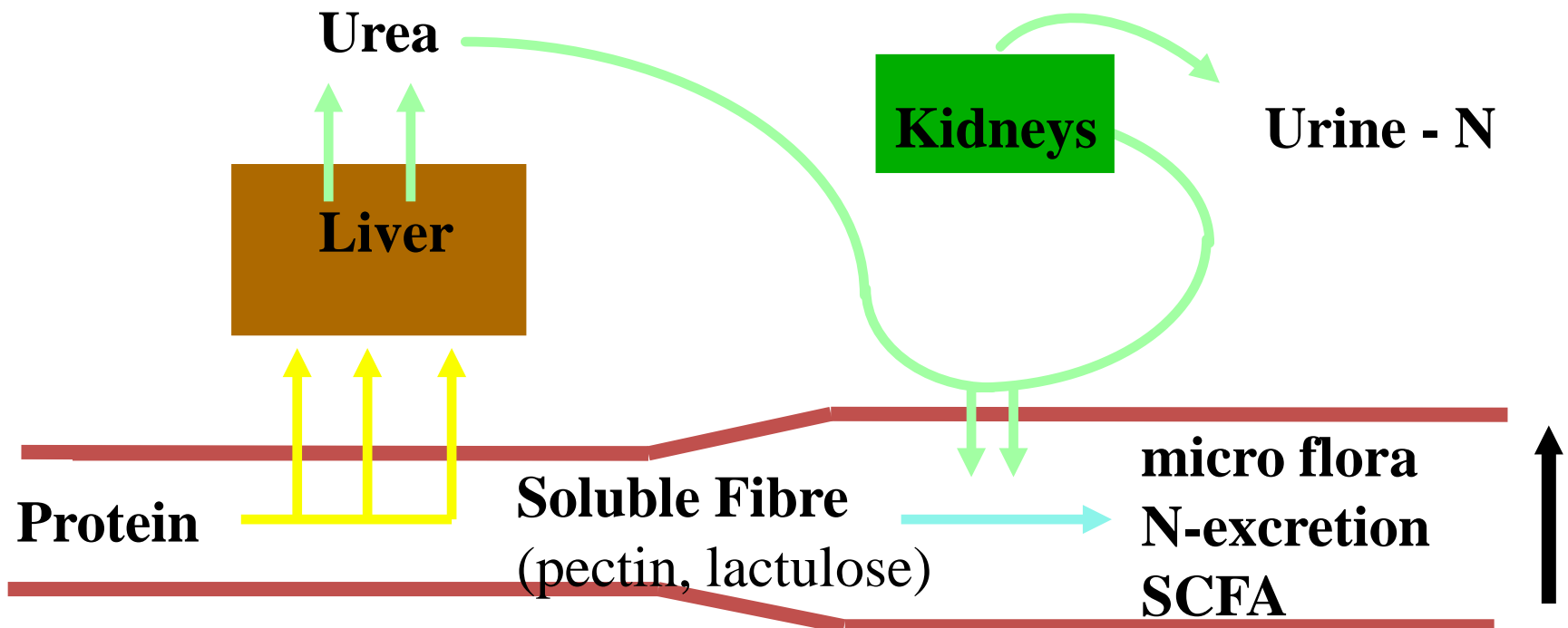
Pancreatitis

Usefull effects of soluble fiber in dietetic of CRF: **Nitrogen Trap**

Fixation of ammonia and polyamids through e.g. pectin



Nultsch 2001; Ochoa-Villarreal et al. 2012



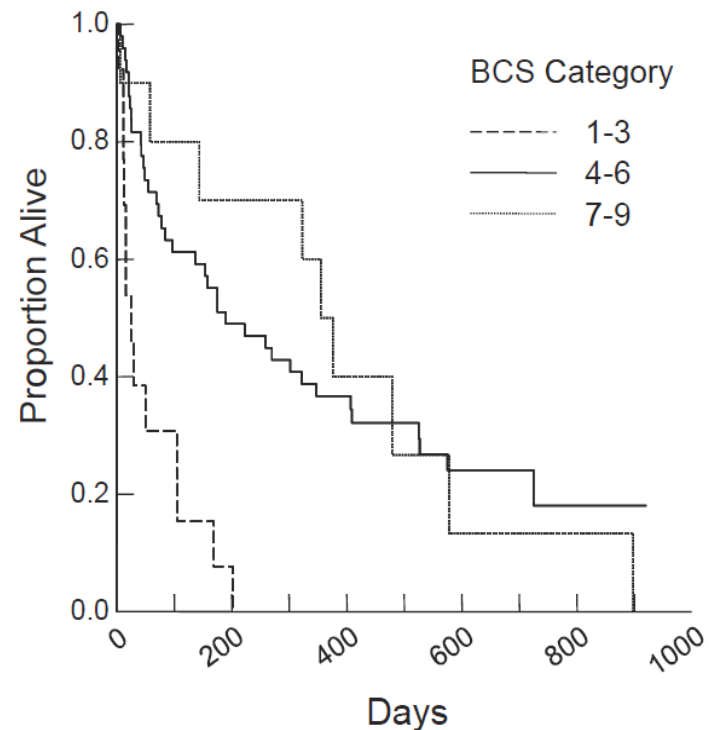


Benefit of renal diet in dogs



- Clinical 2y double-blind study*, 38 dogs w naturally occurring CRF: renal diet** vs. typical maintenance diet
 - Delayed onset of uremic crises (615 vs. 252 days)
 - Improved quality of life: 72% less likely to have clinical signs
 - Improved survival time: lived more than twice as long when fed renal diet

- CKD dogs with lower BCS live shorter***



Pancreatitis: Nutritional considerations

- Common practice: nothing per os in order to „rest“ the pancreas
 - little evidence for that
- Nutritional support is crucial → oral feeding if not vomiting (use antiemetics)
 - ~12 h after patient stops vomiting → offer small amount of fresh water → no vomiting → offer small amount of low-fat food → no vomiting: repeat this offer every few hours
- NPO only if vomiting cannot be controlled
- In canine patients: low-fat diet

Dietary recommendations

CRF

- Protein and Phosphorus ↓
(according to blood values)
- Protein quality ↑
- Fat and cereals ↑
- Sodium (↓), potassium (↑)
according to serum profile
- B vitamins ↑
- Additionally: pectin (soluble fiber)
- Avoid anorexia

Pancreatitis

- Highly digestible diet
- Fat ↓
- Polyunsaturated fatty acids ↑
- Avoid anorexia

Important information for pet owners

- Diet will improve live through slow-down of progression but will not cure CRF
- Lifelong feeding of diet is required
- Dietary failure (snacks, exceptions) can cause worsening of the symptoms
- A pet with CRF needs more care and will be more expensive than a healthy pet
- Be careful with learned dietetic aversions (cats)

Actual feeding (december) - survey

CRF, dog 34kg, BCS 2.5 /5	Amount (g/d)	ME (MJ)	Cp (g)	Ca (mg)	P* (mg)	Sodium (mg)
Recommendation*		7.6	46	1830	1098	366
Content		7.6	116	3540	3192	2888
Cooked whole egg (without shell)	80	0.6	10	40	192	88
RC Hypoallergenic mod. energy, dry	200	3	46	1600	1200	800
RC Hypoallergenic, can	1000	4	60	1900	1800	2000
*chronic renal failure: Cp reco= 60% and P reco = 80% of healthy dog						

Key factors	
Cp/ME (g/MJ)	15.3
Ca/P	1.1
CHO/DM	46.1
CFi/DM	5.2
EE/DM	15.9
P/ME (mg/MJ)	420
Sodium/ME (mg/MJ)	380
MJ/DM	
(MJ/100gDM)	1.6

Recommended diet

*CRF, dog 34kg, BCS 2.5 /5	Amount (g/d)	ME (MJ)	Cp (g)	Cfa (g)	Ca (mg)	P (mg)	Sodium (mg)
Recommendation*		7.6	46		1830	1098	366
Content		7.6	84	58	3026	1416	347
Cooked whole egg	80	0.6	10	10	40	192	88
Potatos	600	1.9	13	1	60	360	6
Carotts	300	0.6	3	0	150	105	90
Rice, cooked	400	1.8	9	0	8	151	8
Canola oil	7	0.3	0	7	0	0	0
Pork escalope	100	0.7	21	8	10	140	70
Salmon oil capsules	3	0.1	0	2	0	0	0
Curd (40% Fat/DM)	250	1.6	28	29	238	438	85
CaCO3	7	0	0	0	2520	0	0

*chronic renal failure: Cp reco= 60% and P reco = 80% of healthy dog
 Plus pectin (0.5-1 g/kg BW/day, start with low dosis)
 Plus phosphate binder

Key factors		
Cp/ME (g/MJ)	11.1	↓
Ca/P	2	↑
CHO/DM	58.2	↑
CFi/DM	1.6	↓
EE/DM	13.8	↓
P/ME (mg/MJ)	186	↓
Sodium/ME (mg/MJ)	46	↓
MJ/DM (MJ/100gDM)	1.8	↑

What the dog got instead till mid February

*CRF	Amount (g/d)	ME (MJ)	Cp (g)	Ca (mg)	P (mg)	Sodium (mg)
Recommendation*		7.6	46	1830	1098	366
Content		7.9	83	3794	1912	1115
Cooked whole egg	80	0.6	10	40	192	88
Potatos	400	1.2	8	40	240	4
Carotts	300	0.6	3	150	105	90
Rice, cooked	400	1.8	9	8	151	8
Canola oil	10	0.4	0	0	0	0
Curd (40% Fat/DM)	250	1.6	28	238	438	85
CaCO3	7	0	0	2520	0	0
RC Hypoallergenic, can	420	1.7	25	798	756	840

Key factors	
Cp/ME (g/MJ)	10.5
Ca/P	2
CHO/DM	57
CFi/DM	3.1
EE/DM	14.6
P/ME (mg/MJ)	242 ↑
Sodium/ME (mg/MJ)	141 ↑
MJ/DM	
(MJ/100gDM)	1.7

No pork, but still can food , no pectin, no phosphate binder and a few days without CaCo3

Blood chemistry and bodyweight

Serum parameter	Reference values	19.12.2014	05.02.2015	
Urea mg/dl	9-29	97	118	↑
Crea mg/dl	<1.4	5.6	6	↑
P mmol/l	0.9-1.7	2.1	3.7	↑
Ca mmol/l	2.1-2.9	2.7	2.8	
Potassium mmol/l	3.9-5.8	4.9	5.0	
α-amylase U/l	< 1264	3176	2235	↑
Lipase U/l	< 298	713	141	
cPLI* µg/l	> 200** >400***	446	346	↓
Albumin g/dl	2.8-4.3	2.8	2.5	↓
Total protein g/dl	5.4-7.6	6.6	5.6	
*Canine pancreatic lipase, **questionable, ***suspected pancreatitis				
Bodyweight (kg)		34	32,5	↓

IRIS
Stage 4

Questionable
pancreatitis

Dietary Recommendation 2

*CRF	Amount (g/d)	ME (MJ)	Cp (g)	Cfa (g)	Ca (mg)	P (mg)	Sodium (mg)
Recommendation*		7.6	46		1830	1098	366
Content		7.6	55	68	2869	1083	229
Potatos	650	2	14	1	65	390	7
Carotts	300	0.6	3	0	150	105	90
Rice, cooked	450	2	10	0	9	170	9
Canola oil	7	0.3	0	7	0	0	0
Salmon oil capsules	3	0.1	0	2.5	0	0	0
Curd (40% Fat/DM)	120	0.8	13	14	114	224	41
CaCO3	7	0	0	0	2520	0	0
Pork belly	100	1.7	12	42	10	140	70
Pork liver	15	0.1	3	1	1	54	12

Plus pectin (0.5-1 g/kg BW/day, start with low dosis)

Plus phosphate binder , plus vitamins and tracelements

Key factors		
Cp/ME (g/MJ)	7.2	↓
Ca/P	2	
CHO/DM	62.9	↑
CFi/DM	1.7	
EE/DM	16.4	↑
P/ME (mg/MJ)	143	↓
Sodium/ME (mg/MJ)	30	↓
MJ/DM		
(MJ/100gDM)	1.8	

Blood chemistry

8 weeks after reco 2

Serum parameter	reference values	19.12.2014	05.02.2015	24.04.15	
Urea mg/dl	9-29	97	118	175	↑
Crea mg/dl	<1.4	5.6	6	14.9	↑
P mmol/l	0.9-1.7	2.1	3.7	4.4	↑
Ca mmol/l	2.1-2.9	2.7	2.8	3.0	↑
Potassium mmol/l	3.9-5.8	4.9	5.0	4.9	
α-amylase U/l	< 1264	3176	2235	1960	
Lipase U/l	< 298	713	141	141	
cPLI* µg/l	> 200** >400***	446	346	199	↓
Albumin g/dl	2.8-4.3	2.8	2.5	2.7	
Total protein g/dl	5.4-7.6	6.6	5.6	6.4	
*Canine pancreatic lipase, **questionable, ***suspected pancreatitis					
Bodyweight (kg)		34	32,5	31,8	↓

IRIS
Stage 4

Stronger
Focus on
CRF

Begin of May

- Reduced overall health: vomiting and lethargy, reduced appetite and anorexia
- Treatment:
 - Antiemetic: Metoclopramid (MCP)
 - S.c. infusion of NaCl
 - Homeopathy treatment e.g. Heel Suc and Heel Hepa
 - Because of very low appetite: Owner feed what ever he eats (with phosphate binder Ipakitine)
- Only short improvement of overall health -> euthanasia



**Dietetic adaptations
and compliance**
is crucial in multimorbid
patients!



**Nutritional management of chronic
renal insufficiency, pancreatitis and
diabetes mellitus
in a senior cat**

Case Report

16.09.2015

Anna Lineva

Chair of animal nutrition LMU Munich

- Male neutered cat, 15 years old
- BW: 3.45 kg, BCS 5/9
- Diagnosed with chronic renal insufficiency (CRI): 2-BP (0.2) -AP2 (170)
- Pancreatitis and secondary EPI
- Clinical examination: anaemia

	22.06.2015	Normal ranges
Urea	19.8	5.4 — 12.1 mmol/l
Creat	233	70 — 165 µmol/l
fPLI	50	< 5,4 µg/l
Glu	8.4	6.8 mmol/l
Phosphate	1.79	1.1 — 2.30 mmol/l

Management of dehydration

Medication:

- Amlodipine
- Prednisolone
- Kreon (Pancreatin)
- Aranesp

Nutritional consultation



Chronical kidney insufficiency

- Moderate protein, low phosphorus
- K and Na at requirements
- Vit. A at requirements
- Vit. D and Vit B x 2
- ω -3 FA
- Soluble fibre
- Water intake management

Pancreatitis

- Moderate fat
- High quality of nutrients
- ω -3 FA
- B12

Actual diet at first presentation

- 184 kcal / cat / day
- Home-made diet: chicken, eggs, rice, wheat bran, beet, cucumber
- High protein, moderate fat and carbohydrates
- Ca, trace elements deficient, invers Ca/P, high Na, low K
- Vitamin A deficiency

Nutrient	CP (g/d)	CFa (%DM)	Ca (mg/d)	P (mg/d)	Na (mg/d)	taurine
Requirements (NRC)	11		153	119 ↓	36	0.1
Ration	21	15	65	193	219	0.3

Recommended diets 1, 2

- The same level of ME
- High calorie / low protein meat sources (duck)
- Protein at reduced level (12.2 g/MJ ME)
- Moderate fat (+ ω -3 FA) / high carbohydrate level (rice)
- Phosphorus at reduced level (90% NRC)
- Complete supplementation (minerals, vitamins B x 2)
- Fermentable fiber (pectin, vegetables that were used before ↗)

Nutrient	CP (g/d)	CFa (%DM)	CH (%DM)	Ca (mg/d)	P (mg/d)
Requirements (NRC)	11			153	119
Ration	11	12.2 → 15	48.8 → 40	167	124

- Acceptance of diet # 2 was better
- BW: 3.45 kg → 3.15 kg
- The owner asked for some changes:

Different protein sources (pork), less carbohydrates (+ potato mash)

	22.06.2015	07.08.2013	02.09.2013	Normal ranges
Urea	19.8	19.4	18.7	5.4 — 12,1 mmol/l
Creat	233	208	261	70 — 165 µmol/l
α-amylase, total	2454	1556	1478	500 — 1200 U/l
fPLI	50	27	5	< 5,4 µg/l
Glu	8.4	4.6	6.3	6.8 mmol/l
Phosphate	1.79	1.49	1.43	1.1 — 2.30 mmol/l

Recommended diet 3

- High calorie / low protein meat sources
- Higher fat / low carbohydrate level
- Protein at reduced level (12.2 g/MJ ME)
- Phosphorus at reduced level (90% NRC)
- Complete supplementation (minerals, vitamins)

Nutrient	CP (g/d)	CFa (%DM)	CH (%DM)	Ca (mg/d)	P (mg/d)
Requirements (NRC)	11			153	119
Ration	11	28.6	37.1	166	116

- Different variants of diet components
- Protein and phosphorus at reduced levels
- Fat and carbohydrates: variable
- Liver parameters and glucose slightly elevated

	22.06.2015	07.08.2013	02.09.2013	29.10.2013	12.04.2014	Normal ranges
Urea	19.8	19.4	18.7	16.2	20.3	5.4 — 12.1 mmol/l
Creat	233	208	261	223	172	70 — 165 µmol/l
α-amylase, total	2454	1556	1478	2458	2206	500 — 1200 U/l
fPLI	50	27	5	5.2	5.0	< 5,4 µg/l
Glu	8.4	4.6	6.3	5.9	11.0	6.8 mmol/l
Phosphate	1.79	1.49	1.43	1.22	1.77	1.1 — 2.30 mmol/l

- + Diagnosis „Diabetes mellitus“

	02.09.2013	29.10.2013	12.04.2014	10.07.2014	Normal ranges
Urea	18.7	16.2	20.3	22	5.4 — 12.1 mmol/l
Creat	261	223	172	247	70 — 165 µmol/l
AST	31	44	94	165	12 — 45 U/l
ALT	50	33	92	206	18 — 60 U/l
Glu	6.3	5.9	11.0	13.8	6.8 mmol/l
Phosphate	1.43	1.22	1.77	1.49	1.1 — 2.30 mmol/l

- **No simple carbohydrates: beet or pumpkin**
- **Moderate carbohydrate level** (as acceptable)
- **Pearl barley** (low glycemic index)
- **Reduced protein and phosphorus levels**
- **Higher level of fermentable fibre**
- **High level of fat** (as tolerated)

Nutrient	CP (g/d)	Cfa (% DM)	CH (%DM)	Cfi (%DM)	Ca (mg/d)	P (mg/d)
Requirements (NRC)	11				153	119
Ration	12	33.3	19	7.4	163	113

- **Glucose: fasting blood level returned to normal**
- **Insulin: no substitution recommended**
- **The patient was stable on diet #4 next 6 months**
- **Monthly monitoring of Urea, Crea, ALT, AST, fPLI, Glucose**

	29.10.2013	12.04.2014	10.07.2014	30.07.2014	Normal ranges
Urea	16.2	20.3	22	23	5.4-12.1 mmol/l
Creat	223	172	247	250	70-165 µmol/l
Glu	5.9	11.0	13.8	6.1	6.8 mmol/l
Phosphate	1.22	1.77	1.49	1.5	1.1-2.30 mmol/l

- Insulin 1 IU x twice daily
- First signs of muscle dystrophy
- Albumin and whole protein in blood normal
- The cat died in march 2015 from cardiac arrest
- Autopsy: no critical internal pathology
- IRIS stage of CKI 3 – BP – 1

	12.04.2014	10.07.2014	30.07.2014	01.02.2015	Normal ranges
Urea	20.3	22	23	25	5.4 — 12.1 mmol/l
Creat	172	247	250	267	70 — 165 µmol/l
Glu	11.0	13.8	6.1	12.5	6.8 mmol/l
Phosphate	1.77	1.49	1.5	1.5	1.1 — 2.30 mmol/l

- National Research Council, NRC (2006): Nutrient requirements of dogs and cats
- IRIS Guidelines: Staging of CKD
- Hand, Thatcher, Remillard, Roudebush: Klinische Diätetik für Kleintiere
- Forman MA, Marks SL, De Cock HE, et al. Evaluation of serum feline pancreatic lipase immunoreactivity for the diagnosis of feline pancreatitis
- Simpson KW. Feline pancreatitis. Waltham Focus 2005
- Williams DA. Diseases of exocrine pancreas
- Hertel-Bähnke P, Demmel A, Kienzle E, Dobenecker B (2014): Dietary P excess influences renal function in cats
- Kienzle E (1989): Untersuchungen zum Intestinal- und Intermediärstoffwechsel von Kohlenhydraten (Stärke verschiedener Herkunft und Aufbereitung, Mono-, Disaccharide) bei der Hauskatze
- Benett N, Greco DS, Peterson ME, et al. Comparison of low carbohydrate-low fiber diet and a moderate carbohydrate-high fiber diet in the management of feline diabetes mellitus
- Biourge VC. Feline diabetes mellitus: nutritional management



Cushing's disease and obesity in a mare

Dr. Julia Katharina Mack

Supervisor: Prof. Dr. Ellen Kienzle, Chair of Animal Nutrition and Dietetics,
Ludwig-Maximilians-University Munich, Germany

10th Residency class Sept 15th-16th 2015, Toulouse, France



Details on “Wiebke”

- 21 y old Warmblood mare
- 154 cm height at withers (stick)
- Easy keeper horse according to owner (i.e. thrifty phenotype)
- Current estimated BW ~ 550 kg
- Ideal BW ~ 500 kg
- Leisure horse, light work (5-6x/week trail ride for 1-1.5 h, occasionally dressage)
- Open stabling, on straw bedding, daily access to pasture during summertime

“Wiebke” - Medical history

- Podotrochlosis since the age of 6
- Arthritis of coffin joints in both forelegs
- Recurring inflammations of tendons, tendon lesions
- Overweight for several years
- March: ACTH on upper margin of reference range of 20 - 50 pg/ml¹
- Skin alterations (neck, shoulders) since fall (shortly before nutrition consultation in November)
- October: ACTH 300 pg/ml => diagnosed with Equine Cushing's disease by local vet
- Treatment 1 mg/d Prascend[®] (pergolide mesylate = agonist of dopamine receptor)



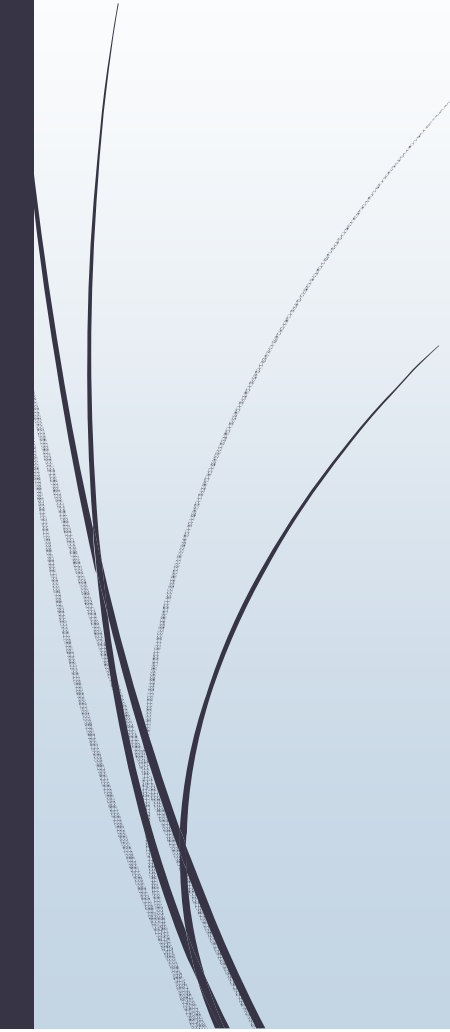
Reason for presentation to the nutrition consultation service

- ➔ Request of the owner to check the current ration and to recommend changes to ration (if necessary), based on medical history of “Wiebke”



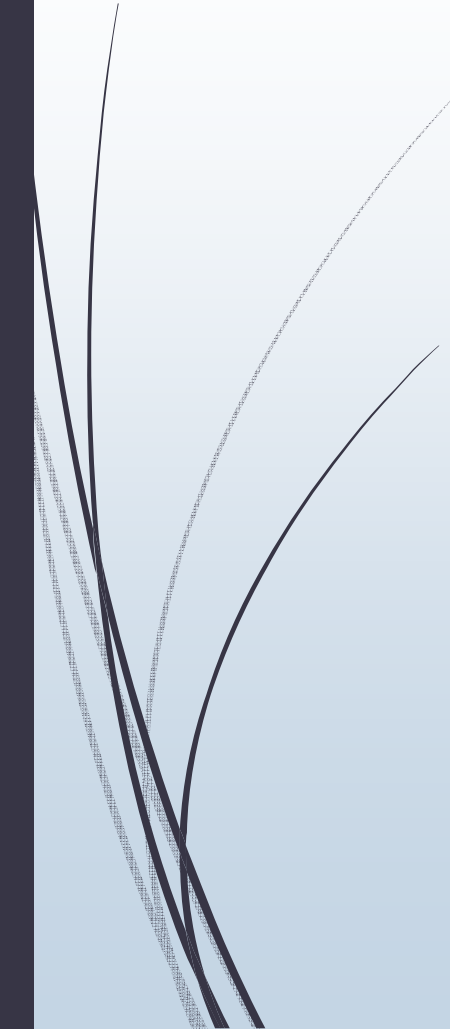


Equine Cushing's disease

- 
- Syn.: pituitary *pars intermedia* dysfunction (PPID)
 - Common neurodegenerative endocrine disease associated with ageing
 - Loss of hypothalamic inhibition due to oxidative damage and in consequence higher production of pro-opiomelanocortin; increased circulating plasma concentrations of the cleavage products result in various clinical signs associated with PPID²
 - With time, melanotroph hypertrophy, eventually adenomatous changes²
 - ~ 20% of horses aged ≥ 15 years affected (PPID also seen in younger horses³)



Common clinical signs in PPID

- 
- ▶ Laminitis (esp. in mature/elderly horses)⁴ – probably esp. in horses with insulin dysregulation as comorbidity²
 - ▶ Hypertrichosis, abnormal hair-shedding patterns⁴
 - ▶ Muscle atrophy leading to a “pot-belly” a/o “wasted topline” appearance⁴
 - ▶ Abnormal fat distribution (especially periorbitally)⁴
 - ▶ Lethargy, PD/PU, excessive sweating, susceptibility to secondary infections, infertility and (rarely) seizures⁴
 - ▶ Suspensory ligament degeneration⁵

Laboratory diagnostics with PPID



- No 'gold standard' diagnostic test that can reliably identify every horse with PPID²
- Therefore, early onset difficult to diagnose unequivocally²
- Recommended diagnostic tests according to Durham et al.⁴ are for example
 - Basal plasma ACTH concentration
 - Overnight dexamethasone suppression test
 - TRH stimulation test (measuring ACTH)
- Circannual variation in plasma ACTH⁶ => consider when interpreting results



Obesity – possible causes and consequences



► Possible causes:

- Overfeeding⁷
- Disruption of seasonal patterns of feed intake and BW regulation⁷
- Genetics⁷
- Altered hormonal regulation of appetite and energy balance⁷
- Lack of physical activity⁷

► Possible consequences:

- Orthopaedic disorders such as laminitis, osteoarthritis⁷
- Endocrine and metabolic disorders (equine metabolic syndrome, insulin resistance, glucose intolerance, hyperinsulinaemia, dyslipidaemia, hyperlipaemia and hepatic lipidosis⁷
- Abdominal/intestinal disorders, e.g. pedunculated lipomas, small intestinal strangulation⁷
- Miscellaneous, such as heat intolerance, exercise intolerance, exacerbation of an ageing-related pro-inflammatory state⁷

Dietary history of “Wiebke”

Ration during summertime	Ration during wintertime
5 kg late-maturity grass hay	5 kg late-maturity grass hay
10 kg pasture grass	1 kg late-maturity haylage
0.5 kg wheat straw	2.75 kg wheat straw
0.8 kg carrots	0.8 kg carrots
1 apple, 1 banana (2-3 x per week)	1 apple, 1 banana (2-3 x per week)
0.2 kg oats	0.2 kg oats
0.2 kg barley, crushed	0.2 kg barley, crushed
0.2 kg maize, crushed	0.2 kg maize, crushed
0.35 kg cereal concentrate for seniors	0.35 kg cereal concentrate for seniors
0.1 kg standard pellets	0.1 kg standard pellets
0.2 kg commercial mash mixture	0.2 kg commercial mash mixture
30 g mineral supplement	30 g mineral supplement
10 g brewer's yeast	10 g brewer's yeast
0.1 kg commercial treats	0.1 kg commercial treats
~ 59 MJ ME/d	~ 59 MJ ME/d



Key data in “Wiebke’s” diet

- ▶ Average ME intake ~ 59 MJ/d

(maintenance requirements $0.52 \text{ MJ/ME/kg BW}^{0.75}$, i.e. ~ 55 MJ ME/d for ideal BW of 500 kg)⁸

- ▶ Summertime: Zn, Se deficient (Na: salt lick)

- ▶ Wintertime: Zn, Se, Vit. E deficient (Na: salt lick)

- ▶ Other nutrients meet or (slightly) exceed requirements⁸



Nutritional management of Equine Cushing's disease

- ▶ In horses without laminitic episodes up to date
 - ▶ Good quality forage (pasture a/o hay)⁷
 - ▶ Low starch adult or „senior“ product with <3% added molasses and restricted starch from grains, if necessary to maintain BW/BCS⁷
 - ▶ Vitamin-mineral supplement
- ▶ In horses that already had laminitic episodes
 - ▶ Restricted access to pasture, when fructan/NCS* accumulation is greatest (early spring/late autumn or stressed pasture)⁷
 - ▶ Forage-based diet (preferably grass hay with low NCS content) with a forage balancer (vitamin-mineral supplement)⁷
 - ▶ No grain or sweet feeds (rich in starch a/o sugars)⁷

*NCS non-structure carbohydrates



Management of obesity

- “eat less – exercise more” – management recommendations by Geor et al.⁷:
 - Assessment of “baseline data” such as BW, BCS, other morphometric measurements, assessment of hooves for “founder lines”; monitoring of these parameters during weight loss programme
 - Increase recognition of trainers/owners for overweight/obesity
 - **Evaluation of current feeding programme and housing**
 - **Decrease/removal of grains/calorie-dense feed/treats**
 - **Evaluation of quality of current forage => preferably later maturity hay with low energy content**
 - **Vitamin-mineral supplement (or low calorie “ration balancer” with high quality protein)**
 - **Restricted access to pasture grazing (maybe with muzzle - high risk for colic/laminitis etc., if lost unnoticed while on pasture)**
 - Assessment of workload
 - Setting of goals for weight loss (weight loss of ~ 0.5 % of BW per week reasonable)
 - Gradual increase of physical activity (intensity and duration), if possible (laminitis); increased workload should be maintained even after goal BW/BCS is obtained

Dietary recommendations for “Wiebke”

Ration during summertime	Ration during wintertime
5 kg late maturity grass hay	5.5 kg late maturity grass hay
10 kg pasture grass	
0.5 kg wheat straw	2.5 kg wheat straw
1.25 kg carrots	1.75 kg carrots
0.1 kg wheat bran	0.1 kg wheat bran
0.25 kg “low glycaemic prebiotic” (commercial product for horses with EMS or PPID)	0.25 kg “low glycaemic prebiotic” (commercial product for horses with EMS or PPID)
80 g vitamin-mineral supplement	70 g vitamin-mineral supplement
25 g selenium supplement	25 g selenium supplement
10 g brewer's yeast	10 g brewer's yeast
50 g low energy commercial treats	50 g low energy commercial treats
~ 48.5 MJ ME/d	~ 48.5 MJ ME/d

EMS Equine metabolic syndrome



Key data on „Wiebke’s“ dietary recommendation and follow-up

- Decrease in daily energy supply of 17 – 18 %
(gradual weight loss mandatory, since horses with PPID combined with overweight have bad prognosis due to the risk of developing laminitis)
- Supply with sufficient amounts of other nutrients
- Reduction of non-structure carbohydrates in the diet
- Increase of physical activity, if possible
- Outcome:
 - “Wiebke” lost weight gradually and under treatment with pergolide the plasma concentration of ACTH returned to the reference range
 - After 2 months the commercial product used to make “Wiebke” eat her supplements was replaced by a similar product from another manufacturer, since “Wiebke” refused to eat it any longer
 - “Wiebke’s” medical situation stabilised under treatment and dietary adjustment

References

1. Reference range from: http://www.laboklin.de/pdf/de/news/laboklin_aktuell/lab_akt_1103.pdf (as of July 10th 2015).
2. Sojka-Kritchevsky, S.; Johnson, P.J. (2014). Current status and future directions: Equine pituitary pars intermedia dysfunction and equine metabolic syndrome. Equine Veterinary Journal ISSN 0425-1644 DOI: 10.1111/evj.12194.
3. McGowan T. et al (2013): Prevalence and risk factors for equine pituitary pars intermedia dysfunction in aged horses. Equine Veterinary Journal 45 (1), 74-79.
4. Durham et al. Dealing with equine pituitary pars intermedia dysfunction (equine cushing's disease) in equine practice.
http://www.prascend.nl/content/dam/internet/ah/prascend/nl_NL/documents/CONSENSUS%20VIEW%202012-%20DEALING%20WITH%20EQUINE%20PPID.pdf (as of July 10th 2015)
5. Hofberger et al. (2015). Suspensory ligament degeneration associated with pituitary pars intermedia dysfunction in horses. The Veterinary Journal 203 (3), 348 – 350.
6. Copas, V.E.N.; Durham, A.E. (2011): Circannual variation in plasma adrenocorticotrophic hormone concentrations in the UK in normal horses and ponies, and those with pituitary pars intermedia dysfunction. Equine Veterinary Journal ISSN 0425-1644 DOI: 10.1111/j.2042-3306.2011.00444.x
7. Geor et al. (2013): Equine applied and clinical nutrition. Saunders Elsevier, Edinburgh.
8. Gesellschaft fuer Ernährungsphysiologie (2014): Empfehlungen zur Energie- und Nährstoffversorgung von Pferden (Recommendations for energy and nutrient supply to horses). DLG-Verlag, Frankfurt (Main), Germany.

THE Zn SIGNIFICANCE IN WEANING PIGS

Jenifer Molina Tena. Hospital Clinic Veterinari UAB.
Barcelona (Spain)



OUTLINE

- **INTRODUCING Zn**
- **Zn METABOLISM**
- **Zn DEFICIENCY**
- **Zn EXCESS**
- **Zn AS ANTIDIARRHEAL TREATMENT**
- **SUMMARY**

INTRODUCING Zn

- Zn: Essential mineral that is naturally present in some foods, added to others, and available as a dietary supplement.
- Zn is used as a cofactor and structural element > 300 enzymes. Zn is involved in numerous aspects of cellular metabolism and in many biological functions (*solomons, 2013*).



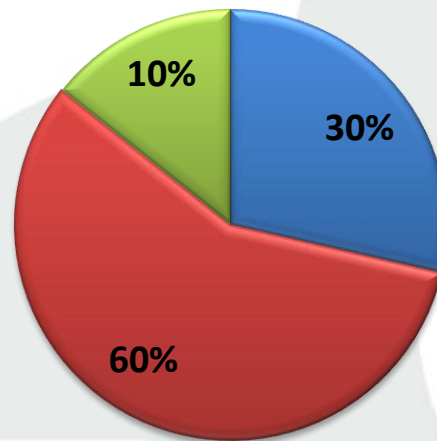
Food groups	Zn content (mg/Kg)	Phytate content (g/Kg)
Liver, kidney (beef, poultry)	42-61	0
Meat (beef, pork)	29-47	0
Poultry (chicken, duck)	18-30	0
Seafood (fish, etc.)	5-52	0
Eggs	11-14	0
Dairy (milk, cheese)	4-31	0
Seeds, nuts (sesame, almond)	29-78	17.6-47.1
Beans, lentils (soy, chickpea)	10-20	1.1-6.2
Whole-grain cereals (wheat, maize, brown rice)	5-32	2.1-6.2
Refined cereal grains (white, flour, white rice)	4-8	0.3-4.4
Bread	9	0.3
Tubers	3-5	0.9-1.3
Vegetables	1-8	0-1.2
Fruits	0-2	0-0.6

Adapted from the International MiniList

- Best sources: red meat, organ meat and shellfish (↑ bioavailable Zn)



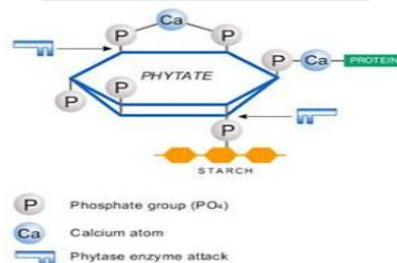
- ✱ Developed countries:



- Legumes and cereals
- Meat
- Dairy products

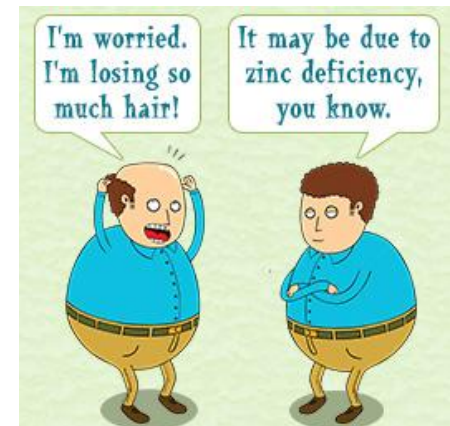
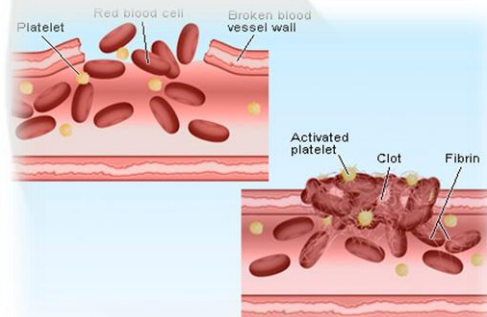
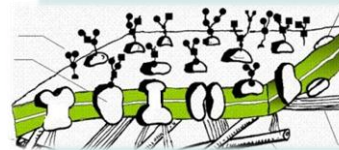
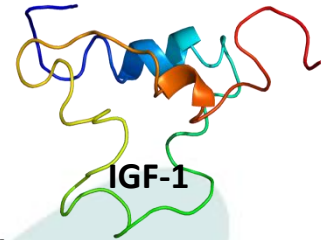


- Major sources in pigs: legumes and cereals (*Gibson, 1994*)
- Whole grain cereals = phytate → inhibit Zn bioavailability



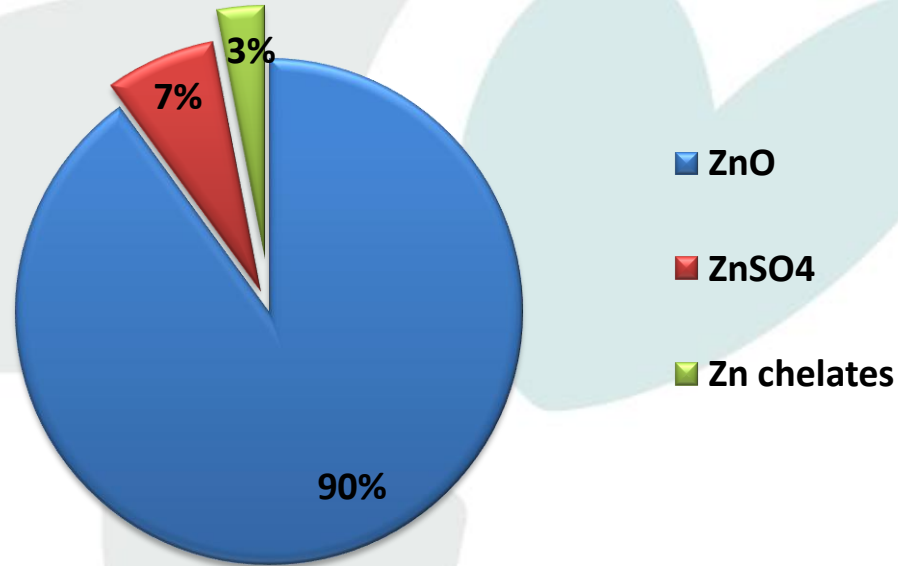
Zn functions

- Growth:
 - ✱ Stimulate connective tissue development and maintenance.
 - ✱ Stimulate bone mineralization
 - ✱ Regulate the function of IGF1
- Essential for innate and adaptative immunity
- Antioxidant agent:
 - ✱ Keep bio membrane stability
- Wound healing
- Stabilization of DNA and RNA
- Blood clotting
- Appetite control
- Nervous system
- Vision system
- Reproduction system



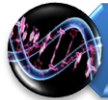
Types of Zn supplementation

- Two categories:
 - Inorganic: oxide, sulfate, chloride, carbonate
 - Organic: lactate, acetate, chelate of aa



- $\text{ZnO} / \text{ZnSO}_4$ = cheaper → commonly used by food industries

- Acetate and sulfate = \uparrow solubility = \uparrow absorbable Zn?
(controversial studies)
- Effects ZnO in-feed:



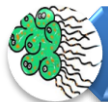
\uparrow Gene expression of antimicrobial peptides in SI



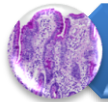
\uparrow IGF-1 and IGF-1R expression in SI mucosa



Positive effect on stability and diversity of microbiota



Bactericide



Electrolyte secretion from enterocytes

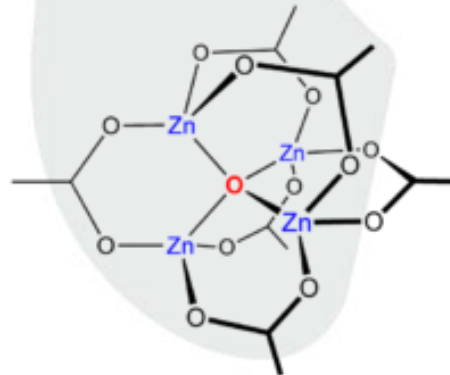
Zn availability



- The absorbed and retained Zn as a % of intake is <50% (*NRC,2012*)
- Variability of ZnO availability 39-88% relative to ZnSO_4 . (*Schell and Kornegay 1996*)



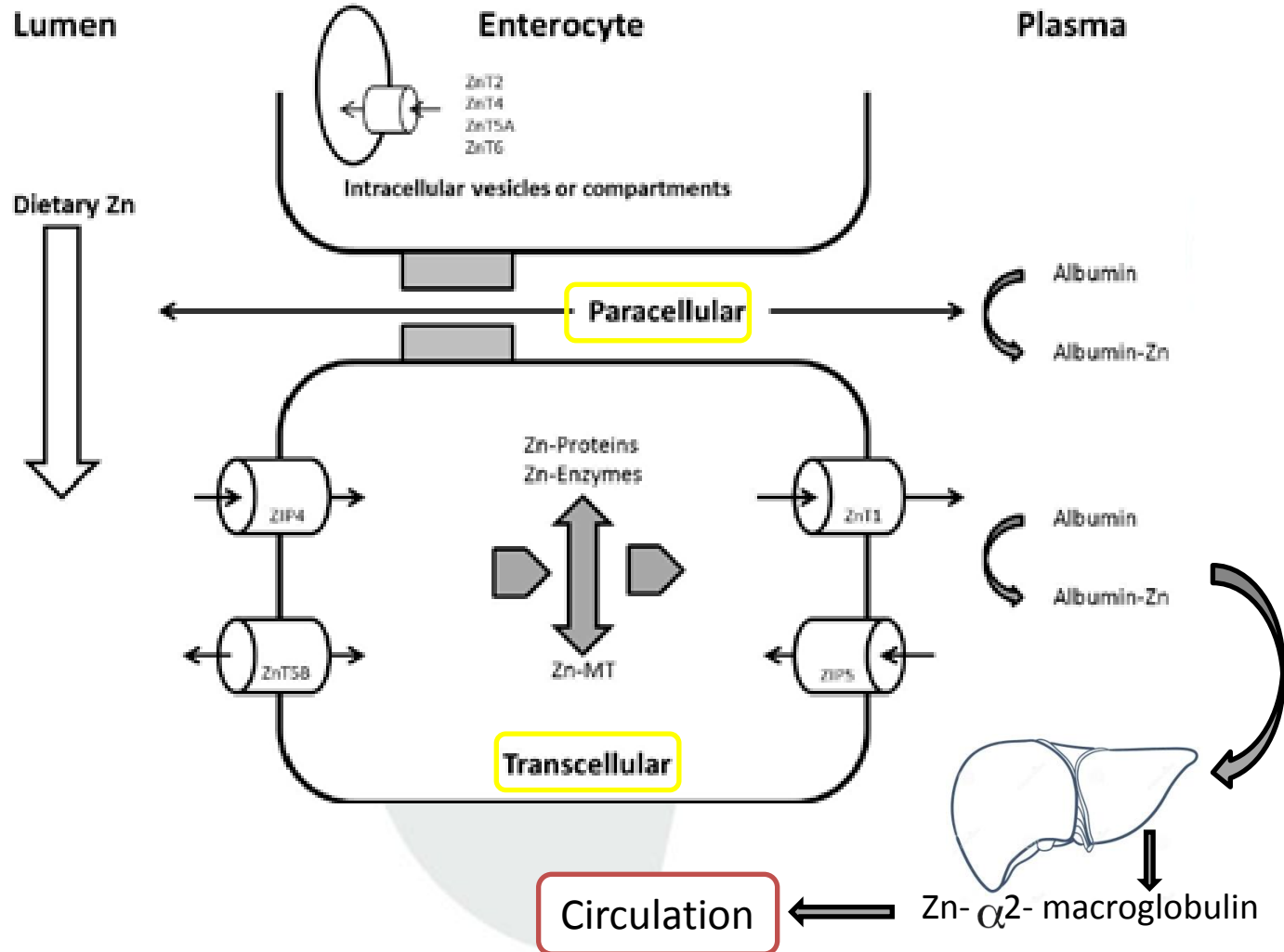
- Bioavailability organic complexes vs. $\text{ZnSO}_4 \rightarrow$ no differences (*cheng et al. 1998*)



Zn: DIGESTION AND ABSORPTION

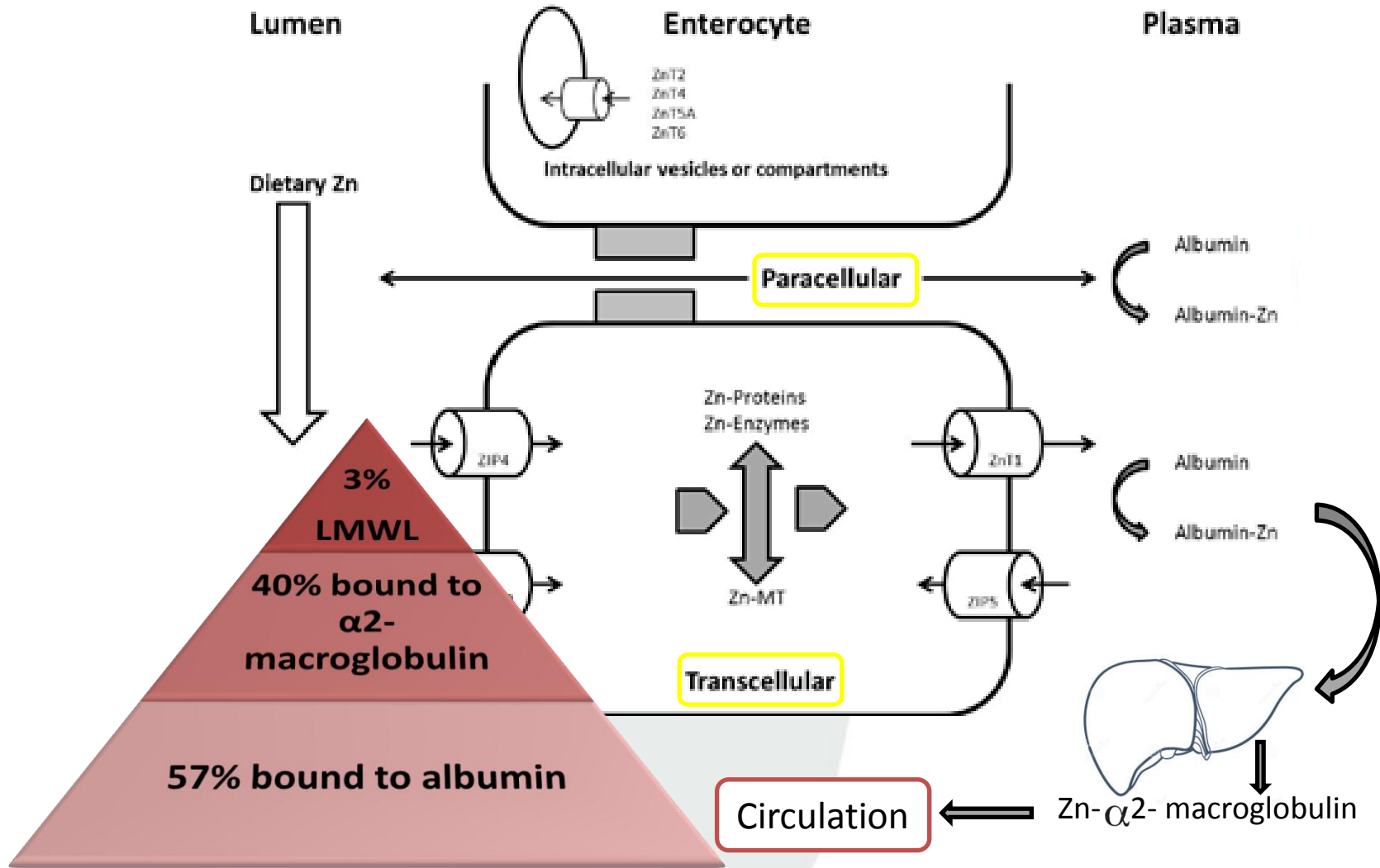
Absorption process in the small Intestine

Mainly in jejunum



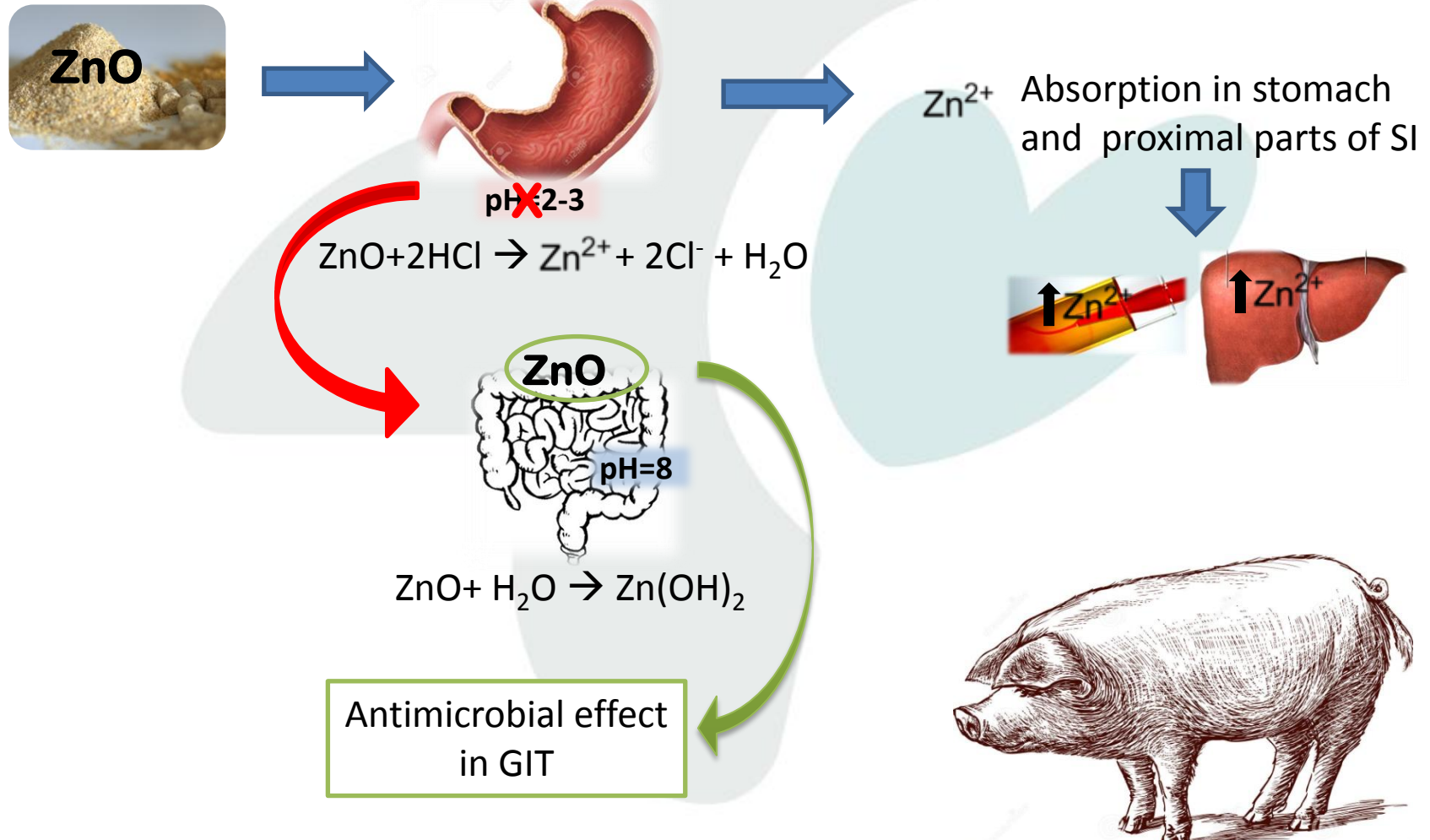
Absorption process in the small Intestine

Mainly in jejunum

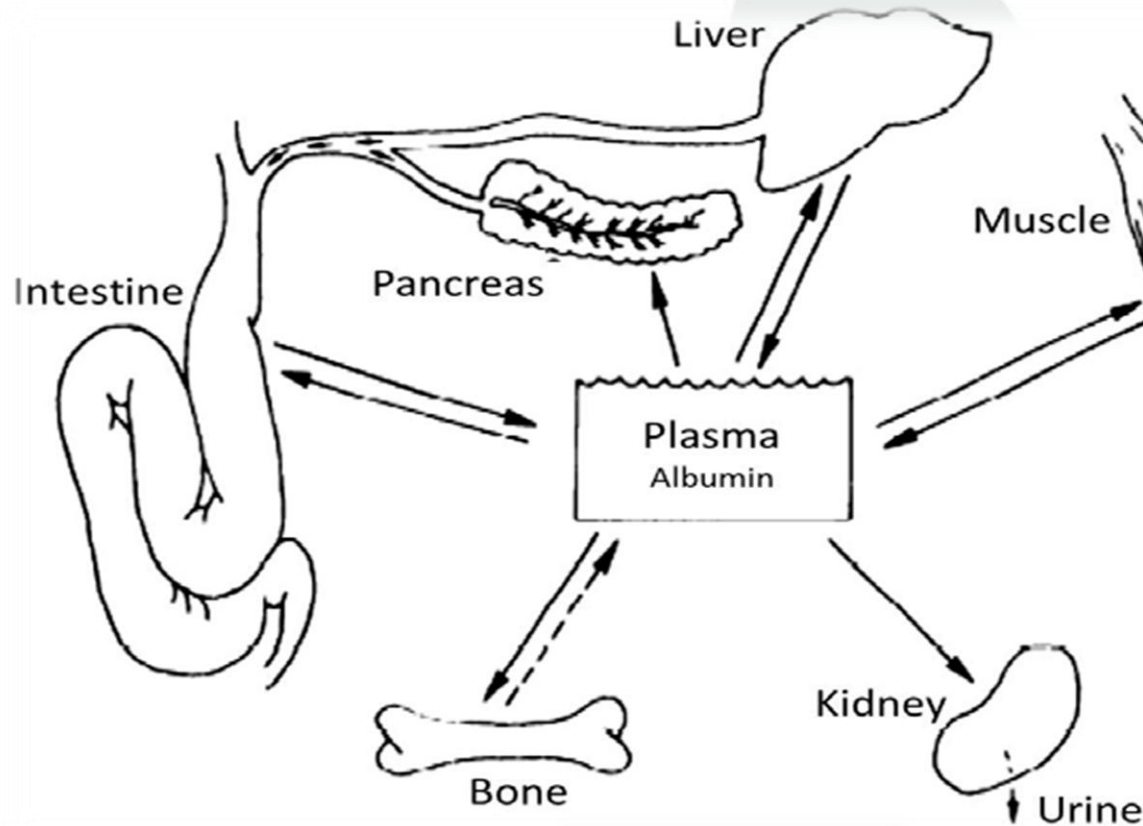


Adapted from Grider, (2013). Model for intestinal zinc absorption.

ZnO absorption process



Zn metabolism



*From Cousins, (1985).
Absorption, transport, and
hepatic metabolism of
copper and zinc.*

- Zn excretion: faeces ($\approx 90\%$); urine ($\approx 10\%$).
- Endogenous Zn GI secretions (pancreatic, bile,...) > consumed in the diet \rightarrow most of it can be reabsorbed.

Zn DEFICIENCY IN PIGS

● Causes:

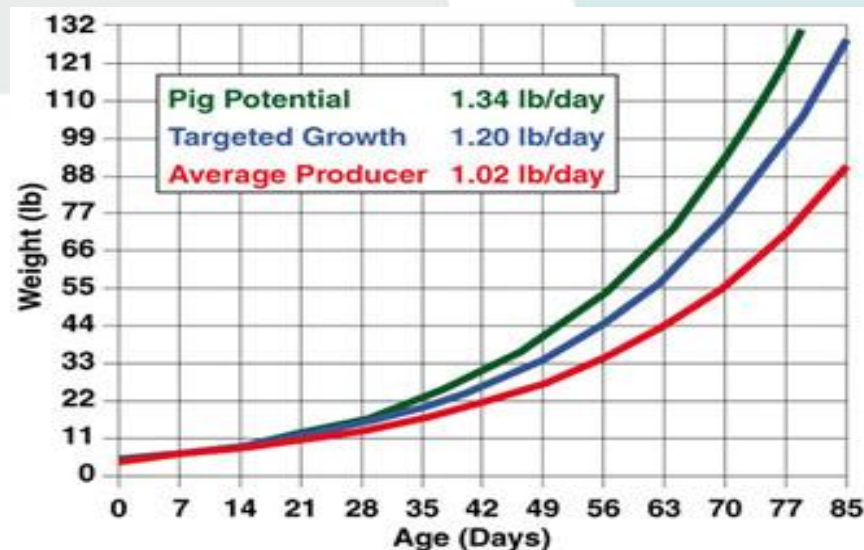
- ▶ Genetic (1ary)
- ▶ Poor intake due to ↑phytate, malabsorption states (IBD...) or long term parenteral nutrition (2ary)
- ▶ Increased utilization: sepsis, trauma, Vit.A and Vit. D deficiency and Fe deficiency.
- ▶ Diarrhoea

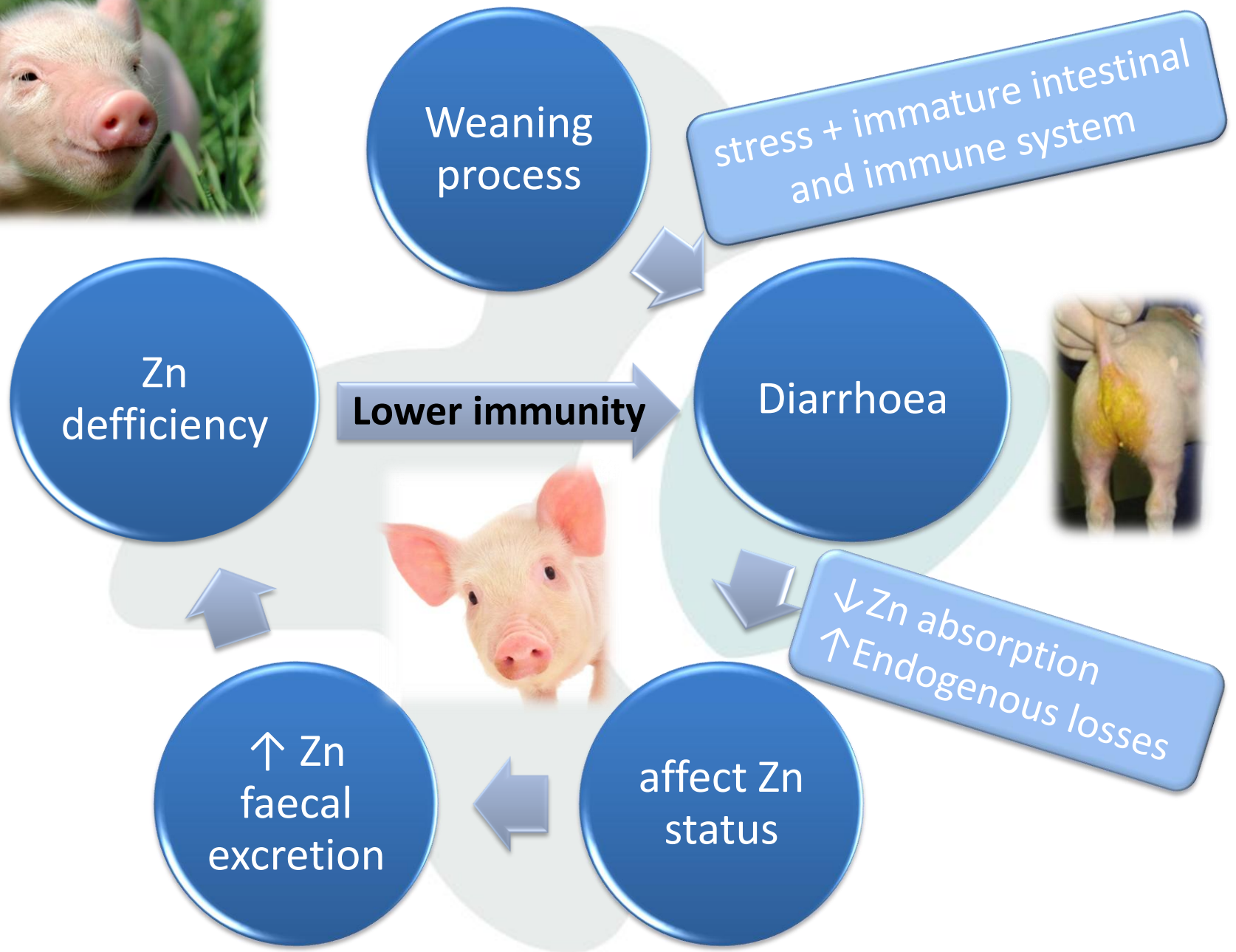
**Difficult to
diagnose**

● Growth retardation

● Depletion of enzyme activity in tissues.

- First symptoms: ↓ appetite and ↓ growth (few days).
- Other symptoms: ↑ risk of infections (↓ immunity), ↓ taste and smell, alopecia, impaired wound healing and infertility.





Zn EXCESS/TOXICITY IN PIGS

- As general rule → Zn is not toxic consumed in the diet (*Grider, 2013*).
- More probable in long term exposure.
- In piglets:
 - ▶ P deficiency.
 - ▶ Poor performance, inflammation and haemorrhages in multiple organs (*Brink et al., 1959*).
 - ▶ ↑ Growth? Unclear!
- Optimum dosage for diarrhoea control = 2500 mg Zn/Kg diet.
- Dose = 4000-5000 mg Zn/Kg diet → adverse effects.

12 Foods High In Zinc



SIGNIFICANCE OF Zn IN PIGLETS

- Commercial conditions → weaning at 21-28 days → stress - immature intestinal and immune system → changes in GI tract physiology, microbiology and immunology.



Environmental
Social
Dietary

- Period after weaning = sub-optimal growth and ↑ incidence of intestinal disturbances (diarrhoea) = ↑ mortality.

Pre-weaning situation



- Micronutrients depends on the input during later gestation and lactation.
 - ✱ *Caine et al., 2009* → supplementing gestating sows with 250 mg/Kg of Zn = ↑ serum [Zn] in days 7 and 14 after birth.
 - ✱ Zn content: colostrum (≈ 15.70 mg/Kg) > later milk (≈ 5.69 mg/kg).
- > parturitions = poorer mineral status (total body mineral content), but not in milk.





Post-weaning situation

- DECREASED FEED INTAKE → sub-optimal growth.

Changes in GIT

- Size
- Protein turnover rate
- Microbiota mass

Alterations in GIT functions

- Digestive
- Absorptive
- GIT barrier
- Immune functions

Affected Zn

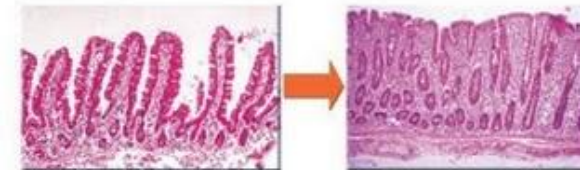
- Bioavailability
- Absorption

- ↓ gastric acid secretion capacity (\uparrow pH), ↓ gastric motility and ↓ emptying rate



POST-WEANING DIARRHOEA

- Villus atrophy, crypt hyperplasia, alteration of brush border enzymes



MALABSORPTION OF NUTRIENTS.

Zn AS ANTIDIARRHEAL TREATMENT

- Main problem nowadays in piglets (after weaning).

- Treatment:

- ▶ AB → controversial (resistance + effect in the human consume meat)



- ▶ ZnO – major used supplement → concerns about the environment.



- Zn supplementation of 2000-3000 mg/Kg:
 - ▶ ↓ diarrhoea
 - ▶ ↑ growth rates
- Mechanisms of action unknown. Hypothesis:
 - ▶ ZnO control the pathogenic bacterial
 - ▶ ↓ Fermentation of digestible nutrients in the proximal part of the GIT = ↑ E available = ↑ growth
- Zn treatments → plasma Zn values ≈ 1.5 mg/L → No weight gain with values < 1.5 or > 3 mg/L.



ENVIRONMENTAL CONSEQUENCES OF ZN SUPPLEMENTATION

↑ Levels Zn supplementation >10 days



Excretion of Zn in faeces



Toxicity to plants and soil microorganisms



Environmental concern in pig farm areas

ZnO has to be registered as a drug.



- Recommended posology: 100 mg ZnO/Kg BW for 14 days post-weaning.
- Used in ↑[] and > days → under veterinary prescription.



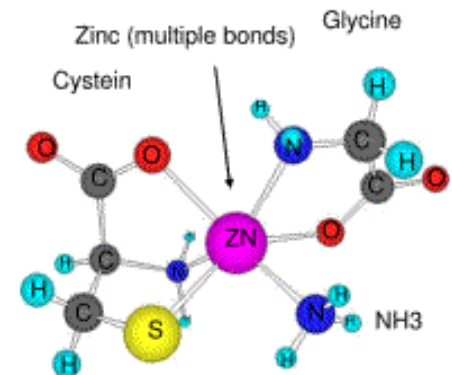
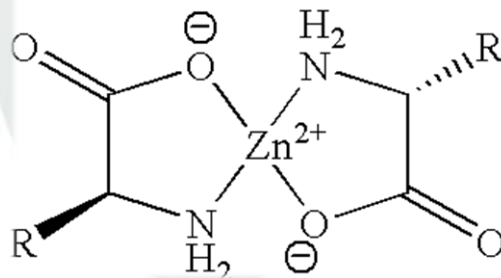
No control on the use.

Maximum content of Zn in feed additives: 150 mg/Kg (SCAN, 2003)

Alternatives to ZnO



- Organic Zn compounds: amino acid chelates - Zn methionine, Zn lysine,... → more environmentally friendly.
 - ✱ Results are inconsistent (*Van Heugten et al., 2003*)
 - ✱ Kind of chelate is an important factor (*Nitrayova et al., 2012*)
- Better with the environment, but no data about the antidiarrheal effect.



SUMMARY



- Weaning in commercial conditions produces a drop in [Zn] plasma, reaching the lowest level 2-3 days post-weaning.
- The drop in [Zn] plasma produce changes in GI tract physiology, microbiology and immunology leading to diarrhoea and increasing the piglets mortality.
- The use of Zn as a treatment is empirical → not accepted studies about its mode of action.
- The use of Zn as ZnO in pig feed industry is accepted for prevention and treatment of diarrhea in early weaned pigs.



SUMMARY



- ZnO < soluble than Zn sulfate, Zn chloride, Zn acetate or Zn chelates and is related with environmental issues.
- ZnSO_4 could be an alternative to ZnO , but is not able to $\uparrow[\text{Zn}]$ in serum in piglets and have palatability concerns.



THANKS FOR YOUR ATTENTION



QUESTIONS?

REFERENCES

- Brink, M.; Becker, D.; Terrill, S.; Jensen, A., 1959: Zinc toxicity in the weanling pig. *Journal of Animal Science.*, 18, 836–842.
- Caine, W. R.; Metzler-Zebeli, B. U.; McFall, M.; Miller, B.; Ward, T. L.; Kirkwood, R. N.; Mosenthin, R., 2009: Supplementation of diets for gestating sows with zinc amino acid complex and gastric intubation of suckling pigs with zinc-methionine on mineral status, intestinal morphology and bacterial translocation in lipopolysaccharide-challenged early-weaned pigs. *Research in veterinary science.*, 86, 453–462.
- Cheng, J.; Kornegay, E. T.; Schell, T., 1998: Influence of dietary lysine on the utilization of zinc from zinc sulfate and a zinc-lysine complex by young pigs. *Journal of animal science.*, 76, 1064–1074.
- Cousins, R. J., 1985: Absorption, transport, and hepatic metabolism of copper and zinc: special reference to metallothionein and ceruloplasmin. *Physiological reviews.*, 65, 238–309.
- Fukada, T.; Civic, N.; Furuichi, T.; Shimoda, S.; Mishima, K.; Higashiyama, H.; Idaira, Y.; Asada, Y.; Kitamura, H.; Yamasaki, S., 2008: The zinc transporter SLC39A13/ZIP13 is required for connective tissue development; its involvement in BMP/TGF- β signaling pathways. *PLoS One.*, 3, e3642.
- Gibson, R. S., 1994: Zinc nutrition in developing countries. *Nutrition Research Reviews.*, 7, 151–173.
- Golden, M. H. N., 1989: The diagnosis of zinc deficiency. *Zinc in human biology*. Springer-Verlag, London, United Kingdom, pp. 323–333.
- Grider, A., 2013: Zinc, Copper, and Manganese. In: Stipanuk, M. H. & M. A. Caudill (eds.), *Biochemical, physiological, and molecular aspects of human nutrition*. St Louis, . Elsevier, pp. 828–848.

REFERENCES

- Keen, C. L.; Hanna, L. A.; Lanoue, L.; Uriu-Adams, J. Y.; Rucker, R. B.; Clegg, M. S., 2003: Developmental consequences of trace mineral deficiencies in rodents: acute and long-term effects. *The Journal of nutrition.*, 133, 1477S–80S.
- King, J.; Keen, C., 1999: Zinc. In: Shils, M., J. Olson, M. Shike & R. AC (eds.), *Modern Nutrition in Health and Disease*. 9th edn. Lea & Febiger, Philadelphia.
- King, J. C., 2011: Zinc: an essential but elusive nutrient. *The American journal of clinical nutrition.*, 94, 679S–84S.
- Murakami, M.; Hirano, T., 2008: Intracellular zinc homeostasis and zinc signaling. *Cancer science.*, 99, 1515–1522.
- Nitrayova, S.; Windisch, W.; von Heimendahl, E.; Müller, A.; Bartelt, J., 2012: Bioavailability of zinc from different sources in pigs. *Journal of animal science.*, 90, 185–187.
- Nriagu, J., 2007: Zinc deficiency in human health. [http://www.extranet.elsevier.com/homepage_about/mrwd/nvrn/Zinc%20Deficiency%20in%20Humans.pdf].).
- Powell, S. R., 2000: The antioxidant properties of zinc. *Journal of Nutrition.*, 130, 1447S–1454S.
- Prasad, A. S.; Oberleas, D., 1971: Changes in activities of zinc-dependent enzymes in zinc-deficient tissues of rats. *Journal of applied physiology.*, 31, 842–846.
- Prasad, A. S., 2009: Zinc: role in immunity, oxidative stress and chronic inflammation. *Current opinion in clinical nutrition and metabolic care.*, 12, 646–652.
- Plum, L. M.; Rink, L.; Haase, H., 2010: The Essential Toxin : Impact of Zinc on Human Health. *International Journal of Environmental Research and Public Health.*, 7, 1342–1365.

REFERENCES

- Rink, L.; Gabriel, P., 2000: Zinc and the immune system. *Proceedings of the Nutrition Society.*, 59, 541–552.
- Schell, T. C.; Kornegay, E. T., 1996: Zinc concentration in tissues and performance of weanling pigs fed pharmacological levels of zinc from ZnO, Zn-methionine, Zn-lysine, or ZnSO₄. *Journal of animal science.*, 74, 1584–1593.
- Scott, B. J.; Bradwell, A. R., 1983: Identification of the serum binding proteins for iron, zinc, cadmium, nickel, and calcium. *Clinical chemistry.*, 29, 629–633.
- Solomons, N. W., 2013: Zinc. Editorial. *Annals of nutrition & metabolism.*, 62, 5–6.
- Steel, L.; Cousins, R. J., 1985: Kinetics of zinc absorption by lumenally and vascularly perfused rat intestine. *American Journal of Physiology-Gastrointestinal and Liver Physiology.*, 248, G46–G53.
- Sturniolo, G. C.; Fries, W.; Mazzon, E.; Di Leo, V.; Barollo, M.; D'inca, R., 2002: Effect of zinc supplementation on intestinal permeability in experimental colitis. *Journal of Laboratory and Clinical Medicine.*, 139, 311–315.
- Van Heugten, E.; Spears, J. W.; Kegley, E. B.; Ward, J. D.; Qureshi, M. A., 2003: Effects of organic forms of zinc on growth performance, tissue zinc distribution, and immune response of weanling pigs. *Journal of animal science.*, 81, 2063–2071.
- Yamaguchi, M., 1998: Role of zinc in bone formation and bone resorption. *The Journal of Trace Elements in Experimental Medicine.*, 11, 119–135.

ECVCN Residents Class 2015

Ketogenic diet in a dog with refractory idiopathic epilepsy

Elena Pagani, DMV, ECVCN Resident (1^o Year)

Department of Veterinary Sciences

University of Turin

Largo Paolo Braccini 2

10095 Grugliasco (TO)

BACKGROUND

Epilepsy is one of the most common serious neurological conditions in dogs and the prevalence is estimated to be from 0.5% to 5.7%

Most dogs have idiopathic epilepsy and they are often managed successfully with standard antiepileptic drugs, but 30% of cases are refractory to treatment

Refractory Epilepsy,
when its quality of life is compromised by:

- frequent and severe seizures despite of an appropriate drug therapy
- side effects of the medication



BACKGROUND

Currently, many dogs with refractory epilepsy are eventually euthanased or die during uncontrollable seizures (Arrol et al., 2012)

Therefore, non-pharmacological treatment options are becoming important

The Antiepileptic Effect Of Fasting was noted almost 100 years ago (Geyelin, 1921) and the ketogenic diet (KD) was introduced in that same year for the treatment of epilepsy (Wilder, 1921).

KETOGENIC DIET is high in fat, low in carbohydrates and has adequate amounts of protein, based on minimum daily requirements (Kossoff, 2004)

BACKGROUND

KETOGENIC DIET – CLINICAL TRIAL

IN HUMAN:

Clinical trials have demonstrated that approximately 50% of children with refractory epilepsy who receive the KD will have at least 50% reduction in seizures (Henderson et al., 2006, Neal et al., 2008, Kossoff et al., 2009 and Kessler et al., 2011)

IN DOG:

Only two abstracts describe the use of a KD in dogs with refractory idiopathic epilepsy (Patterson et al., 2005; Paganí et al. 2014).

Dogs receiving the ketogenic food over a period of 2 months had significantly decrease of seizure frequency than controls, but there was no significant difference in urine ketosis.

CLINICAL CASE

EMMA

Border Collie, intact female, 5 years,
17 Kg, BCS= 4/9

- **October 2013**: Diagnosis of idiopathic epilepsy
- Cluster seizures (6-7 for 15 seconds) every two months
- Seizures refractory to treatment with standard antiepileptic drugs (phenobarbital 6 mg/Kg BID and potassium bromide 18 mg/Kg BID): genetic resistance to Phenobarbital (ABCD-1)



KETOGENIC DIET

December 2014: non-pharmacological treatment options

EMMA received a KETOGENIC FOOD over a period of 2 months

The ketogenic diet was high in fat (65 % d.m.), low in Nfe (7% d.m.) and had adequate amounts of protein (25% d.m.), based on minimum daily requirements

11% of total fat was composed of medium-chain triglyceride (MCT)

An Adequate fluid intake has been necessary to prevent constipation and kidney stones

During the clinical trial, the treatment with antiepileptic drugs was kept constant and equal to that administered before starting

KETOGENIC DIET

$$\text{DER: } 110 \times (17) \times 0,75 = 920 \text{ Kcal/die}$$

Ingredients	Gramme	%
Pork meat	165	47,02
Carrots	90	25,64
Butter	90	25,64
MCT oil	3	0,85
Mineral and Vitamine supplement	3	0,85
Total	351	100

content of MCT in coconut oil: 58,2%

content of MCT in butter: 6,3%

11% of total fat (65%) was composed of medium-chain triglyceride
(MCT)

GESTIONE RAZIONI

Codice Razione

Data Razione

Descrizione

Categoria

Attività

Peso

BCS

000262

ketogenica 7

Cane

Mantenimento

17

5

Numero Cuccioli

Settimane

Tipo Lavoro

Ore Settimanali

Peso Adulto

Razione Fabb. / die		Imp	Caratteristica	STQ	SS	!	(SS A)	(SS B)
Kcal	982 920		SOSTANZA SECCA %	39,64	99,99		100	
			UMIDITA' %	60,35	0		0	
			LIPIDI %	25,57	64,5		5,5	31
			PROTIDI %	10,22	25,78		10	
			FIBRA %	0,79	1,99			
			CENERI %	0	0	!		
			E.I. %	2,51	6,33	!		
			EM kcal/100g	279,59	705,25	!		
			Proteine / Kcal EM	0	0	!		
			Calcio / Fosforo	0	0	!		
			AC.LINOLEICO %	1,27	3,2	!	1,1	6,5
			AC.LINOLENICO %	0,4	1,01	!	0,044	
			AC.ARACHIDONICO %	0,01	0,03	!		
			Na %	0,05	0,13	!	0,04	1,5
			Ca %	0,23	0,58	!	0,4	
			P tot %	0,21	0,53	!	0,3	

Materia	Grammi	%	Caratteristica	STQ	SS
MAIALE LEGGERO LOMBO	165	47,01	SOSTANZA SECCA %	29,3	100
CAROTE	90	25,64	UMIDITA' %	70,7	0
BURRO	90	25,64	LIPIDI %	7	23,89
INTEGRATORE (ALS TEKNOFARMA)	3	0,85	PROTIDI %	20,7	70,65

Elimina Alimento

Calcola

Completa

FOLLOW UP

FOLLOW UP PERIOD of seizure frequency and laboratory results:

- the day before starting the therapy (T0)
- at 15 days (T1)
- at the end of the trail food period of 2 month (T2)

LABORATORY TESTS performed has been the evaluation of :

- Levels of urinary ketones by a urinalysis strips (Siemens MULTISTIX 10SG: in the presence of acetoacetic acid produces a color change : Acetone and B-hydroxybutyric acid are not detected with this method)
- Complete blood analysis
- Phenobarbitalemia and Bromuremia

SEIZURE FREQUENCY was recorded 24 hours 24 by the owners and analyzed by the neurologist

FOLLOW UP

SEIZURE FREQUENCY : important decrease of seizure frequency (only one episode (2 crises during 5-8 seconds) over a period of 6 months)

URINARY KETONE BODIES: changeable urine concentration of acetoacetic acid

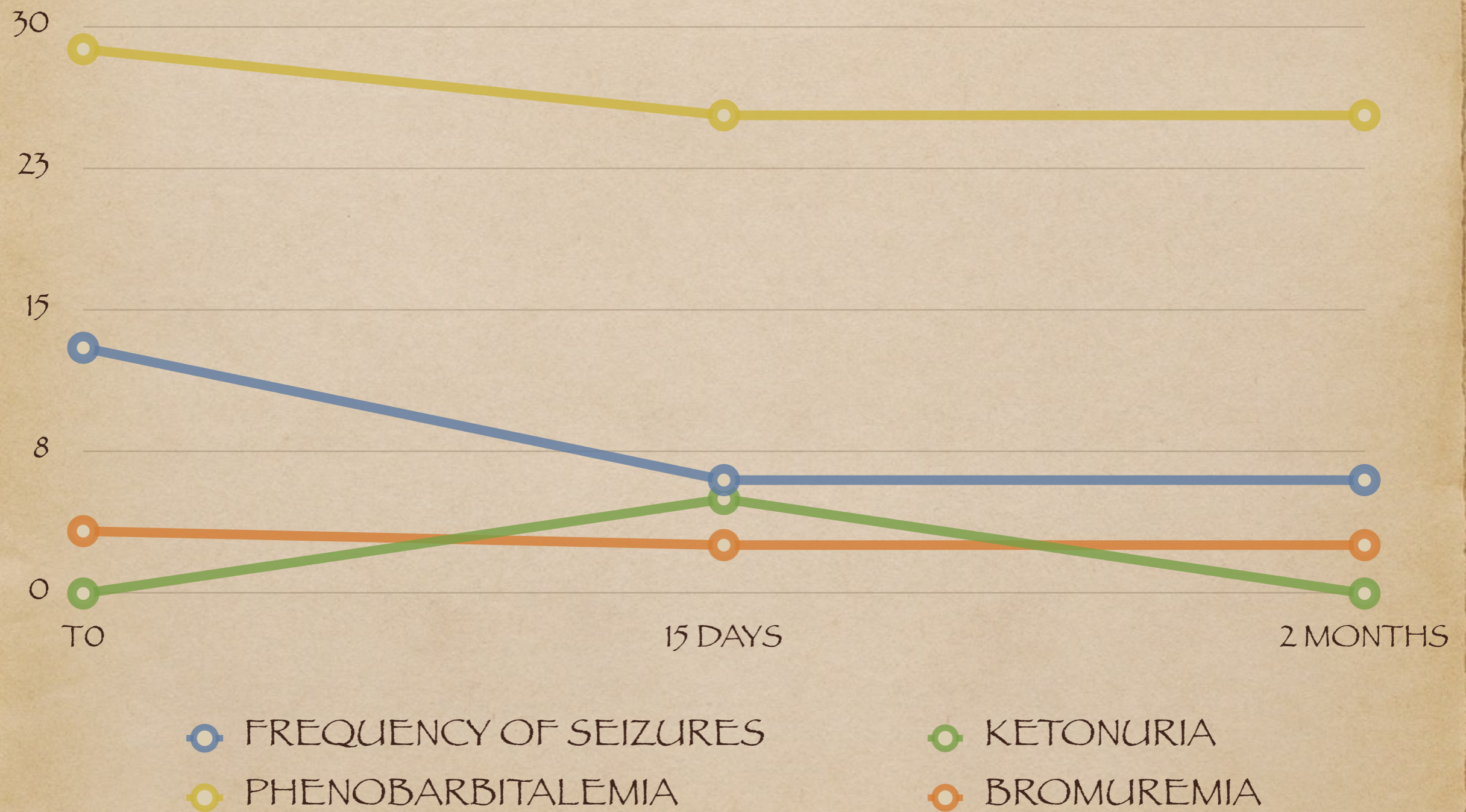
BODY WEIGHT : increase from 17 Kg to 19,6 Kg

CLINICAL SIGNS: After 6 months of ketogenic food: arise acute episode of VOMITING after eating

FOLLOW UP

Analysis	T0	T1	T2
Ketonuria (mg/dl)	no detectable	5	no detectable
Phenobarbitalemia (20-35microg/ml)	28,8	/	25,3
Bromuremia (1000-2000 microg/ml)	3309	/	2564

FOLLOW UP



DISCUSSION

WHY “UNSTABLE URINARY KETONE BODIES, BUT CLINICAL IMPROVEMENT”?

- A. URINALYSIS STRIPS uses sodium nitroprusside reagent, which, in the presence of acetoacetic acid produces a color change, BUT during ketosis, the normal ratio of 1:1 of β -hydroxybutyrate (β HB) and acetoacetic acid shift to an important elevation of β HB acid.

It would be useful to include in future cases the simultaneous evaluation of blood concentration of **β -hydroxybutyrate acid**

DISCUSSION

WHY “UNSTABLE URINARY KETONE BODIES, BUT CLINICAL IMPROVEMENT”?

- B. The precise antiepileptic mechanism of action of the KD still remains unknown (Schwartzkroin, 1999; McNally and Hartman, 2012),
BUT IS PRESUME TO BE MULTIFACTORIAL:

KETONE BODIES

- **Acetone:** suppresses seizures in animal model (Likhodii SS, 2003)
- **Acetoacetate:** neuroprotective against the excitatory neurotransmitter glutamate (Massieu L, 2003)
- **β -hydroxybutyrate:** structurally similar to GABA, inhibitory neurotransmitter (Morris AA, 2005)
- **Ketosis:** increase of oxaloacetate consumption: glutamate is shunted to GABA synthesis (Yudkoff M, 2004)

CHANGE IN LIPIDS

ACIDOSIS AND
DEHYDRATION

ALTERED ENERGY
STATE

DISCUSSION

WHY “arise acute episode of VOMITING after eating”?

11% of total fat was composed of medium-chain triglyceride (MCT): MCT oil is rapidly absorbed by the gastrointestinal tract, it is often associated with symptoms including abdominal cramps, diarrhea, nausea, and vomiting

Human study suggests to change MCT oil with corn oil without loss of seizure efficacy (Woody RC, 1988)

WHY “weight gain”?

Pet-owner: more energy-dense foods tend to be more palatable but learn to consume them in smaller portion sizes.

REFERENCES

- Arrol LI, Penderis J, Garosi L, Cripps P, Gutierrez-Quintana R, Gonçalves R. Aetiology and long-term outcome of juvenile epilepsy in 136 dogs. *Vet Rec.* 2012 Mar;170(13):335.
- Geyelin HR. Fasting as a method for treating epilepsy. *Medical Record* 1921;99:1037-9.
- Henderson CBI, Filloux FM, Alder SC, Lyon JL, Caplin DA. Efficacy of the ketogenic diet as a treatment option for epilepsy: meta-analysis. *J Child Neurol.* 2006 Mar;21(3):193-8.
- Kessler SKI, Neal EG, Camfield CS, Kossoff EH. Dietary therapies for epilepsy: future research. *Epilepsy Behav.* 2011 Sep;22(1):17-22.
- Kossoff EH, Hartman AL. Ketogenic diets: new advances for metabolism-based therapies. *Curr Opin Neurol.* 2012 Apr;25(2):173-8.
- Kossoff EH. More fat and fewer seizures: dietary therapies for epilepsy. *Lancet Neurol.* 2004 Jul;3(7):415-20.
- Likhodii SS, Serbanescu I, Cortez MA, et al.: Anticonvulsant properties of acetone, a brain ketone elevated by the ketogenic diet. *Ann Neurol* 2003, 54:219-226.
- Massieu L, Haces ML, Montiel T, et al.: Acetoacetate protects hippocampal neurons against glutamate-mediated neuronal damage during glycolysis inhibition. *Neuroscience* 2003, 120:365-378.
- McNally MAI, Hartman AL. Ketone bodies in epilepsy. *J Neurochem.* 2012 Apr;121(1):28-35.
- Morris AA: Cerebral ketone body metabolism. *J Inher Metab Dis* 2005, 28:109-121.
- Neal EG, Chaffe H, Schwartz RH, Lawson MS, Edwards N, Fitzsimmons G, Whitney A, Cross JH. A randomized trial of classical and medium-chain triglyceride ketogenic diets in the treatment of childhood epilepsy. *Epilepsia.* 2009 May;50(5):1109-17.
- Pagani E, Síviero T, Prola L. Ketogenic diet for dogs with refractory epilepsy. *Proceeding of ESVCN Congress* 2014
- Patterson E.E., Muñana K.K., Kirk C.A., Lowry S.R., Armstrong P.J.: Results of a ketogenic food trial for dogs with idiopathic epilepsy. *Journal of Veterinary Internal Medicine* 2005;19:421.
- Schwartzkroin PAI. Mechanisms underlying the anti-epileptic efficacy of the ketogenic diet. *Epilepsy Res.* 1999 Dec;37(3):171-80.
- Wilder RM 1921 The effect of ketonemia on the course of epilepsy. *Mayo Clin Bull* 2:307
- Woody RC, Brodie M, Hampton DK: Corn oil ketogenic diet for children with intractable seizures. *J Child Neurol* 1988, 3:21-24.
- Yudkoff M, Daikhin Y, Nissim I, et al.: Ketogenic diet, brain glutamate metabolism and seizure control. *Prostaglandins Leukot Essent Fatty Acids* 2004, 70:277-285.

Thank you for your attention



Food allergy and genetic predisposition to dilated cardiomyopathy in a female Doberman

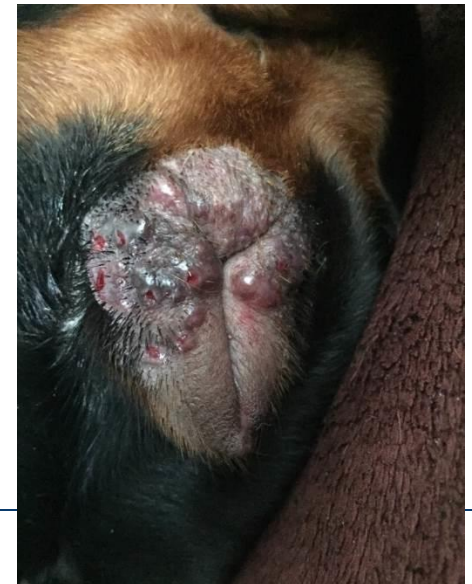
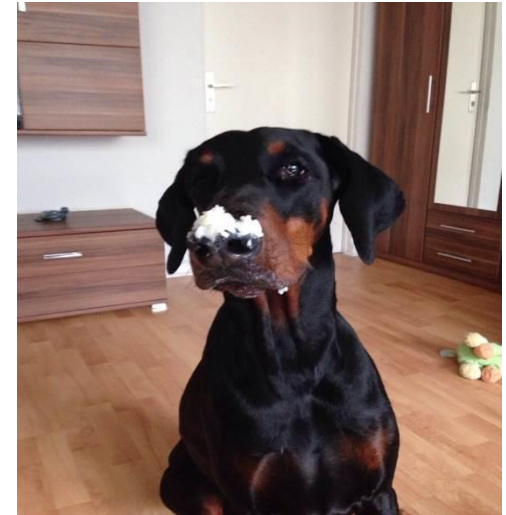
Dr. Nadine Paßlack

Institute of Animal Nutrition

Freie Universität Berlin, Germany

Case description / Anamnesis

- „Mercedes“: Doberman, female, intact, 6 years old
- Suspected food allergy (dermatological signs, especially paws and vulva)
- Initial appointment at the Nutrition Consultation Service: March 23, 2015



Case description / Anamnesis

- Mercedes is healthy otherwise, but shows a genetic predisposition to dilated cardiomyopathy (DCM) (parents and brothers died)
- Request of the owner:
 1. Home-cooked diet for the treatment of the food allergy
 - Mercedes tolerates salmon and potatoes
 2. Supplements to support heart function (?) -> Taurine, L-carnitine, vitamin E,...

Dietary recommendations

- Diets:

Ingredients	Diet 1	Diet 2	Diet 3
Salmon¹	425 g	425 g	425 g
Rice²	320 g	-	-
Noodles²	-	300 g	-
Potato flakes³	-	-	320 g
Oil (e.g. linseed oil, fish oil)	28 g	28 g	40 g
Vitamin-Optimix Sensitive⁴	10 g	10 g	8 g
Calcium carbonate	1 g	1 g	2,5 g
VMP-pills⁵	-	-	2 g
Cellulose	10 g	10 g	-

¹ Amount given for raw salmon, but it should be cooked after weighing

² Amount given for raw noodles/rice, but it should be cooked after weighing

³ Amount given for raw potato flakes, but they should be mixed with warm water and soak for approximately 5 minutes

^{4, 5} Vitamin and mineral supplements

Background

- **Supplements to support heart function: Taurine:**
 - **Kittleson et al. (1997):** American cocker spaniels with DCM and taurine deficiency → supplementation of taurine and L-carnitine → blood values within the normal range and improvement of cardiac parameters
 - **Sanderson et al. (2001):** Dogs fed protein-restricted diets showed taurine deficiency; development of canine DCM secondary to taurine deficiency; taurine supplementation led to an improvement of cardiac parameters
 - **Fascetti et al. (2003):** Taurine deficiency in dogs with DCM → improvement of cardiac function with supplementation of taurine
 - **Bélanger et al. (2005):** Reversible taurine-deficient DCM in golden retrievers
 - **Ko et al. (2007):** Large dogs showed lower taurine biosynthesis compared to small dogs
 - **Vollmar et al. (2013):** Taurine deficiency occurred in dogs with and without DCM

Background

- Supplements to support heart function: L-carnitine
 - **Costa and Labuc (1994):** Supplementation of carnitine did not resolve DCM in boxers
 - **Freeman (1998):** Carnitine might not be a causative factor in the pathogenesis of canine DCM; carnitine deficiency is possibly a secondary event in some dogs with DCM

Background

- Supplements to support heart function: n-3-fatty acids
 - **Freeman et al. (1998):** Improved cardiac cachexia and muscle mass; no effect on heart size or heart function
 - **Freeman et al. (1998; 2006):** Increased n-3-plasma-concentration after supplementation
 - **Smith et al. (2007):** Fish oil reduced arrhythmia in Boxers with arrhythmogenic right ventricular cardiomyopathy
 - **Smith et al. (2007); Lavie et al. (2009); Freeman (2010):** Anti-inflammatory, anti-arrhythmogenic effects, improved endothelial function, reduced platelet aggregability; antithrombotic effects

Background

- Supplements to support heart function: Antioxidants
- **Sagols and Priymenko (2011):** Oxidative stress → heart cell damage; supplementation of antioxidants (e.g. Coenzyme Q10, vitamins, polyphenols) for neutralization of free radicals
- Little data available in dogs with heart disease
 - **Tripathi and Hegde (1997):** Alpha-tocopherol pretreatment in dogs with experimentally induced left anterior descending coronary artery occlusion → myocardial infarct size ↓, percent necrosis in the left ventricular mass ↓ compared to untreated animals
 - **Freeman et al. (2005):** Some antioxidants ↓ and biomarkers of oxidative stress ↑ in dogs with congestive heart failure

Background

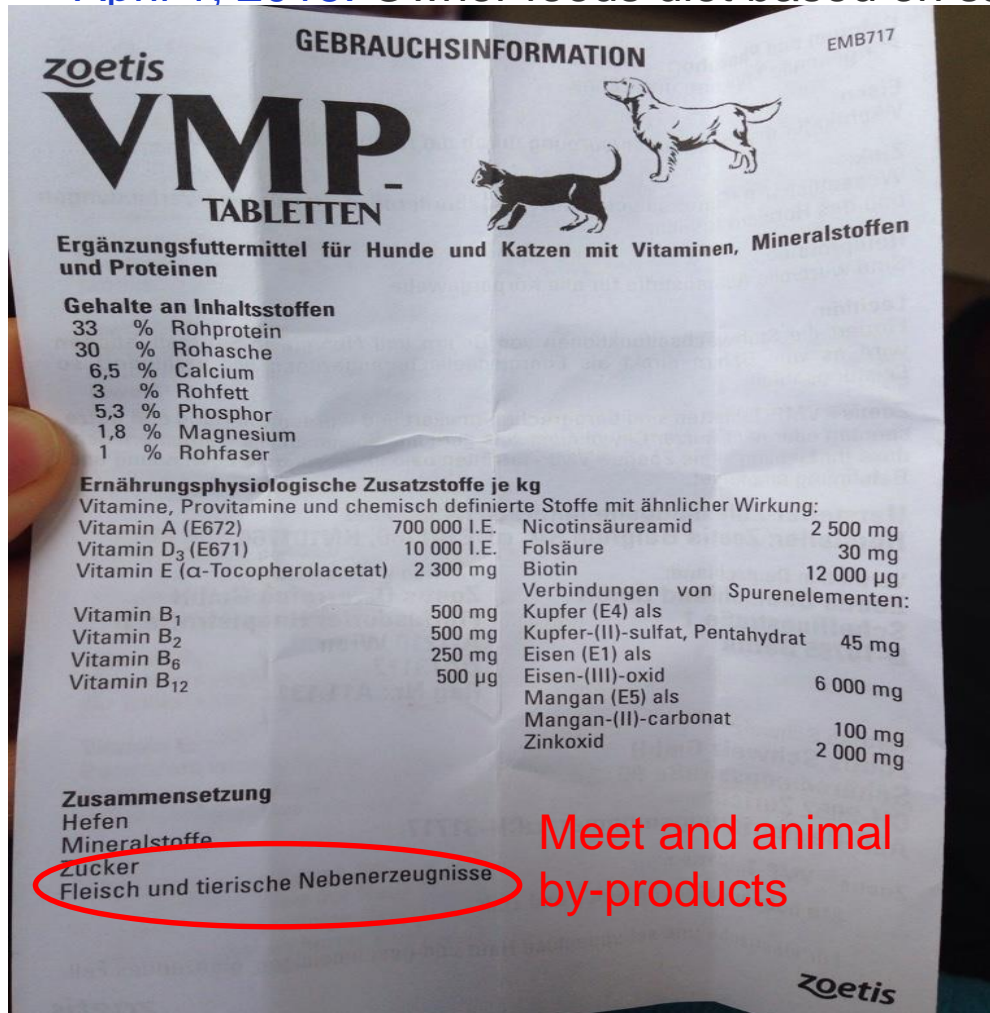
- Recommendations in the present case:
 - Supplementation of taurine and carnitine especially in case of deficiencies
 - N-3-fatty acid supplementation (e.g. fish oil) might be beneficial
 - Due to the vitamin supplements in the calculated diets, no additional supplementation of antioxidants like vitamin E is necessary

Follow-up

- **April 1, 2015:** Owner feeds diet based on salmon and rice without vitamins and minerals (as recommended for the first weeks); dermatological signs ↑, diarrhea
 - Recommendation: potato flakes instead of rice
 - Feedback: Dog tolerates diet based on salmon and potato flakes, dermatological signs ↓
- **May 21, 2015:** pustules on vulva when feeding VMP-pills (vitamin and mineral supplement)

Follow-up

- April 1, 2015: Owner feeds diet based on salmon and rice without vitamins and minerals; dermatological signs ↑, diarrhea



Follow-up

- **Recommendation:** to increase the amount of „Vitamin-Optimix Sensitive“ in order to remove the VMP-pills

Ingredients	Diet 3
Salmon ¹	425 g
Potato flakes ²	330 g
Oil (e.g. e.g. linseed oil, fish oil)	40 g
Vitamin-Optimix Sensitive ³	10 g
Calcium carbonate	2,5 g

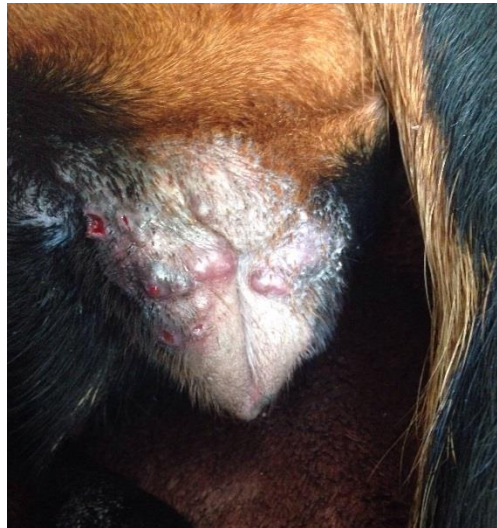
¹ Amount given for raw salmon, but it should be cooked after weighing

² Amount given for raw potato flakes, but they should be mixed with warm water and soak for approximately 5 minutes

³ Vitamin and mineral supplement

Follow-up

- **June 10, 2015:** Dog tolerates the diet based on salmon and potato flakes with all supplements; no dermatological signs
- **July 2, 2015:** Pustules on vulva



Follow-up

- **Recommendation:** to replace the dietary protein source -> pig instead of salmon; supplementation of biotin and zinc

Ingredients	Diet 4	Diet 5
Pig meat ¹	320 g	360 g
Potato flakes ²	280 g	-
Corn flakes ³	-	195 g
Oil (e.g. e.g. linseed oil, fish oil)	32 g	40 g
Vitamin-Optimix Sensitive ⁴	11 g	11 g
Canestro Biotin Forte ⁵	1 g	1 g
Iodized table salt	-	0.5 g

¹ Amount given for raw pig meat, but it has to be cooked after weighing

² Amount given for raw potato flakes, but they should be mixed with warm water and soak for approximately 5 minutes

³ Amount given for raw corn flakes, but they should be cooked and soak for a few minutes

⁴ Vitamin and mineral supplement

⁵ Biotin and zinc supplement

Follow-up

- **Feedback (July 24, 2015):** Owner did not change the protein source to date, since dermatological signs improved; owner noticed that dog tolerates cooked but not raw salmon
 - Change of allergenic potential of protein due to heat treatment?
- Owner will stop feeding raw salmon and observe dermatological signs. In case that pustules still occur, dietary protein source will be replaced

...To be continued...

Discussion

- Some things to discuss...

...Mineral and vitamin supplements: Animal protein →
allergy symptoms

...Impact of heat process on allergenic potential of protein?

...(Further) recommendations for dogs with a predisposition to DCM?



References

- **Bélanger MC, Ouellet M, Queney G, Moreau M (2005).** Taurine-deficient dilated cardiomyopathy in a family of golden retrievers. J Am Anim Hosp Assoc 41:284-91.
- **Costa ND, Labuc RH (1994).** Case report: efficacy of oral carnitine therapy for dilated cardiomyopathy in boxer dogs. J Nutr 124(12 Suppl): 2687S-2692S.
- **Fascetti AJ, Reed JR, Rogers QR, Backus RC (2003).** Taurine deficiency in dogs with dilated cardiomyopathy: 12 cases (1997-2001). J Am Vet Med Assoc 223: 1137-1141.
- **Freeman LM (1998).** Interventional nutrition for cardiac disease. Clin Tech Small Anim Pract 13: 232-237.
- **Freeman LM, Rush JE, Kehayias JJ, Ross JN Jr, Meydani SN, Brown DJ, Dolnikowski GG, Marmor BN, White ME, Dinarello CA, Roubenoff R (1998).** Nutritional alterations and the effects of fish oil supplementation in dogs with heart failure. J Vet Intern Med 12: 440–448.
- **Freeman LM, Rush JE and Markwell PJ (2006).** Effects of dietary modification in dogs with early chronic valvular disease. J Vet Intern Med 20: 1116–1126.
- **Freeman LM (2010).** Beneficial effects of omega-3 fatty acids in cardiovascular disease. J Small Anim Pract 51: 462–470.

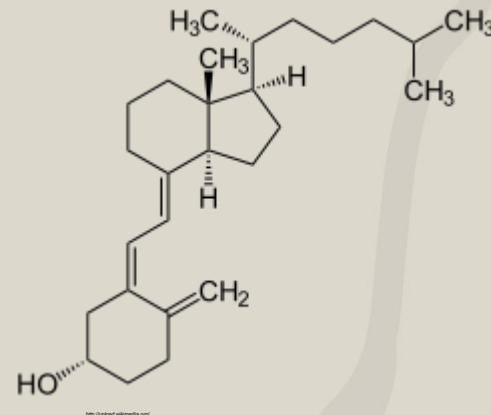
References

- **Kittleson MD, Keene B, Pion PD, Loyer CG (1997).**Results of the multicenter spaniel trial (MUST): Taurine- and carnitine-responsive dilated cardiomyopathy in American Cocker Spaniels with decreased plasma taurine concentration. J Vet Intern Med 11: 204-211.
- **Ko KS, Backus RC, Berg JR, Lane MW, Rogers QR (2007).** Differences in taurine synthesis rate among dogs relate to differences in their maintenance energy requirement. J Nutr 137:1171-1175.
- **Lavie CJ, Milani RV, Mehra MR, Ventura HO (2009).** Omega-3 polyunsaturated fatty acids and cardiovascular diseases. J Am Coll Cardiol 54: 584–594.
- **Sagols E, Priymenko N (2011).** Oxidative stress in dog with heart failure: the role of dietary Fatty acids and antioxidants. Vet Med Int:180206. doi: 10.4061/2011/180206
- **Sanderson SL, Gross KL, Ogburn PN, Calvert C, Jacobs G, Lowry SR, Bird KA, Koehler LA, Swanson LL (2001).** Effects of dietary fat and L-carnitine on plasma and whole blood taurine concentrations and cardiac function in healthy dogs fed protein-restricted diets. Am J Vet Res 62(10):1616-23.
- **Smith CE, Freeman LM, Rush JE, Cunningham SM, Biourge V (2007).**Omega-3 fatty acids in Boxer dogs with arrhythmogenic right ventricular cardiomyopathy. J Vet Intern Med 21: 265–273.

References

- **Tripathi Y, Hegde BM (1997).** Effect of alpha-tocopherol pretreatment on infarct size following 90 minutes of ischemia and 4 hours of reperfusion in dogs. *Indian J Physiol Pharmacol* 41: 241-247.
- **Vollmar AC, Fox PR, Servet E, Biourge V (2013).** Determination of the prevalence of whole blood taurine in Irish wolfhound dogs with and without echocardiographic evidence of dilated cardiomyopathy. *J Vet Cardiol* 15: 189-196.

A Case of Vitamin D Intoxication in Alpacas



Christine Ratert

Outline

- **The case:**
 - anamnesis (reported symptoms, diagnostics done before, pathological findings)
 - background information: vit. D intoxication
 - feed analysis
 - results and discussion
 - therapy/feeding advice
 - references



http://pinabay.com/static/uploads/photo/2012/04/26/22/15/alpacas-43324_180.jpg

The case: anamnesis, symptoms

Anamnesis:

- farm with alpacas (including 32 stallions, 42 mares and foals)
- feeding of alfalfa hay and two variants of a special complementary feed for alpacas
- housing on paddocks with only small residuals of grass
- worse body condition and some animals worse general condition
→ consultation of veterinarian



The case: anamnesis, symptoms

Anamnesis: diagnostic of the veterinarian

- blood sample of four animals → high vitamin D levels
- worse general condition

Reception order → clinic for small ruminants, TiHo



The case: pathological findings

Findings: Clinic of small ruminants

Vorberichtlich zeigte die Stute seit dem Vortag ein reduziertes Allgemeinbefinden mit Untertemperatur und vermehrtem Liegen. Eine Vorbehandlung durch den Haustierarzt erfolgte bereits mit Metamizol, Gastrogard und Elektrolyten per os.

Bei der Aufnahmeuntersuchung befand sich die Stute in Brust-Bauchlage und konnte nicht aufgestellt werden. Die Bauchwand war nicht vermehrt gespannt. Das Tier war hochgradig abgemagert. Bei der Manipulation, um einen venösen Zugang zu legen, zeigte das Tier kurzzeitig Maulatmung und geriet in Seitenlagen. Es erfolgte eine erste Versorgung mit einer Infusion, Antibiose und einem Schmerzmittel. Eine Blutuntersuchung ergab Hinweise auf eine Niereninsuffizienz (Creatinin- und Harnstoffwerte waren im Blut erhöht). Aus einer Kotprobe konnte kein okkultes Blut als Hinweis auf das Vorliegen eines Magengeschwürs nachgewiesen werden.

Trotz intensiver Therapie verendete die Stute am Morgen des [REDACTED]. Der Tierkörper wurde in Absprache mit Ihnen an das Institut für Pathologie zur Sektion weitergeleitet. Das klinisch unauffällige Fohlen wurde von Ihnen am selben Tag abgeholt.

Bei der Sektion wies die Stute einen sehr schlechten Ernährungszustand auf, der wahrscheinlich zu dem nachgewiesenen hypoproteinämischen Erguss in der Bauchhöhle geführt hat. Die Stute war tragend mit einem weiblichen Fetus. Im Bereich des ersten Kompartimentes konnte eine gering- bis mittelgradige Gastritis mit einem hochgradigen, fibrinreichen Ödem in der Submukosa (Gewebeschicht unter der Schleimhaut) festgestellt werden. Des Weiteren zeigten beide Nieren eine gering- bis

mittelgradige, chronische, interstitielle Nephritis, eine gering-bis mittelgradige, interstitielle Fibrose sowie hochgradige, intratubuläre mineralisierte Konkreme. Die Ablagerung der Konkreme in den Nieren kann u. a. Folge einer ungenügenden Wasseraufnahme, einer Hyperkalzämie sowie einer Überdosierung von Vitamin D sein. Eine genaue Abklärung der Ursache ist jedoch in den meisten Fällen nicht möglich.

Als Todesursache wurde ein akutes Herz-Kreislaufversagen festgestellt, vermutlich infolge der Veränderungen sowohl an den Nieren als auch am Magensystem.

The case: pathological findings

Anamnesis: diagnostic of the clinic for small ruminants, TiHo

- clinical examination of one mare: cachexia, renal dysfunction (crea↑, urea↑), no signs of gastric ulcer (occult blood)...
- pathological analysis: ascites (hypoproteinaemic, low grade gastritis, low to middle grade interstitial nephritis and low to middle grade interstitial fibrosis, and high grade mineralized intratubular concretions (potential cause: reduced water intake, hypercalcaemia, vit. D intoxication).
Cause of death: cardiovascular failure.



⇒ **Consultation of the Institute of Animal Nutrition – suspected vit. D intoxication**

The case: background information

Hypervitaminosis D (cattle; Stöber 2006):

- **aetiology:** exzessive oral or parenteral supply with vit. D₂, D₃ or metabolites
 - *Trisetum flavescens* in grass or hay
 - other plants containing vit. D or –metabolites
 - iatrogen (prophylaxis of hypocalcaemia)
- **clinical signs:** apathia, circulatory dysfunction, polyuria ...
- **pathological findings:** calcification of soft tissues (endocardium, blood vessels, kidneys, lungs)
- **diagnosis:** mostly post-mortem
- **therapy:** unknown
- **prophylaxis:**
 - prevention of intake of toxic plants
 - treatment according to dosage recommendation



<http://www.botanikus.de>

The case: feed evaluation/feed analyses

Visual appraisal alfalfa hay:

macroscopy: green colour
 no hints on occurrence of trisetum flavescens
 no blossoms visible
 high proportion of stems

smell: aromatic

grip: bulky structure

→ No further analyses



The case: feed evaluation/feed analyses

Visual appraisal complementary feed 1:

macroscopy: green-brown pellets

smell: low-grade roast smell

grip: dry

→ vitamin D-analysis



The case: feed evaluation/feed analyses

Visual appraisal complementary feed 2:

macroscopy: dark green pellets

smell: low-grade smell of fatty acids

grip: dry

→ vitamin D-analysis

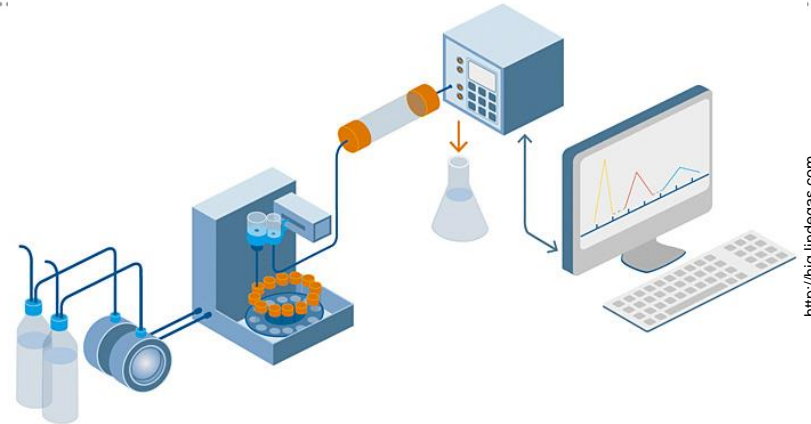


The case: results

Laboratory analysis Vitamin D₃:

Sample: complementary feed 1+2 (as fed)

Method: HPLC



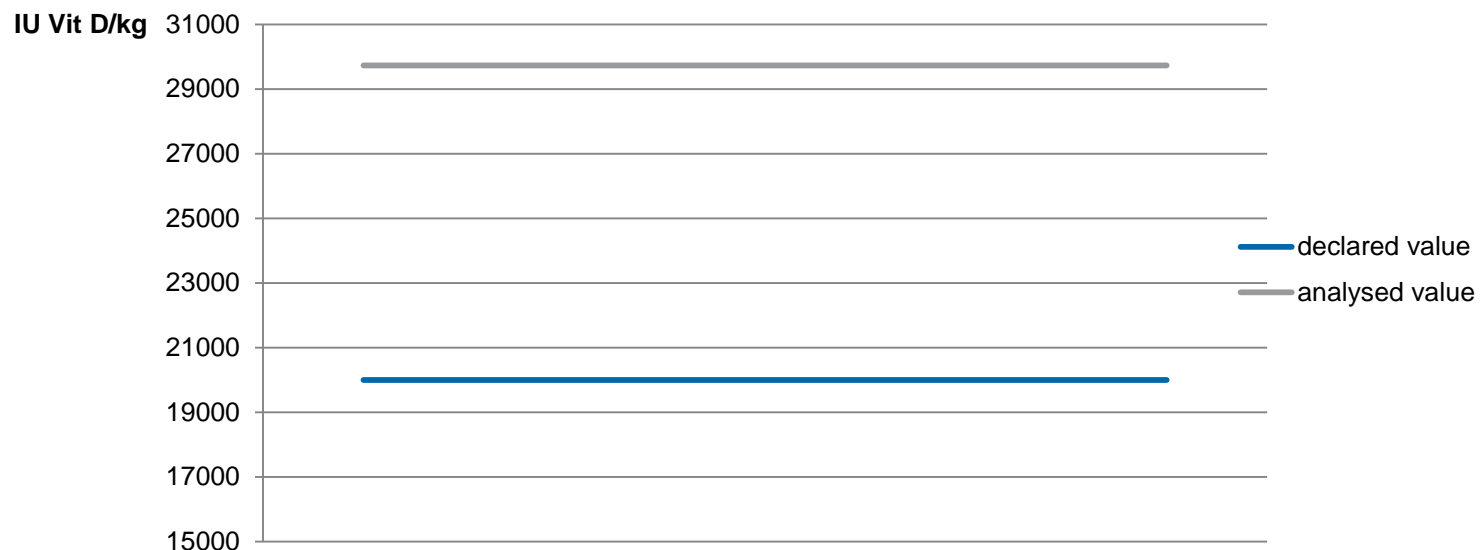
Results: complementary feed 1: < 1000 IU/kg diet (not declared)
complementary feed 2: 29730 IU/kg diet (declared: 20000 IU/kg)



How to evaluate the difference from the declared value?

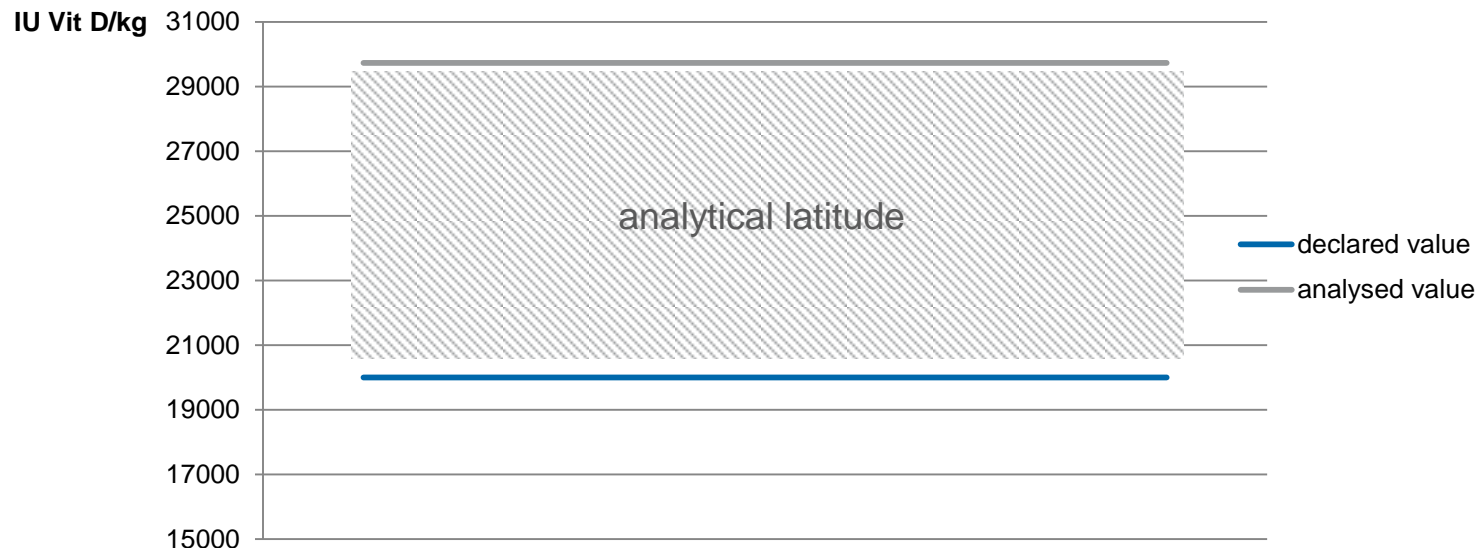
The case: results

technical latitude amounted to: 10 % of the declared content (Reg. (EG) 767/2009)
analytical latitude amounted to: 28 % relative of the analysed value (VDLUFA 2014)



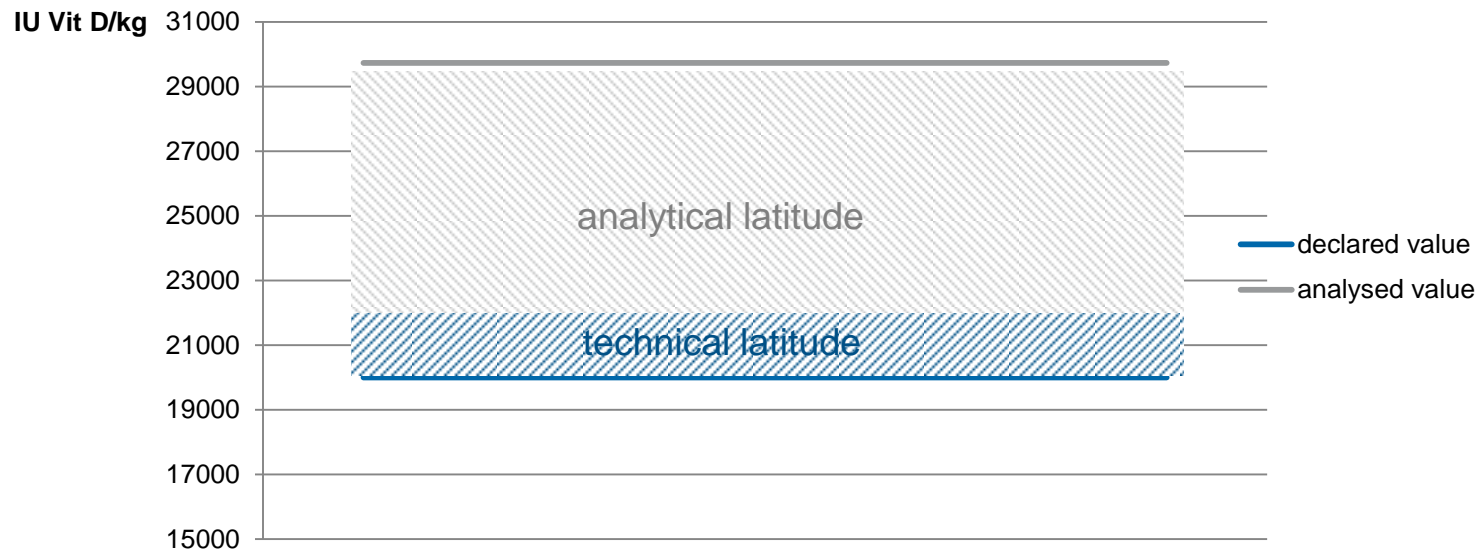
The case: results

technical latitude amounted to: 10 % of the declared content (Reg. (EG) 767/2009)
analytical latitude amounted to: 28 % relative of the analysed value (VDLUFA 2014)



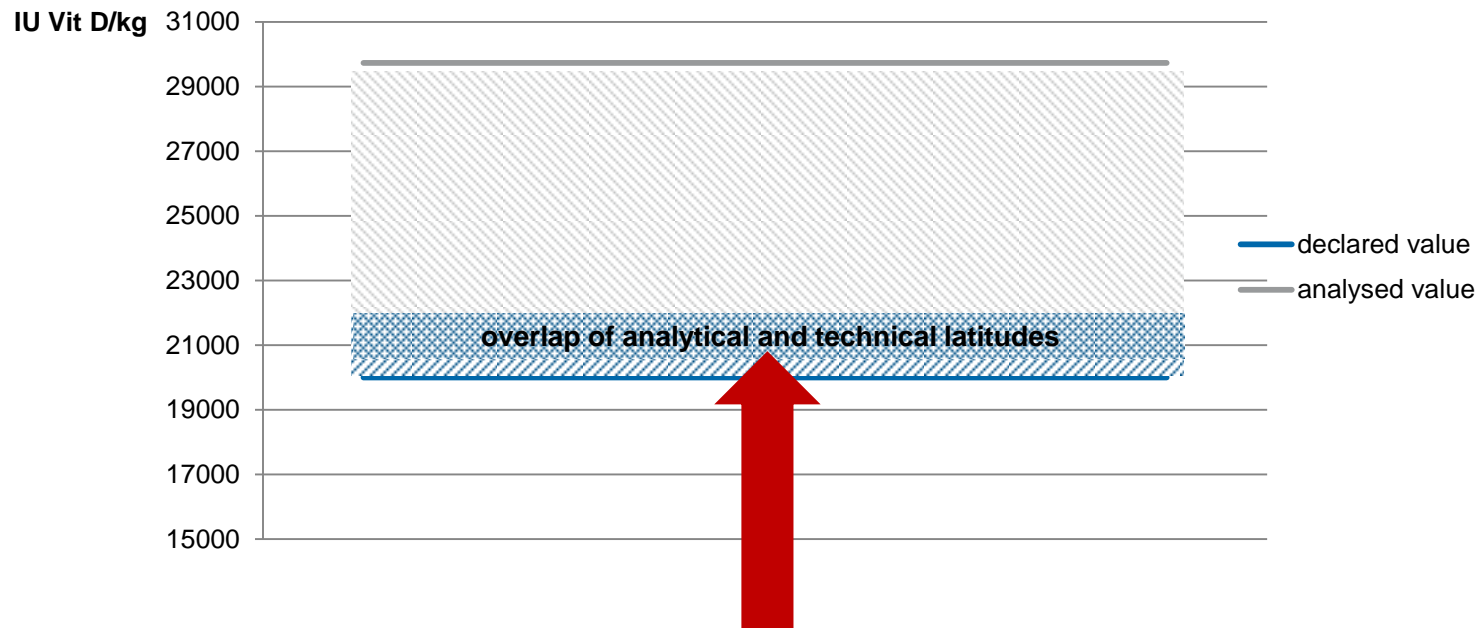
The case: results

technical latitude amounted to: 10 % of the declared content (Reg. (EG) 767/2009)
analytical latitude amounted to: 28 % relative of the analysed value (VDLUFA 2014)



The case: results

technical latitude amounted to: 10 % of the declared content (Reg. (EG) 767/2009)
analytical latitude amounted to: 28 % relative of the analysed value (VDLUFA 2014)



The analysed vit. D content does not deviate beyond the analytical and technical latitudes from the declared value.

→ The analysed content complies with the declared content.

The case: discussion



No feed-related problem?

The case: results and discussion

Gathering of further information

Amount/composition of ration (mares, about 65 kg bw):

1.8 kg complementary feed 1

1.5 kg complementary feed 2

1.76 kg alfalfa hay

The case: results and discussion



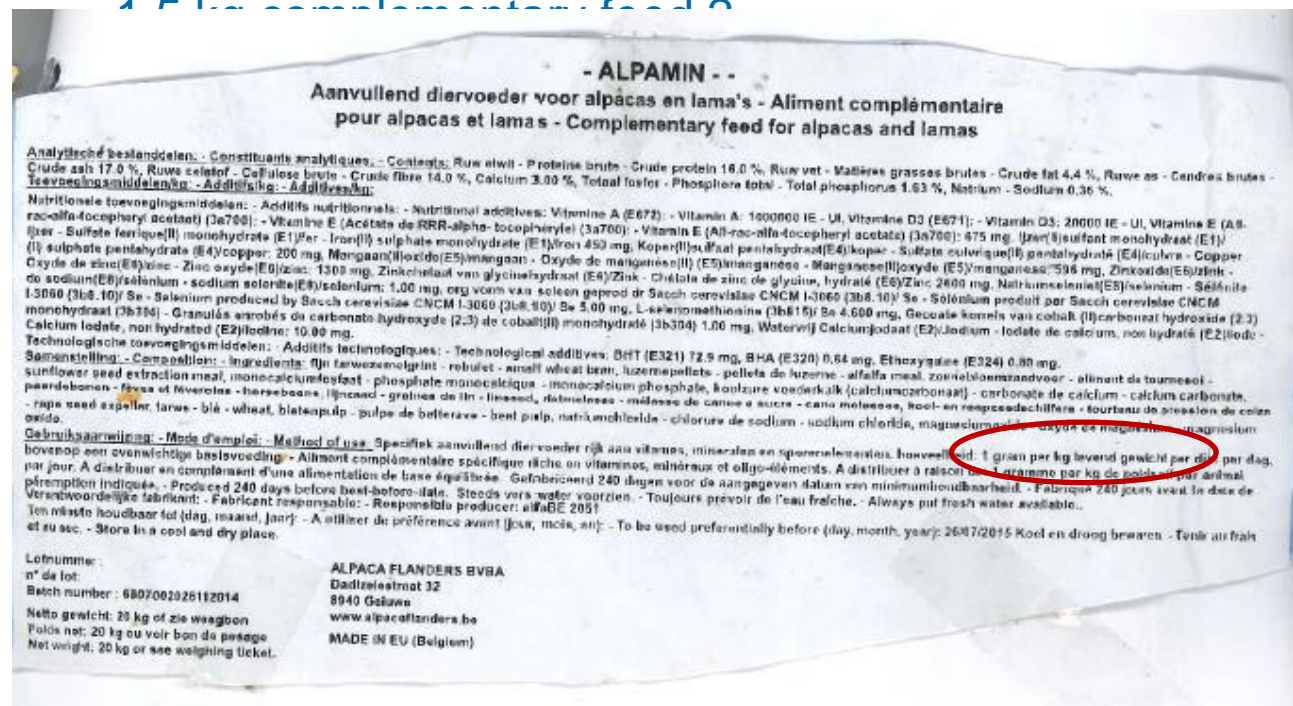
Gathering of further information

Amount/composition of ration (mares, about 65 kg bw):

1.8 kg complementary feed 1

4.5 Feedback system: feed

Complementary feed 2:



The case: results and discussion

Gathering of further information

Amount/composition of ration (mares, about 65 kg bw):

1.8 kg complementary feed 1

1.5 kg complementary feed 2

1.76 kg alfalfa hay

vitamin D requirements of alpacas (Kamphues et al. 2014)

cattle: 5-10 IU/kg bw/day

sheep: 5 IU/kg bw/day

65 kg bw, 10 IU/kg bw/day: requirement - 650 IU vit. D/animal/day

intake of vit. D: not less than **44595 IU/animal/day**

The case: results and discussion

Correct definition of the “complementary feed”?

REGULATION (EC) No 767/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 13 July 2009
on the placing on the market and use of feed, amending European Parliament and Council
Regulation (EC) No 1831/2003 and repealing Council Directive 79/373/EEC, Commission
Directive 80/511/EEC, Council Directives 82/471/EEC, 83/228/EEC, 93/74/EEC, 93/113/EC and
96/25/EC and Commission Decision 2004/217/EC

- ⇒ “**complementary feed**” means compound feed which has a high content of certain substances but which, by reason of its composition, is sufficient for a daily ration only if used in combination with other feed“
- ⇒ “**mineral feed**” means complementary feed containing at least 40 % crude ash”

Crude ash-content in the complementary feed 2: 17 %

⇒ **correct definition!**

The case: therapy/feeding advice



Thank you for your attention!



Questions?

References

KAMPHUES, J., P. WOLF,, M. COENEN, K. EDER, C. IBEN, E. KIENZLE, A. LIESEGANG, K: MAENNER, Q. ZEBELI, J. ZENTEK (2014): Supplemente zur Tierernährung: Für Studium und Praxis. Schaper, Hanover, 354-383

REGULATION (EC) No 767/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 13 July 2009

on the placing on the market and use of feed, amending European Parliament and Council Regulation (EC) No 1831/2003 and repealing Council Directive 79/373/EEC, Commission Directive 80/511/EEC, Council Directives 82/471/EEC, 83/228/EEC, 93/74/EEC, 93/113/EC and 96/25/EC and Commission Decision 2004/217/EC

STOEBER, M. (2006): Hypervitaminose D.

In: DIRKSEN, G., GRUENDER, H.-D., STOEBER, M. (2006): Innere Medizin und Chirurgie des Rindes. Parey in Medizinverlage Stuttgart GmbH & Co. KG

VDLUFA (2014): Analysenspielräume, Version 2014. VDLUFA-Verlag, Darmstadt 1-8

Vitamin D metabolism

Isabelle Ruhnke^{1,2}, Mingan Choct², Jürgen Zentek¹

¹ Freie Universität of Berlin, Berlin, Germany

² University of New England, Armidale, Australia



HOUGHTON
TRUST



Outline

- 1) Vitamin D metabolism
- 2) Mode of action / clinical signs
- 3) Therapeutic use



<https://www.google.fr/imgres?imgurl=http%3A%2F%2Fnutritionbyerin.com%2Fwp-content%2Fuploads%2F2015%2F07%2F549960-59517->

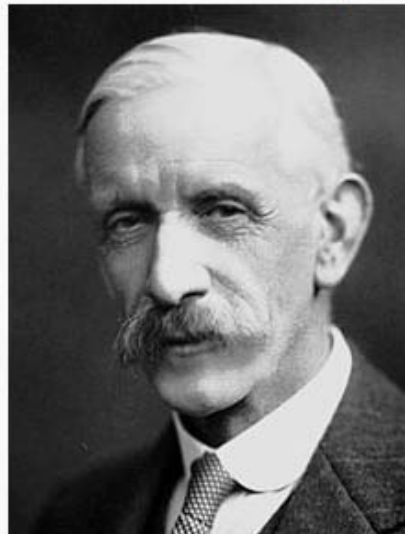


une
University of
New England

Vitamins

- Organic compounds that are required to be consumed in small amounts for normal growth and maintenance of animal life
- Does not take into account:
 - MO providing vitamin in GI tract (Vitamin B)
 - Provitamins that can be synthesised (Vitamin D)

Sir Frederick Gowland Hopkins



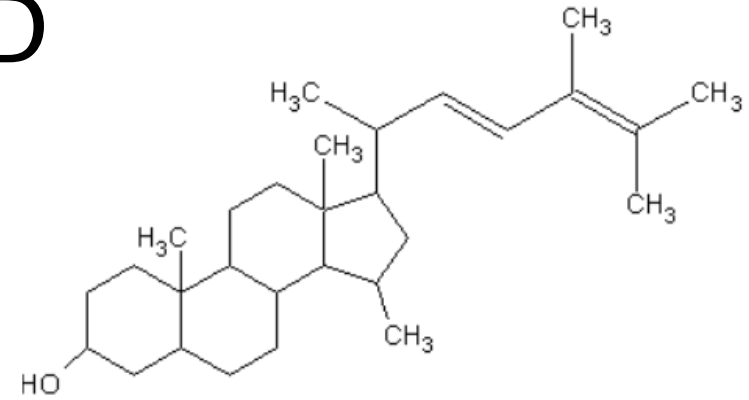
- Improve animal health
- Enhance the quality of the product
- Fat soluble (Vitamins A,D,E,K)
- Water soluble
 - Occurrence and characteristics are related to solubility



Vitamin D

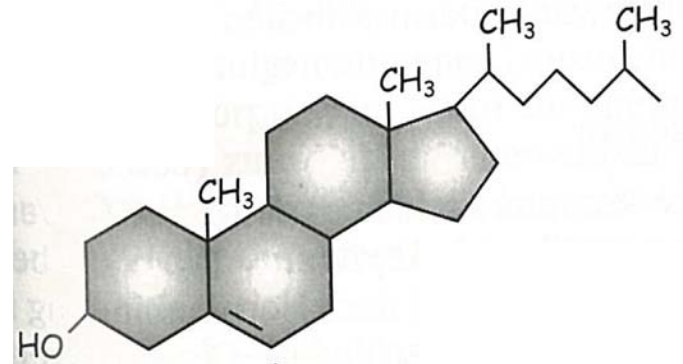
- Vitamin D₂:

- Plant vitamin D, true vitamin
- Ergosterol → ergocalciferol
- UV-light dried roughages, dead leaves



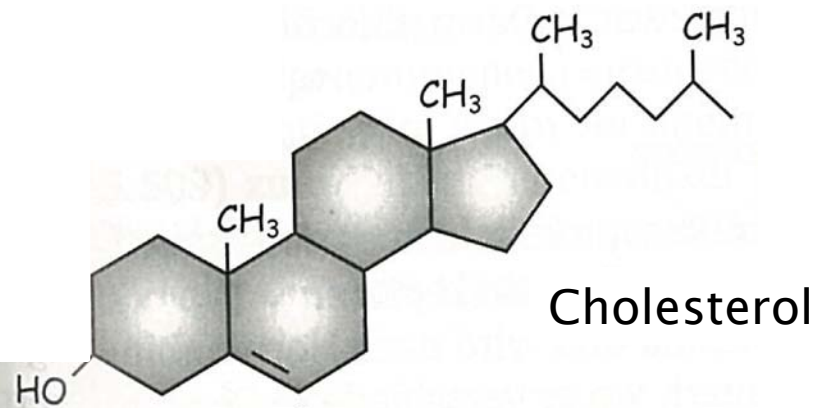
- Vitamin D₃:

- Animal vitamin D, hormone
- Cholesterol → cholecalciferol
- Organ specific (liver, egg yolk)



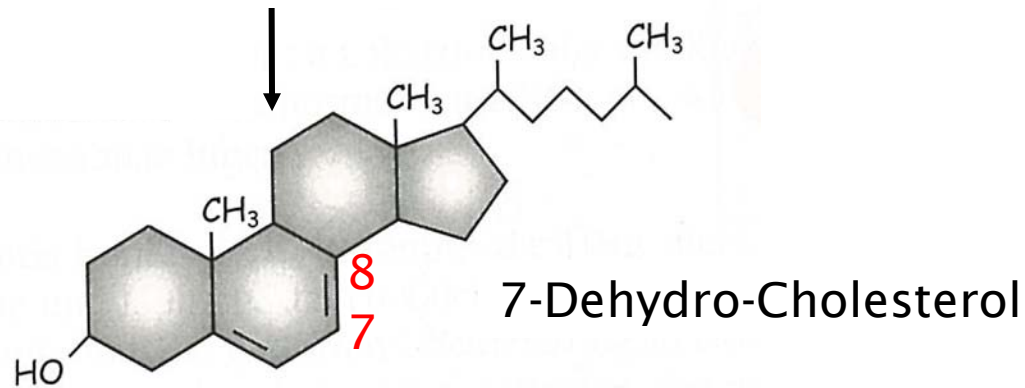
- Vitamin D₁:

- Impure activated sterol, mainly D₂ → abolished



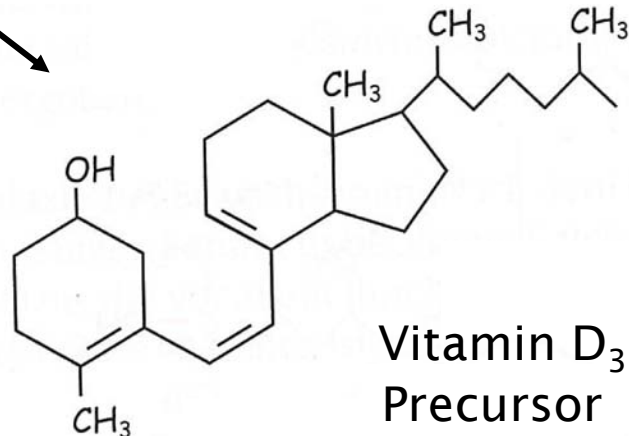
Cholesterol

Cholesterol-Dehydrogenase in Liver



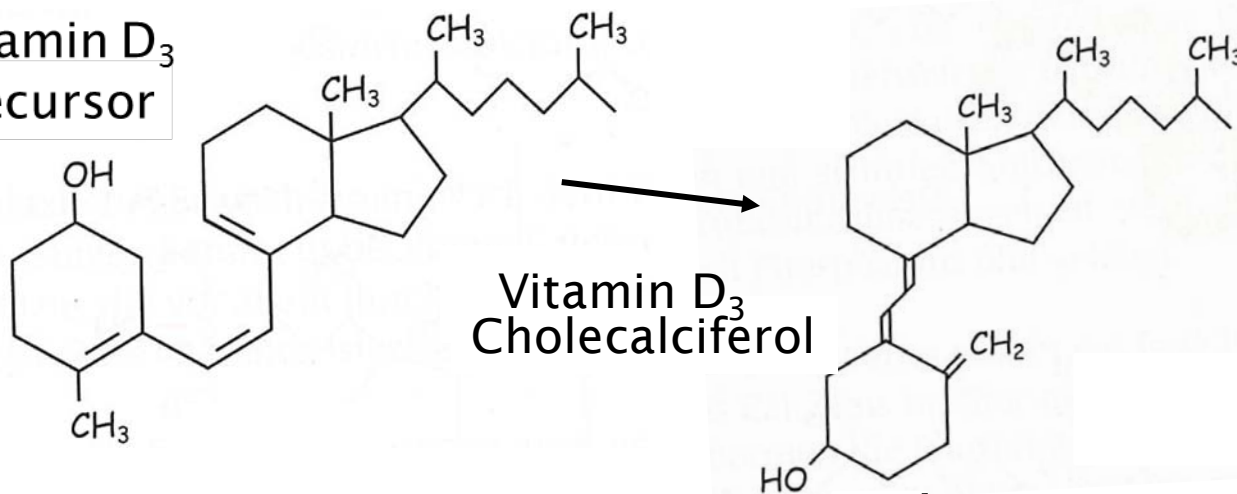
7-Dehydro-Cholesterol

UV Light
290-315 nm

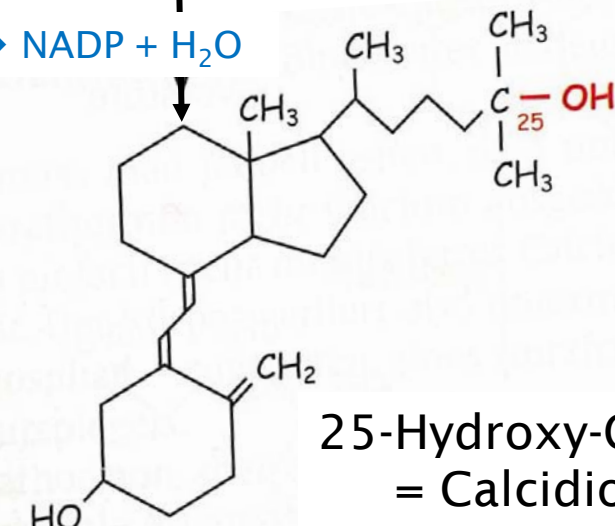
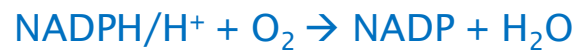


Vitamin D₃
Precursor

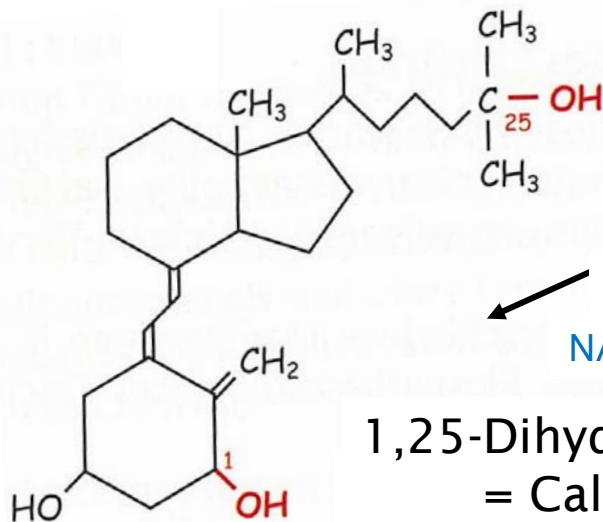
Vitamin D₃
Precursor



C₂₅ Hydroxylase in Liver



C₁ Hydroxylase in Kidney



Horses

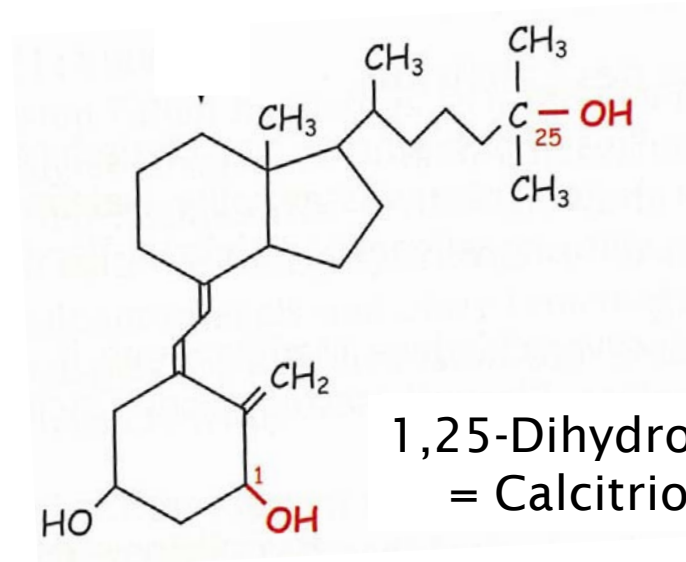
- Extremely low plasma levels (pg/l vs.ng/l)
 - C₁-Hydroxylase activity nearly undetectable
 - CaBP less active
- Vitamin D does not play a key role in C/P homeostasis



Summary 1

- Difference Vitamin D₂/Vitamin D₃
 - hay/liver oil
 - endogenous cholesterol
- Species specifics:
 - Poultry: very limited use of D₂
 - Cats & dogs: food dependent
 - Horses: extremely low metabolic activity
- Newborns are often deficient because of limited uptake and limited enzyme development





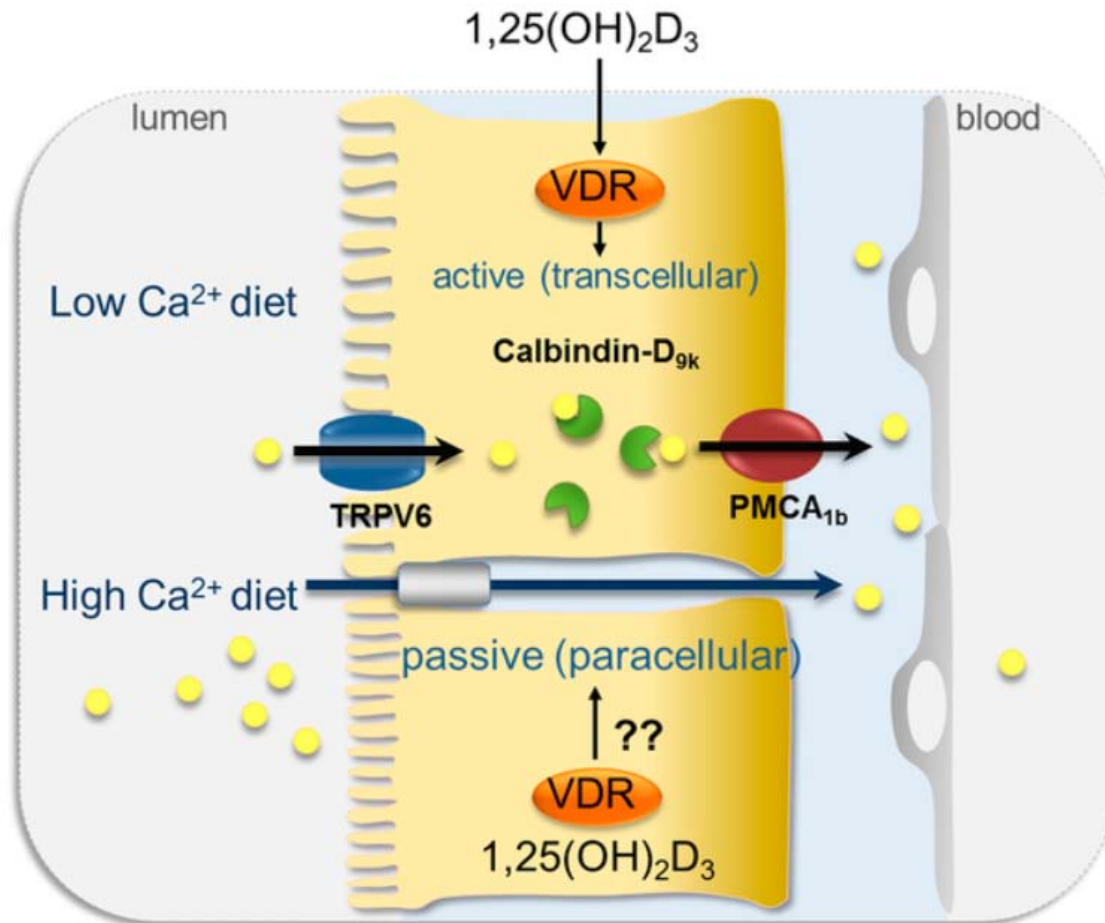
intestine/uterus
CaBP

bones

immune system

- Calcium homeostasis
- Phosphorus reabsorption
- Immune system function

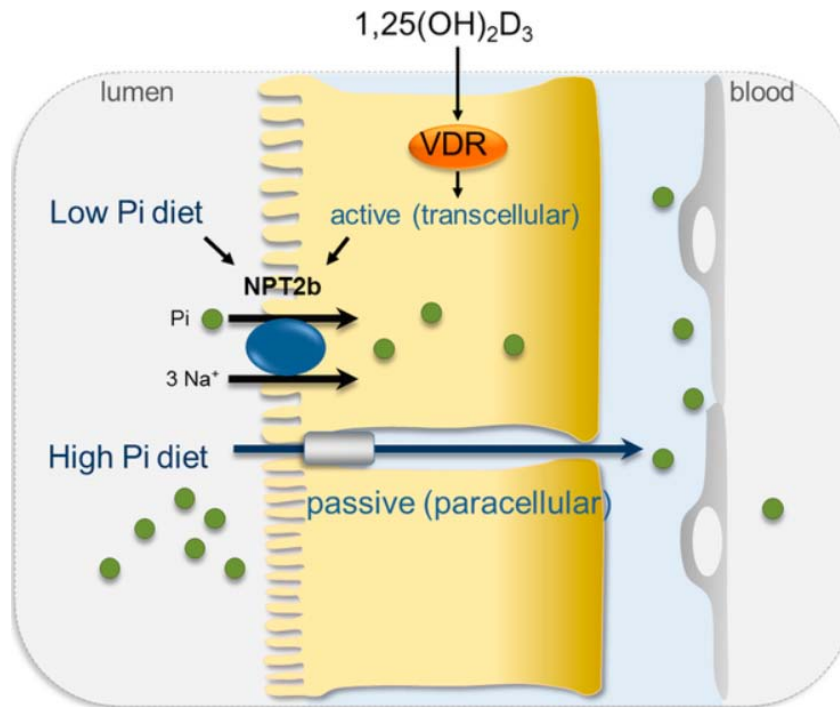
Calcium Binding Protein (CaBP)



Christakos, S., Lieben, L., Masuyama, R., & Carmeliet, G. (2014). Vitamin D endocrine system and the intestine. *BoneKEy reports*, 3.

Phosphorus absorption

- Enhanced intestinal absorption



Christakos, S., Lieben, L., Masuyama, R., & Carmeliet, G. (2014). Vitamin D endocrine system and the intestine. *BoneKEy reports*, 3.

- Enhanced renal absorption

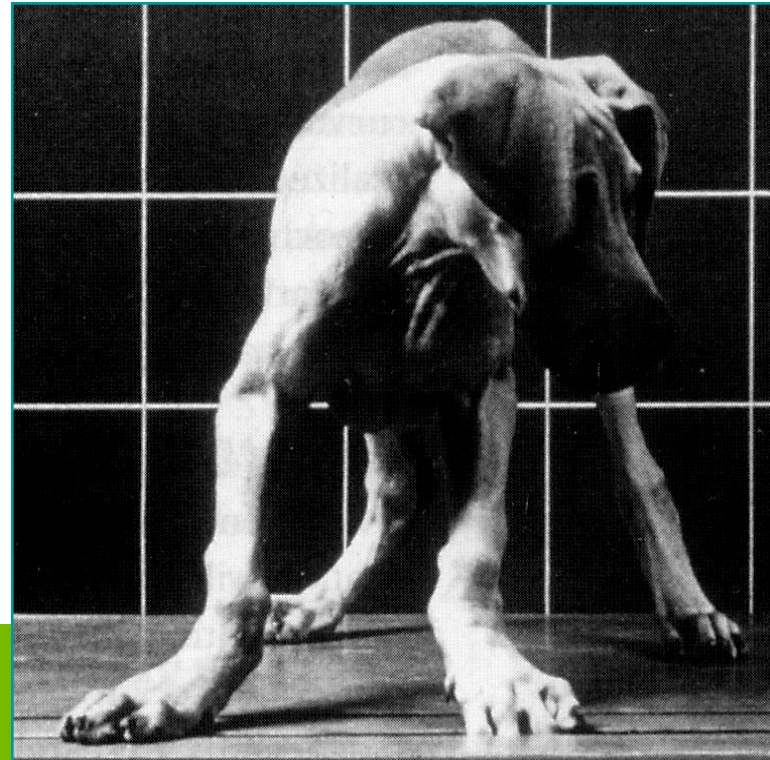
Vitamin D deficiency

- Rickets
 - Cattle: swollen joints, arching back
 - Pigs: enlarged joints, stiff joints, broken bones, paralysis
 - Poultry: bones and beak soft & rubbery, retarded growth, weak legs, reduced egg production, reduced egg shell quality
 - Companion animals: skeletal deformation
- Osteomalacia
 - Uncommon in farm animals (impaired gait, tetanus, reduced egg shell quality, reduced hatchability)
 - Pregnant and lactating animals cave!



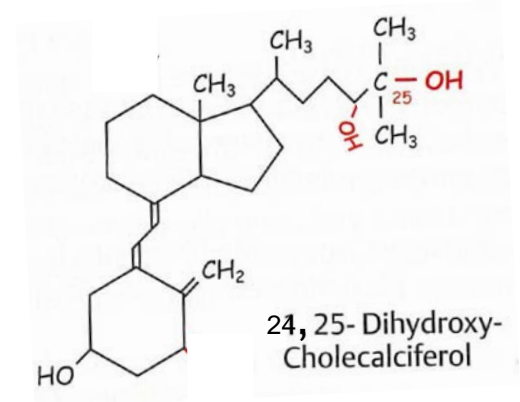
Hypervitaminosis

- Enhanced Calcium mobilization
 - Calcification of arteria
 - Renal tubuli
 - Joints
 - Other organs (liver, spleen, lung)



Excessive Vitamin D:

- Storage form:
24, 25 Dihydroxy-Cholecalciferol
- Excretion via bile, faeces, urine
- 1,25-(OH)₂-Vit D₃:
1, 24 (OH)+glucuronic/sulfuric acid → bile
- Calcitonin:
Secreted from C-cells of thyroid, direct counter play of PTH
→ increases renal Ca & P excretion
→ increases bone mineralisation

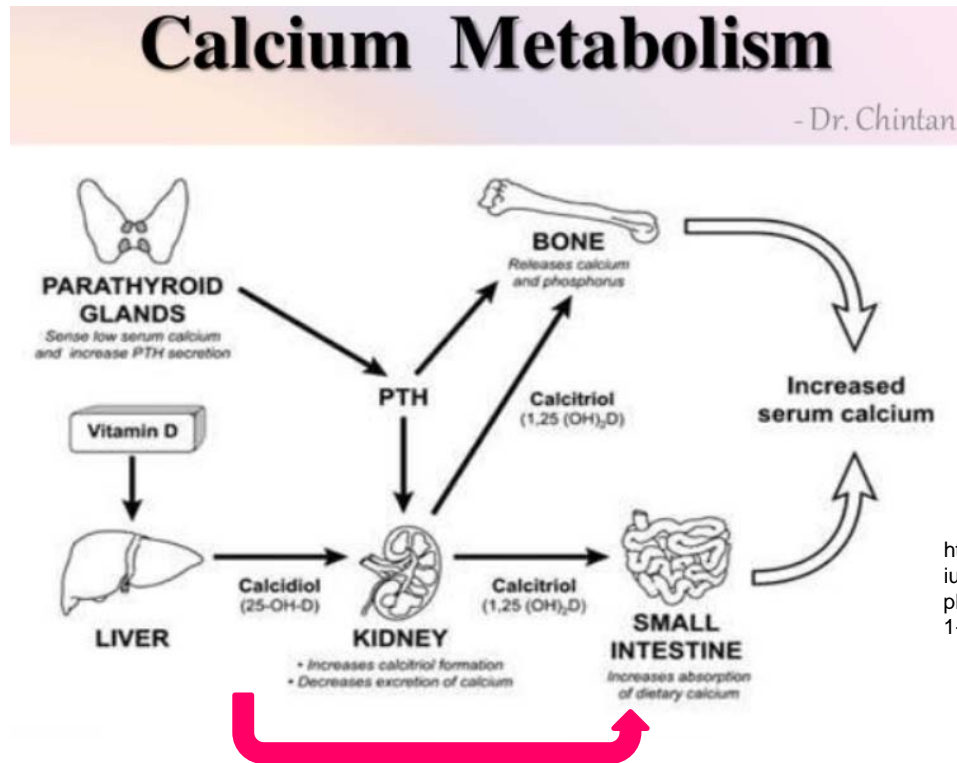


Summary 2

- Hormonal activity
- Difference Calciferol/Calcidiol/Calcitriol/Calcitonin
- Close interplay with Calcium/Phosphorus -> clinical signs



Impact on Calcium re-absorption



- Vitamin D → promotes net bone deposition when given therapeutically (PTH absence)

- Use $25-(\text{OH})_2\text{-D}_3$ (Calcidiol) rather than $1,25-(\text{OH})_2\text{-D}_3$ (Calcitriol)!
 - Bypasses the PTH – control of Vitamin D action
 - Achieve greater bone deposition/reduction in re-absorption
 - Low risk of toxicity
 - Ease of inclusion in feed
 - Potentially more absorption & conversion of Ca in product



- 1 IU of Vitamin D:
Vitamin D activity of 0.025 crystalline Vitamin D₃
- Requirement
 - Minimal: avoids symptoms of deficiency, ensures physiologic metabolic function
 - Optimal: animal can use its full potential
- Recommended standard
 - Safety addition



Vitamin D requirement in humans

25-(OH)-D₃ (Calcidiol) level of

- > 30 nmol/l lower all-cause mortality
- > 78 nmol/l beneficial for bone health
- > 90 nmol/l full cancer prophylaxis
- > 100 nmol/l benefits in countering infections
- > 120 nmol/l lowest mortality

→ Average level in 2/3rd of northern climate population: 67 nmol/l



Immune System

- Direct regulation on IL-40 and others
- Reduced risk for infectious diseases
- Reduced risk for food allergy
- Impact on Inflammatory Bowel Diseases
- Chemopreventative: colorectal cancer



<http://img.medscapestatic.com/pi/meds/ckb/67/35567tn.jpg>



une
University of
New England

Take home message

- Difference Vitamin D₂/Vitamin D₃
- Difference Calciferol/Calcidiol/Calcitriol
- Interplay with Calcitonin/PTH

Be aware of the impact of serum Vitamin D levels on animal health!



<https://www.google.fr/imgres?imgurl=http%3A%2F%2Fwww.wallpaperhi.com%2Fthumbnails%2Fdetail%2F20130226%2Fsunset%252520australia%252520kangaroos%2525201920x1280%252520wallpaper>



une
University of
New England

References

- Wranicz, J., & Szostak-Węgierek, D. (2014). Health outcomes of vitamin D. Part I. Characteristics and classic role. *Rocz Panstw Zakl Hig*, 65(3), 179–184.
- Suaini, N. H., Zhang, Y., Vuillermine, P. J., Allen, K. J., & Harrison, L. C. (2015). Immune Modulation by Vitamin D and Its Relevance to Food Allergy. *Nutrients*, 7(8), 6088–6108.
- Ardesia, M., Ferlazzo, G., & Fries, W. (2015). Vitamin D and Inflammatory Bowel Disease. *BioMed research international*, 2015.
- Kearns, M. D., Alvarez, J. A., Seidel, N., & Tangpricha, V. (2015). Impact of vitamin D on infectious disease. *The American journal of the medical sciences*, 349(3), 245–262.
- McGrath, J., Savage, D., & Godwin, I. (2015). The role and potential advantages of Vitamin D metabolites in maintaining calcium status in high producing dairy herds. *Animal Production Science*.
- Song, M., Garrett, W. S., & Chan, A. T. (2015). Nutrients, foods, and colorectal cancer prevention. *Gastroenterology*, 148(6), 1244–1260.
- Horn, F. (2005). *Biochemie des Menschen: das Lehrbuch für das Medizinstudium*. Georg Thieme Verlag.
- Jeroch, H. Simon, A. & Zentek J. (2014). *Geflügelernährung*. Ulmer Verlag.
- Jeroch, H., Drochner, W., & Simon, O. (1999). *Ernährung landwirtschaftlicher Nutztiere*. Ulmer Verlag.
- McDonald, P. (2002). *Animal nutrition*. Pearson education.
- Breidenbach, A., Schlumbohm, C., & Harmeyer, J. (1998). Peculiarities of vitamin D and of the calcium and phosphate homeostatic system in horses. *Veterinary research*, 29(2), 173–186.



Feeding of an adult mini pig

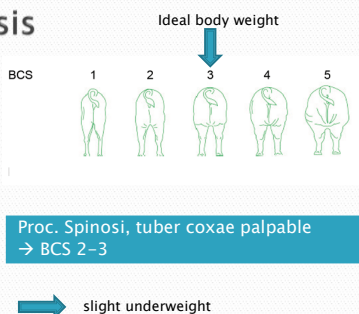
Residency class 15th to 16th september 2015
Stephanie Schmitt

Anamnesis

- ▶ Mini Pig „Berta“
- ▶ 1 year old
- ▶ ca. 30kg



Anamnesis



Diet

- ▶ commercial Mini Pig diet
- ▶ Fruits: apples, banana, grapes, tangerines
- ▶ Vegetables: carottes, salad, potatos, cucumber
- ▶ Other: dried bread, acorns

Diet

Commercial mini pig diet

Ingredients:

CP1 2.5%
crude fat 3%
CA 12.5%
CF 6.5%
lys 0.55%
met 0.23%
Ca 0.75%
P 0.54%
Na 0.15%



Problems in mini pig nutrition

- ▶ **Overweight/obesity**
- ▶ Urolithiasis

→ Diet low in energy
High in fibre
Meeting mineral requirements

BUT

No requirements for mini pigs are defined

Requirements

- ▶ Extrapolation from recommendation of an adult boar (bw 250kg)
- ▶ ME MJ: 5.6 MJ
- ▶ Crude protein: 32g
- ▶ Lysine: 0.8g
- ▶ Calcium: 1.3
- ▶ Digestible phosphorus: 0.4
- ▶ Potassium: 0.16g

Diet revision

feed	Amount [kg]	DM [g]	ME [MJ]	Cp [g]	Lys [g]	Ca [g]	dP [g]	Na [g]
Verselle Pet Pig muesli	0.15	132	1.93	18.8	0.83	1.1	0.41	0.2
Apple	0.18	27	0.36	0.5	0.03	0.0	0.01	0.0
banana	0.1	26.1	0.30	1.2	0.06	0.0	0.01	0.0
Dried bread	0.025	23	0.22	0.1	0.04	0.0	0.02	0.1
Carottes	0.1	13	0.20	1	0.04	0.1	0.02	0.0
Grapes	0.1	19	0.24	0.7	0.02	0.0	0.01	0.0
tangerine	0.1	14	0.17	0.7	0.03	0.0	0.01	0.0
Salad	0.1	8.5	0.06	1.7	0.06	0.0	0.01	0.0
potato	0.1	22	0.31	2.1	0.06	0.0	0.03	0.0
Cucumber	0.05	2	0.03	0.3	0.01	0.0	0.00	0.0
acorns	0.1	67	0.21	0.8	0.00	0.1	0.00	0.0
supply	1.105	354	4.0	28	1.2	1.3	0.5	0.4
requirement			5.6	32	0.8	1.3	0.4	0.2

- ➔ Energy supply: 77% of estimated requirements
Crude protein supply meet 81% of supposed requirements

Aim of diet improvement

- ▶ Increase of ME not minerals
- ▶ Satisfaction of chewing needs

Diet recommendation

- ▶ Commerical pet pig muesli
 - High mineral concentration
 - ➔ Amount = / ↓
- ▶ Fruits
 - High in energy
 - High in fibre
 - ➔ Amount ↑
- ▶ Vegetables
 - high in fibre
 - ➔ Amount ↑ ↑

Diet adaptation

feed	Amount [kg]	DM [g]	ME [MJ]	Cp [g]	Lys [g]	Ca [g]	dP [g]	Na [g]
Verselle Pet Pig muesli	0.14	123.2	1.8	17.5	0.8	1.1	0.38	0.2
Apple	0.15	22.5	0.3	0.5	0.02	0.0	0.01	0.0
banana	0.15	39.15	0.5	1.8	0.1	0.0	0.02	0.0
Dried bread	0.03	23	0.2	0.1	0.04	0.0	0.02	0.1
Carottes	0.3	39	0.6	3	0.1	0.2	0.05	0.1
Grapes	0.15	28.5	0.4	1.1	0.02	0.0	0.01	0.0
tangerine	0.15	21	0.3	1.1	0.05	0.0	0.02	0.0
Salad	0.3	25.5	0.2	5.1	0.2	0.1	0.03	0.0
potato	0.15	33	0.5	3.2	0.1	0.0	0.05	0.0
Cucumber	0.3	12	0.2	1.8	0.1	0.0	0.03	0.0
acorns	0.1	67	0.2	0.8	0	0.1	0.00	0.0
supply	1.915	434	5.0	36	1.5	1.5	0.6	0.5
requirement			5.6	32	0.8	1.3	0.4	0.2

- ➔ Diet higher in energy, but still moderate
Diet higher in crude protein
Diet only a little bit higher in Ca and P



Faculty of Health and Medical Sciences



A combination of commercial and homemade diet for a Greyhound suffering from concurrent protein losing nephropathy, azotemia and acute pancreatitis.

Kathrine Stenberg, DVM, Ph.D. Student, resident ECVCN

Supervisor Charlotte R. Bjornvad, DVM, Ph.D.

Dipl. ECVCN, Professor in Companion Animal Internal Medicine



Agenda

1. History, clinical presentation, previous and current diagnostics
2. Nutritional problem list
3. Nutritional recommendations for a dog with protein losing nephropathy and for a dog with acute pancreatitis respectively
4. Calculations
5. Diet formulation
6. Conclusion
7. Considerations
8. Follow up, owner compliance



History

- "Sixten", 6.5 year old Greyhound, intact male
- History of polydipsia
- Exercise intolerance and stiffness in the neck, treated with physiotherapy
- Father died of renal failure at the age of 8 years
- Sixten is a carrier of a neuropathy gene seen in Greyhounds (A deletion in the N-myc downstream regulated gene 1 (NDRG1)¹) , this has currently no effect on his nutritional requirements

1. Drögemüller C et al. PLoS One. (2010) Jun 22;5(6):e11258



Diagnostics performed at referring vet, February 2015-March 2015

- CBC and biochemistry within reference levels
- normal USG 1026-1035 (ref. 1013-1045¹)
- Proteinuria + + +
- UPC 1.1-3.7 (ref. 0-1¹)
- Low T4 (0.5 µg/dl, ref. 1.3-4.5 µg/dl)
- Normal TSH (0.25 ng/ml, ref. <0.6 ng/ml)
- Low free T4 (2.9 pmol/L, ref. 7.7-47.6 pmol/L)
- Low free T3 (3.2 pmol/L, ref. 3.7-9.2 pmol/L)

1. Stockham SL & Scott MA. Fund Vet Clin Path, 2nd Edition



Clinical presentation, April 2015

- BCS 4/9, weight 45 kg
- Diet: RC renal + k/d canned + boiled rice + cooked chicken
- Supplement: Phosphate binder (Pronefra)
- Amounts unknown
- Presenting complaint: increased water intake (600-1000 ml/day), less active the past few months
- Unremarkable clinical exam
 - T: 38.5 °C
 - P: 60 per min
 - R: 24 per min
 - BP systolic 132-162.



Diagnostics, April 2015 at University Hospital

- CBC and biochemistry within reference levels
- Normal TEG coagulation analysis
- USG 1029 (ref. 1013-1045¹)
- Proteinuria + + + +, increased UPC (2.2, ref. 0-1¹)
- Snap test Borrelia and Anaplasma - neg
- Normotensive (systolic: 150 mm Hg, diastolic: 93 mm Hg, ref. 150/95²)
- Diagnosis: Low grade protein losing nephropathy without azotemia or hypoalbuminemia, USG within reference level, normotensive
- Treatment: ACE inhibitor (Fortekor vet, Novartis, 0,5 mg/kg SID)

1. Stockham SL & Scott MA. Fund Vet Clin Path, 2nd Edition
2. Ettinger & Feldman. Textbook Vet Int Med, 6th Edition



Clinical presentation, May 2015

- Recheck PLN and thyroid status
- BCS 4/9, weight 45 kg
- Presenting complaint: diarrhea today, exercise intolerance
- Clinical exam
 - T: 38.3 °C
 - P: 64 per min
 - R: 20 per min
 - Signs of pain during abdominal palpation in the cranial abdomen



Diagnostics, May 2015 at University Hospital

- CBC and biochemistry within reference levels, except creatinine: 132 $\mu\text{mol/L}$ (40-130 $\mu\text{mol/L}$)
- USG 1022-1032 (ref. 1013-1045¹)
- Proteinuria + + +, increased UPC (2.5, ref. 0-1¹)
- Low T4 (6.85 nmol/L, ref. 11.2-40.8 nmol/L)
- Normal TSH (0.14 ng/ml, ref. 0-0.5 ng/ml)
- Low free T4 (7.53 pmol/L, ref. 7.7-47.6 pmol/L)

- Diagnosis: Low grade protein losing nephropathy with azotemia, USG within reference level, normotensive. Hypothyroidism- possible euthyroid sick syndrome.

- Treatment: Levothyroxine sodium (Forthyron flavoured vet, 10 $\mu\text{g/kg}$ BID)
- Continue treatment: ACE inhibitor (Fortekor vet, Novartis, 0,5 mg/kg SID)

1. Stockham SL & Scott MA. Fund Vet Clin Path, 2nd Edition



Clinical presentation, June 2015

- Presenting complaint: diarrhea the past week, flatulent, depressed today, anorexia today
- Clinical exam
 - T: 38.5 °C
 - P: 64 per min
 - R: 20 per min
 - Signs of pain during abdominal palpation in the mid-caudal abdomen



Diagnostics, June 2015 at University Hospital

- cPLI: positive
- Quantitative cPLI: 250 µg/L (ref. 0-200 µg/L)
- Ultrasound: no abnormal findings on abdominal ultrasound
- Diagnosis:
 - Low grade protein losing nephropathy, IRIS stage II (proteinuric + APO)
 - Concurrent hypothyroidism, possible euthyroid sick syndrome
 - Low grade acute pancreatitis
- Treatment:
 - Levothyroxine sodium (Forthyron flavoured vet, 10 µg/kg BID)
 - ACE inhibitor (Fortekor vet, Novartis, 0,5 mg/kg SID)
 - Maropitant (Cerenia, Orion, 1 mg/kg once)
 - Tramadol (Tradoloan, Nordic Drugs, 1,1 mg/kg TID)



Feeding regimen, June 2015

- Stable weight, 45 kg
- Picky eater
- Kidney diet:
 - Royal Canin Renal
 - Hill's k/d canned diet
 - Boiled rice
 - Cooked chicken
 - Phosphate binder (Pronefra, Virbac)
- Changed to Hill's i/d low fat diet due to pancreatitis
- -> Nutrition service contacted



Nutrition problem list

1. Low grade protein losing nephropathy
2. Azotemia IRIS stage II (proteinuric + AP0)
3. Acute low grade pancreatitis
4. Possible hypothyroidism
5. Picky eater

We were asked to

- Evaluate the feeding regimen
- Owner would like to continue feeding a diet based on kidney diets but supplemented with chicken and rice
- Propose a well balanced feeding regimen for the adult dog with PLN and concurrent azotemia and pancreatitis based on Royal Canin Renal dry food and Hill's k/d canned food and providing supplements



Recommendations

PLN and azotemia

- Protein 14-20 %DM
- P 0.2-0.5 %DM
- Na <0.3 %DM
- K 0.4-0.8 %DM
- Omega-3 0.4-2.5% DM

Pancreatitis

- Protein 15-30 %DM
- Fat ≤ 15 %DM
non-obese and non-hypertriglyceridaemic dogs
- Fat ≤ 10 %DM
obese and hypertriglyceridaemic dogs

Jacob F et al. JAVMA. (2002) 220; 1163-1170

Jacob F et al. Proc ACVIM. (2004) 828

Kerl ME & Johnson PA. Clin Tech in Small Animal Pract. (2004) 19;1; 9-21

Parker VJ & Freeman LM. Compend Contin Educ Vet. (2012) Jul; 34(7):E6

Hand et al, Small Animal Clinical Nutrition, 5th edition

Residency class 2015, Toulouse

Slide 13



Calculations of energy and nutrient requirements

- Energy requirement calculations (NRC 2006)
 - Inactive pet dog, Ideal body weight: 45 kg.
 - $DER = 95 \times BW^{0.75} = 1650 \text{ kcal}$
- Protein
 - NRC recommended allowance: $3.28 \text{ g/kgBW}^{0.75} \Rightarrow 57.1 \text{ g protein /day}$
 - NRC minimal requirement: $2.62 \text{ g/kgBW}^{0.75} \Rightarrow 45.6 \text{ g protein /day}$
- Fat
 - NRC recommended allowance: $1.8 \text{ g/kgBW}^{0.75} \Rightarrow 31.32 \text{ g fat /day}$
 - NRC adequate intake: $1.3 \text{ g/kgBW}^{0.75} \Rightarrow 22.62 \text{ g fat /day}$
 - NRC safe upper limit: $10.8 \text{ g/kgBW}^{0.75} \Rightarrow 187.92 \text{ g fat /day}$



Calculations of nutrient requirements

- Essential fatty acids (EPA + DHA)
 - NRC recommended allowance: $0.03 \text{ g/kgBW}^{0.75} \Rightarrow 0.52 \text{ g EPA + DHA /day}$
 - Safe upper limit $0.37 \text{ g/kgBW}^{0.75} \Rightarrow 6.44 \text{ g/day}$
- P
 - NRC recommended allowance = adequate intake: $0.1 \text{ g/kgBW}^{0.75} \Rightarrow 1.74 \text{ g P /day}$
- Na
 - NRC recommended allowance: $26.2 \text{ mg/kgBW}^{0.75} \Rightarrow 455.9 \text{ mg Na /day}$
 - NRC minimal requirement: $9.85 \text{ mg/kgBW}^{0.75} \Rightarrow 171.39 \text{ mg Na /day}$
 - Safe upper limit $> 15 \text{ g/kg DM at energy density } 4000 \text{ kcal/kg} \Rightarrow > 6.12 \text{ g /day}$
- K
 - NRC recommended allowance = adequate intake: $0.14 \text{ g/kgBW}^{0.75} \Rightarrow 2.44 \text{ g K /day}$



Royal Canin renal dry diet

As fed:

Energy: 3995 kcal/ 1000 g

Protein: 16%

Fat: 18%

EPA+DHA: 0.41%

P: 0.2%

Na: 0.2%

K: 0.7%

Moisture: 9.5%

DM:

Energy: 4.41 kcal/g DM

Protein: 17.7% DM

Fat: 19.9% DM

EPA+DHA: 0.45%

P: 1.28% DM

Na: 0.22% DM

K: 0.77% DM

Data from Danish product book, Royal Canin

Residency class 2015, Toulouse
Slide 16

Analyse	Mængde
Arachidonsyre (%)	0.07
Aske (%)	4.3
Biotin (mg/kg)	1.1
Calcium (%)	0.72
Fibre (%)	2.2
Diætetiske fibre (%)	7.2
DL-methionin (%)	0.33
EPA/DHA (%)	0.41
Fedt (%)	18.0
Linolsyre (%)	3.85
Lutein (mg/kg)	5.0
Omsættelig energi (beregnet med NRC85) (kcal/kg)	3840.0
Omsættelig energi (målt) (kcal/kg)	4090.0
Methionin Cystin (%)	0.6
Vand (%)	9.5
Nitrogenfri ekstrakt (NFE) (%)	50.0
Omega-3 (%)	0.82
Omega-6 (%)	3.99
Fosfor (%)	0.2
Protein (%)	16.0
Stivelse (%)	45.0
Taurin (mg/kg)	2000.0
A-Vitamin (IE/kg)	19000.0
C-Vitamin (mg/kg)	200.0
E-Vitamin (mg/kg)	600.0
Polyfenoler fra grøn te og vindruer (mg/kg)	1280.0



Hill's k/d canned diet

As fed:

Energy: 1390 kcal/ 1000 g

Protein: 4.5%

Fat: 7.9%

Omega-3: 0.57%

P: 0.07%

Na: 0.05%

K: 0.11%

Moisture: 70.3%

DM:

Energy: 4.67 kcal/g DM

Protein: 15% DM

Fat: 26.5% DM

Omega-3: 1.9% DM

P: 0.24% DM

Na: 0.17% DM

K: 0.37% DM

Data from Danish product book, Hill's

Residency class 2015, Toulouse
Slide 17

	FÆRDIGT PRODUKT	TØRSTOF	kcal/100g
A-vitamin ¹⁰	10000 IU/kg	33647 IU/kg	720 IU
Beta-karoten	0.45 mg/kg	1.5 mg/kg	0.03 mg
C-vitamin ¹⁰	21 mg/kg	71 mg/kg	1.5 mg
D-vitamin ¹⁰	490 IU/kg	1649 IU/kg	35 IU
E-vitamin ¹⁰	165 mg/kg	555 mg/kg	12 mg
Fedt	7.9 %	26.5 %	5.7 g
Fibre (rå)	0.1 %	0.5 %	0.1 g
Fosfor	0.07 %	0.24 %	50 mg
Kalcium	0.23 %	0.77 %	166 mg
Kalium	0.11 %	0.37 %	79 mg
Kulhydrat (NFE)	16.1 %	54.1 %	11.6 g
Magnesium	0.04 %	0.12 %	26 mg
Natrium	0.05 %	0.17 %	36 mg
Omega-3 fedtsyrer	0.57 %	1.92 %	410 mg
Omega-6 fedtsyrer	1.29 %	4.34 %	929 mg
Protein	4.5 %	15 %	3.2 g
Taurin	0.03 %	0.11 %	23 mg
Vand	70.3 %	0 -	50.6 g

	FÆRDIGT PRODUKT	TØRSTOF
kcal/100g	139	467
kJ/100g	581	1955
kcal/dåse	514	
Non-Proteinholdige kalorier	89 %	
Mål urin pH	6.8 - 7.2	



Diet formulation

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
3	Foderberegninger til hund, proteinbærende nefropati + azotæmi+pancreatitis																				
4	Ejer ønsker at supplere kommercielt foder med kylling og ris																				
5	(requirements protein, rask hund, 175 g/kg DM (44-70 g/1000 kcal ME), fat 85 g/kg DM (21,3 g/1000 kcal), calcium 12 g/kg DM (3 g/1000 kcal ME), phosphor 10 g/kg DM (2,5 g/1000 kcal ME)																				
6	Energifordeling anbefaling fra Ca and Fe nutrition, rask hund: vedligehold: prot 24%, fedt 38%, kulhydrat 38%																				
7	Anbefaling fra SACN ved prot bærende nefropati og azotæmi: prot 14-20 %DM; P 0,2-0,5 %DM; Na <0,3% DM, K 0,4-0,8% DM																				
8	Anbefaling fra SACN ved pancreatitis: Prot 15-30%DM, fedt ≤ 15 %DM																				
10		DM		protein % as fed	fedt % as fed	kulhydrat % as fed	fiber % as fed	Ca % as fed	P % as fed	Na % as fed	Mg % as fed	K % as fed	EPA/DHA/Omega 3 % as fed	energi, kJ/100 g	beregnet						
11	k/d vådfoder	29,7	4,5	7,9	16,1	0,1	0,23	0,07	0,05	0,04	0,11	0,57	581	636,72							
12	Renal tørfoder	90,5	16	18	45	2,2	0,7	0,2	0,2	na	0,7	0,41	1671	1684,09							
13	kylling uden skind	22,80	19,30	2,70	0,00	0,00	0,01	0,20	0,06	na	0,32		448,00	421,02							
14	Oksekød (hakket, magert)	31,70	20,70	10,00	0,00	0,00	0,01	0,19	na				749,00	716,77							
15	Hytteost 4,5% fedt (vælges pga lav Cu indhold)	21,10	12,50	4,50	2,70	0,00	0,06	0,13	0,4	0,01			431	420,1924							
16	grøntsager kogte eller dase	10,00	2,00	0,10	6,00	1,00	0,12	0,09	0,20	na			1130,00	136,47							
17	kogt ris (hvide)**	27,40	2,00	0,10	24,10	0,10	0,04	0,10	0,37	na	0,03		109,00	436,78							
18	kogt ris (brune)**	30,00	2,50	0,60	25,20	0,30	0,01	0,07	0,28	na			119,00	482,00							
19	kartofler	20,00	2,10	0,10	16,60	0,50	0,01	0,05	0,00	0,03			318,00	314,00							
20	æg	26,30	12,90	11,50	0,90	0,00	0,05	0,21	0,12	0,01			380,00	658,29							
21	Aptus Multidog	85,80	2,60	1,70		4,50	29,00	16,00					106,60								
22	Kanavit 37	100,00	25,00	9,00		0,10	1,00	0,72													
23	Kanavit tabletter (Ca, P, Mg i g per tabl)	100,00	1,00	1,00		1,00	0,12	0,09		0,00											
24	Kanavit pulver (vitamin og mineraler, calcium)	100,00					25,00	0,01		0,82											
25	Kanavit calcium og trace mineraler pr tablet (g)	100,00	5,00	1,00		1,00	0,10	na													
26	vegetabilsk olie	100,00			100,00					na	0,35			3766,00	3733,20						
27	fiskeolie	100,00			100,00						na			3766,00	3733,20						
29		total g	DM	g protein	g fedt	g NFE	g fiber	g calcium	g fosfor	g Natrium	g Magnesium	g Kalium		energi							
30	k/d vådfoder	175,00	51,98	7,88	13,83	28,18	0,18	0,403	0,123	0,088	0,070	0,193	0,998	1016,75	318,36						
31	Renal tørfoder	200,00	181,00	32,00	36,00	90,00	4,40	1,400	0,400	0,400	na	1,400	0,820	3342,00	842,04						
32	kylling uden skind	50,00	11,40	9,65	1,35	0,00	0,00	0,005	0,100	0,030	na	0,160	0,000	224,00	210,51						
33	Oksekød (hakket, magert)	0,00	0,00	0,00	0,00	0,00	0,00	0,000	0,000	na	0,000			0,00	358,39						
34	Hytteost	0,00	0	0,00	0,00	0	0,00	0,000	0,000	0,000	0,000			0	210,0962						
35	grøntsager kogte eller dase	0,00	0,00	0,00	0,00	0,00	0,00	0,000	0,000	0,000	na			0,00	136,47						
36	1 L kogte ris (svarer til 600 g)	500,00	137,00	10,00	0,50	120,50	0,50	0,200	0,500	1,850	na	0,150	0,000	545,00	1310,35						
37	kogt ris (brune)	0,00	0,00	0,00	0,00	0,00	0,00	0,000	0,000	0,000	na			0,00	1445,99						
38	kartofler	0,00	0,00	0,00	0,00	0,00	0,00	0,000	0,000	0,000	0,000			0,00	942,01						
39	æg (1 stk 50 g)	0,00	0,00	0,00	0,00	0,00	0,00	0,000	0,000	0,000	0,000			0,00	658,29						
40	Aptus Multidog (i g, Ca+P, 1 tabl pr 5 kg, 1 tabl = 1,3 g)	0,00	0,00	0,00	0,00	0,00	0,00	0,000	0,000	0,000	0,000			0,00	0,00						
41	Kanavit 37 pulver (g) Ca+P, ca 1-2 g pr 5 kg	0,00	0,00	0,00	0,00	0,00	0,00	0,000	0,000					0,00	0,00						
42	Kanavit tabletter pr tabl (Ca, i g, 1 tabl pr 5 kg)	0,00	0,00	0,00	0,00	0,00	0,00	0,000	0,000		0,000			0,00	0,00						
43	Kanavit pulver (vitamin og mineraler, Ca+P) (i g)(1 ske= ca 5 g, 5 g pr 5 kg)	0,00	0,00	0,00	0,00	0,00	0,00	0,000	0,000	0,000	0,000			0,00	0,00						
44	Kanavit calcium og trace mineraler pr tablet (Ca+P, pr tablet, Ca i g)	0,00	0,00	0,00	0,00	0,00	0,00	0,000	na					0,00	0,00						
45	vegetabilsk olie (3 spsk= 45 ml, 1 tsk=4g, 1 spsk=12g)	0,00	0,00	0,00	0,00					na	0,000			0,00	261,32						
46	Fiskeolie (15 ml = 2 spsk)	0,00	0,00	0,00	0,00						na			0,00	0,00						
47	Total	925,00	381,38	59,53	51,68	238,68	5,08	2,01	1,12	2,37	0,070	1,903	1,818	769,00	5533,43						
48	energi			996,21	1821,96	3960,10															
49	% energi			14,70	26,88	58,42															
50	% pr DM			15,61	13,55	62,58	2,64	0,53	0,29	0,62	0,02	0,50	0,48	Svarer til en Ca:P ratio på	1,79 *						
51	g/1000 kcal ME			36,43	31,62	146,06	3,11	1,23	0,69	1,45	0,04	1,16	1,11	HUSK (1 måleske= 1,5 g):	5 => g fiber total =	10,08					
52																					
53	E behov hund, Sixten, 45 kg, BCS 4/9			Kj/blanding	Kcal/bl	kJ/kg feed	kcal/g DM														
54	MER normal aktiv hund: 1650 kcal/dag			6778,26	1634,10	7327,85	4,28														



Proposed diet

175 g k/d canned food

+

200 g RC Renal dry food

+

50 g cooked chicken without skin, unsalted water

+

500 g boiled white rice, unsalted water

+

5 g Psyllium husks or 5 tbsp. boiled grated zucchini, unsalted water

Energy intake pr. day: 1634 kcal

Total amount of food pr. day: 925 g

	Sixten, proposed diet	Recommended requirements, Amt./kg BW^{0.75} (NRC 2006)	Recommended requirements 95 kcal/BW^{0.75} (fediaf 2014)	Recommended requirements (SACN, 5th ed.), PLN and azotemia	Recommended requirements (SACN, 5th ed.), pancreatitis
Energy density	4.25 kcal/g DM				
Protein	59.53 g/day 15.6 %DM	RA 57.1 g/day Min 45.6 g/day	Min 86.0 g/day	14-20 %DM	15-30 %DM
Fat	51.68 g/day 13.6 %DM	RA 31.32 g/day AI 22.62 g/day SUL 187.9 g/day	Min 22.69 g/day		≤15 %DM
EPA+DHA, Omega-3	1.82 g/day 0.48 %DM	RA 0.52 g/day SUL 6.44 g/day		0.4-2.5 %DM	
Phosphorus	1.12 g/day 0.29 %DM	RA=AI 1.74 g/day	Min 1.91 g/day Max 6.6 g/day	0.2-0.5 %DM	
Sodium	520 mg/day 0.13 %DM	RA 455.9 mg/day Min 171.39 mg/day SUL 6.19 g/day	Min 480 mg/day Max 7.43 g/day	≤0.3 %DM	
Potassium	1.9 g/day 0.5 %DM	RA 2.44 g/day	Min 2.39 g/day	0.4-0.8 %DM	
Fiber	5.08 g/day 2.64 %DM				

Conclusion, the proposed diet

- All nutrients:
 - Above min. requirements and under SUL – NRC
 - Within recommendations – SACN for PLN and pancreatitis
- Protein
 - High in protein – NRC
 - Below recommendations- fediaf
 - Within recommendations - SACN
- Fat, EPA and DHA, Omega-3
 - High, under SUL - NRC and fediaf
 - Within recommendations – SACN
- P
 - Low in P – NRC and fediaf
 - Within recommendations – SACN
- Na
 - High in Na, under SUL – NRC and fediaf
 - Within recommendations – SACN
- K
 - Low in K – NRC and fediaf
 - Within recommendations – SACN



Nutrients compared to NRC recommendations

	Sixten, proposed diet	Sixten, RC renal dry diet	Sixten, Hill's i/d dry diet	Sixten, Hill's i/d low fat dry diet	Recom. Require, Amt./kg BW ^{0.75} (NRC 2006)	Recom. Require, 95 kcal/BW ^{0.75} (fediaf 2014)	Recom. Require, (SACN, 5 th ed.), PLN and nephropa thy	Recom. Require, (SACN, 5 th ed.), pancreati tis
Protein	59.53 g/day 15.6 %DM ↑	66.1 g/day 16 %DM ↑↑	107 g/day 23.5 %DM ↑↑↑	116 g/day 23.5 %DM ↑↑↑↑	RA 57.1 g/day Min 45.6 g/day	86.0 g/day	14-20 %DM	15-30 %DM
Fat	51.68 g/day 13.6 %DM ↑↑	74.34 g/day 18 %DM ↑↑↑↑	59.6 g/day 13 %DM ↑↑↑	36.1 g/day 7.3 %DM ↑	RA 31.32 g/day AI 22.62 g/day SUL 187.9 g/day	22.69 g/day		≤15 %DM

Conclusion

Protein: Proposed diet < renal

Fat: Proposed diet < i/d, Proposed diet > i/d low fat

Proposed diet: high in protein and fat compared to NRC



Conclusion

- The proposed diet meets the SACN¹ recommendations for diets for dogs with PLN with azotemia and dogs with acute pancreatitis.
- The diet is below the fediaf² protein recommendations, but above the NRC³.
- Although the diet is high in fat according to the NRC³ and fediaf² recommendations the diet has an acceptable level of fat as the dog is non-obese and non-hypertriglyceridaemic (SACN¹)
- The amount of protein (g/day) is lower in the proposed diet than a commercial renal diet and the amount of fat (g/day) is lower than in a commercial intestinal diet.
- It is possible to formulate a well balanced diet for a dog with PLN with azotemia and concurrent acute pancreatitis, although one should be aware of the level of fat in the diet when using a renal diet as a main ingredient



Considerations

- NRC recommendations are low in protein compared to fediaf
- This renal diet is high in fat compared to NRC recommendations
- This intestinal diet is high in fat compared to NRC recommendations
- Homemade diets vary considerably in nutrient contents depending on raw ingredients, preparation and methodology¹
- Recipes can be highly variable and result in inappropriate diets. Many recipes would not meet nutritional and clinical needs of individual patients and should be used cautiously for long-term feeding.²

1. Davies M. Vet Rec. (2014) 174: 352

2. Larsen JA et al. J Am Vet Med Assoc. (2012) Mar 1;240(5):532-8.



Follow up, owner compliance

- Sixten is generally in good health
- Has had recurrent diarrhea, colitis, before he started on the kidney diet.
- Improved on probiotics and intestinal diet but recurrence of diarrhea when owner tried to changed to kidney diet
- Positive for Clostridia -> metronidazol and amox+clav treatment at referring vet
- Current diet: Hill's i/d Low fat canned diet + RC GI low fat dry diet + Psyllium husk
- Owner is not interested in change to kidney diet at the moment



Thank you for listening



	Sixten, proposed diet	Sixten, RC renal dry diet	Sixten, i/d dry diet	Sixten, i/d low fat dry diet	Recommen- ded require- ments, Amt./kg BW ^{0.75} (NRC 2006)	Recommen- ded require- ments (SACN), PLN and nephropa- thy	Recommen- ded require- ments (SACN), pancreati- tis
Energy density	4.25 kcal/g DM	4.5 kcal/g DM	3.9 kcal/g DM	3.6 kcal/g DM			
Amount per day	925 g	413 g	458.7 g	494.5 g			
Protein	59.53 g/day 15.6 %DM	66.1 g/day 16 %DM	107 g/day 23.5 %DM	116 g/day 23.5 %DM	RA 57.1 g/day Min 45.6 g/day	14-20 %DM	15-30 %DM
Fat	51.68 g/day 13.6 %DM	74.34 g/day 18 %DM	59.6 g/day 13 %DM	36.1 g/day 7.3 %DM	RA 31.32 g/day AI 22.62 g/day SUL 187.9 g/day		≤15 %DM



COMPRESSION FRACTURES IN A LARGE BREED PUPPY

Moran Tal Gavriel

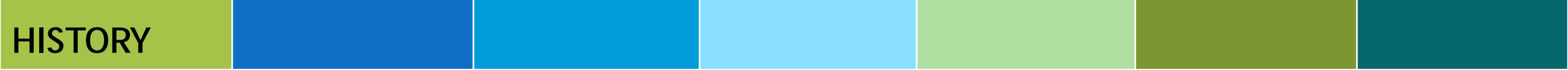
DVM, DVSc Student in Clinical Nutrition

Case Advisors: Dr. Verbrugghe, Dr. Parr
Program Advisor: Dr. Verbrugghe

TESS, 6 MONTHS, FI, GIANT SCHNAUZER

- Presented December 15, 2014
 - Yelped and tried to bite when owner lifted her
 - Hunched and laying down





TESS, 6 MONTHS, FI, GIANT SCHNAUZER

- Reluctance to walk, diarrhea, vomiting, leaking urine (1 month)
- Hematuria (4 days)
- rDVM Urinalysis (free catch) - WBC, pH 8 → Clavamox
CBC - mild anemia
Biochemical panel - elevated Alk Phos
- “Episodes” of lameness (RH)
 - Pain, trembling
 - Could not jump or walk down the stairs
 - Choppy gait

**HOMEMADE
DIET**

TESS, 6 MONTHS, FI, GIANT SCHNAUZER

- Tense, rigid muscles on HL bilaterally
- Severe tachypnea
- Painful on abdominal palpation
- Urinary incontinence when relaxed - UTI?
- Lack of proprioception and hopping bilaterally in HL
- Knuckling bilaterally in HL
- Hunched posture, weakly ambulatory with assistance
- Lumbar pain and pain with extension of hips
- Other - WNL

BW - 20.36kg

BCS - 5/9

MCS - mild muscle wasting

DECEMBER 16, 2014

Pediatric Clinical Pathology

Benita von Dehn, DVM

Vet Clin Small Anim, 2014; 44: 205-219.

➤ CBC

- WBC - $19.7 \times 10^9/L$ ($4.9 - 15.4 \times 10^9/L$)
- Segmented neutrophil count - $16.55 \times 10^9/L$ ($2.9 - 10.6 \times 10^9/L$)

➤ Biochemical Panel

Parameters	Results	AHL Reference Range	Puppy Reference Range (4-6 months)
Ca	2.11 ↓	2.5 - 3 mmol/L	2.5 - 3.3 mmol/L
Alk Phos	473 ↑	22 - 143 U/L	126 - 438 U/L
CK	1058 ↑	40 - 255 U/L	40 - 192 U/L
Amylase	1238	299 - 947 U/L	≤1683

DECEMBER 16, 2014

➤ Urinalysis

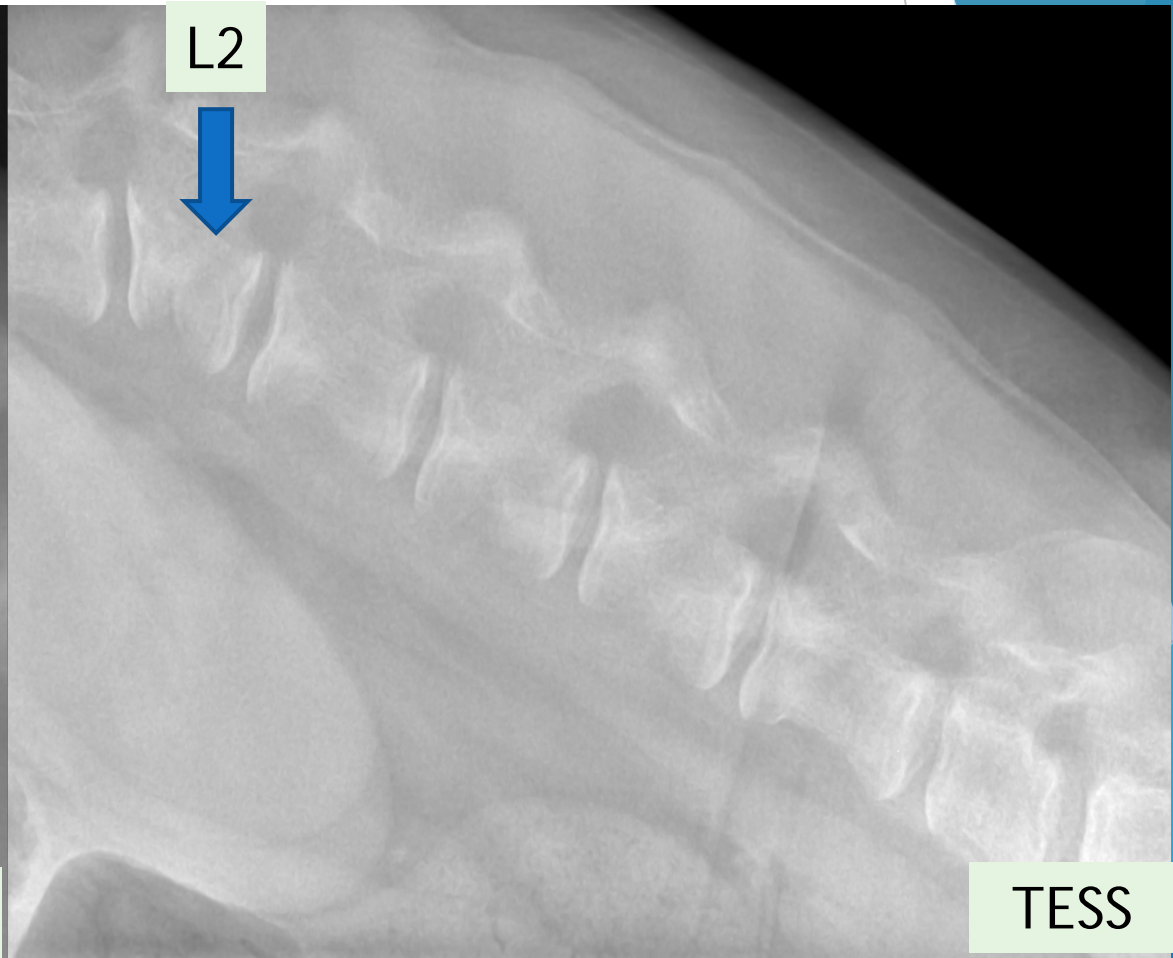
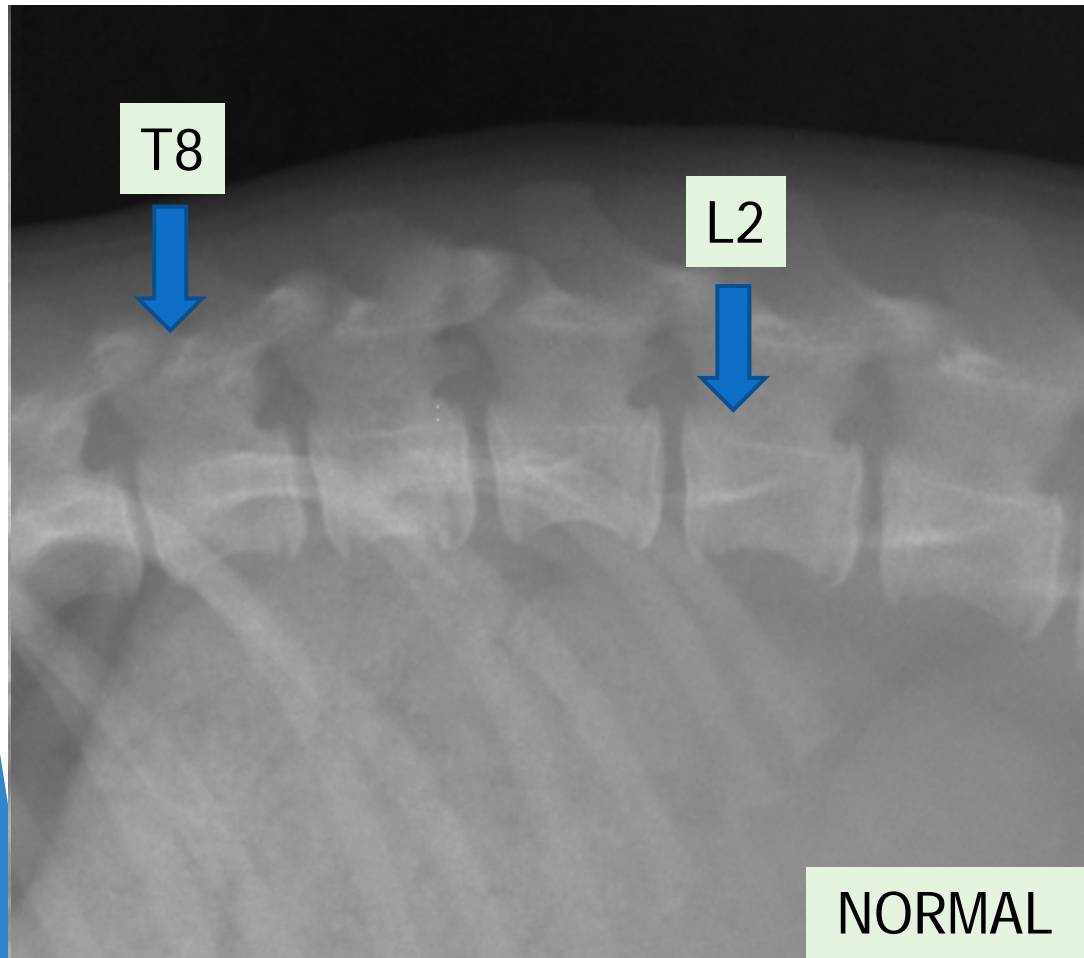
Parameters	Results	Reference Range
RBC	8-10	0 / 400 x
Clarity	Cloudy	
Bacteria	3	
Leukocytes	200-250	0 / 400 x
Urobilinogen	3.2	0 umol/L
Blood	2	0

❑ Beta E. coli (10^5 cfu/mL) (December 18, 2014)

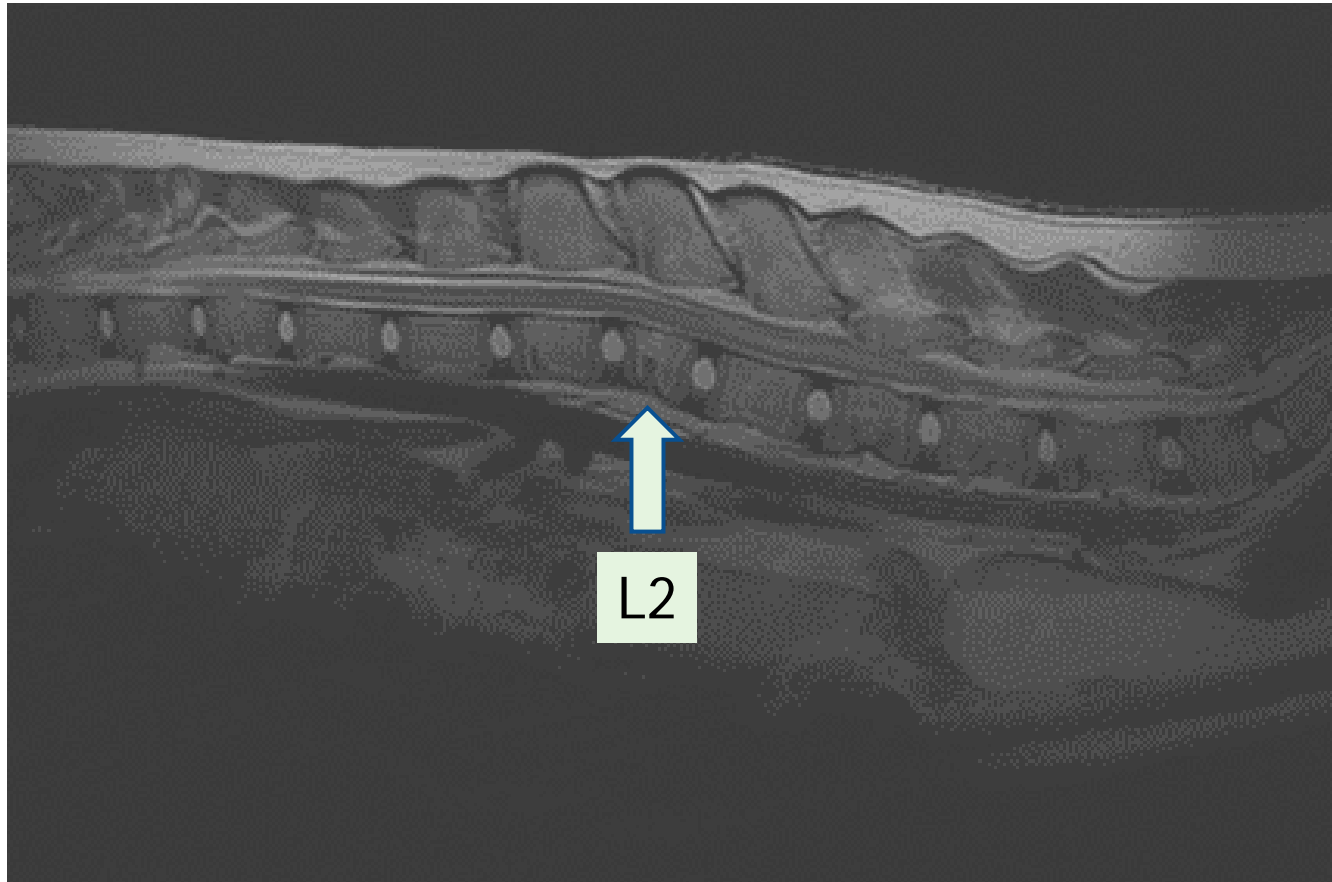
INITIAL DIFFERENTIAL DIAGNOSES

- Discospondylitis
- Autoimmune meningomyelitis
- Spinal empyema
- Trauma (fracture/luxation)
- Parasytic myelitis (toxoplasma, neospora)
- Nutritional secondary hyperparathyroidism

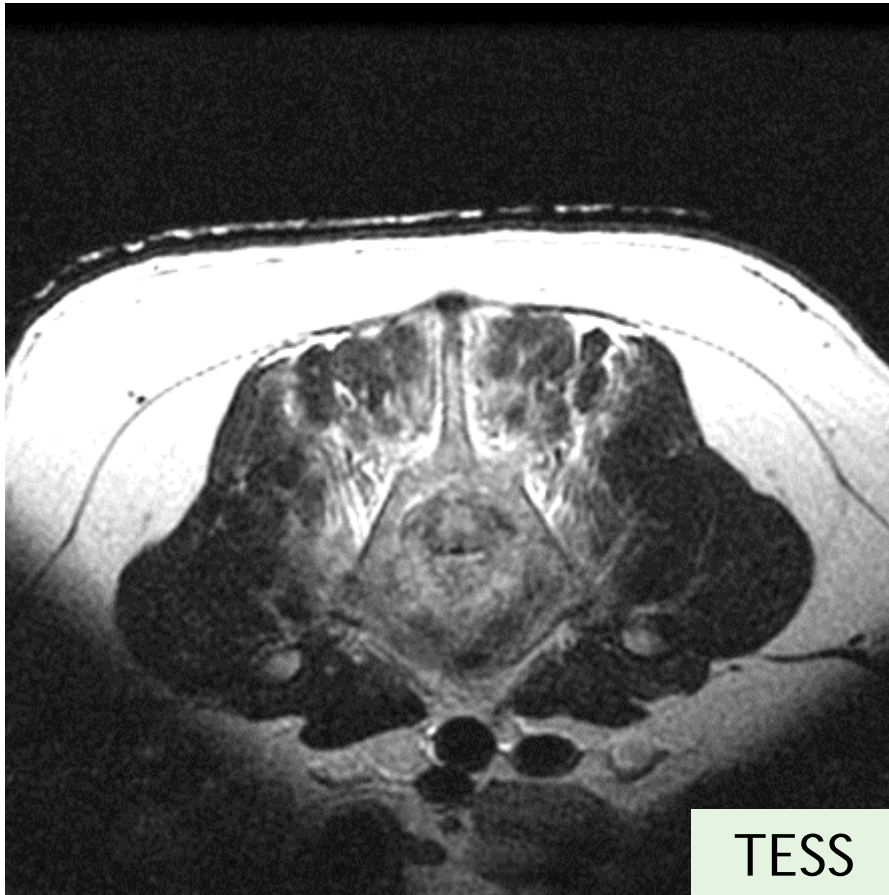
RADIOGRAPHS



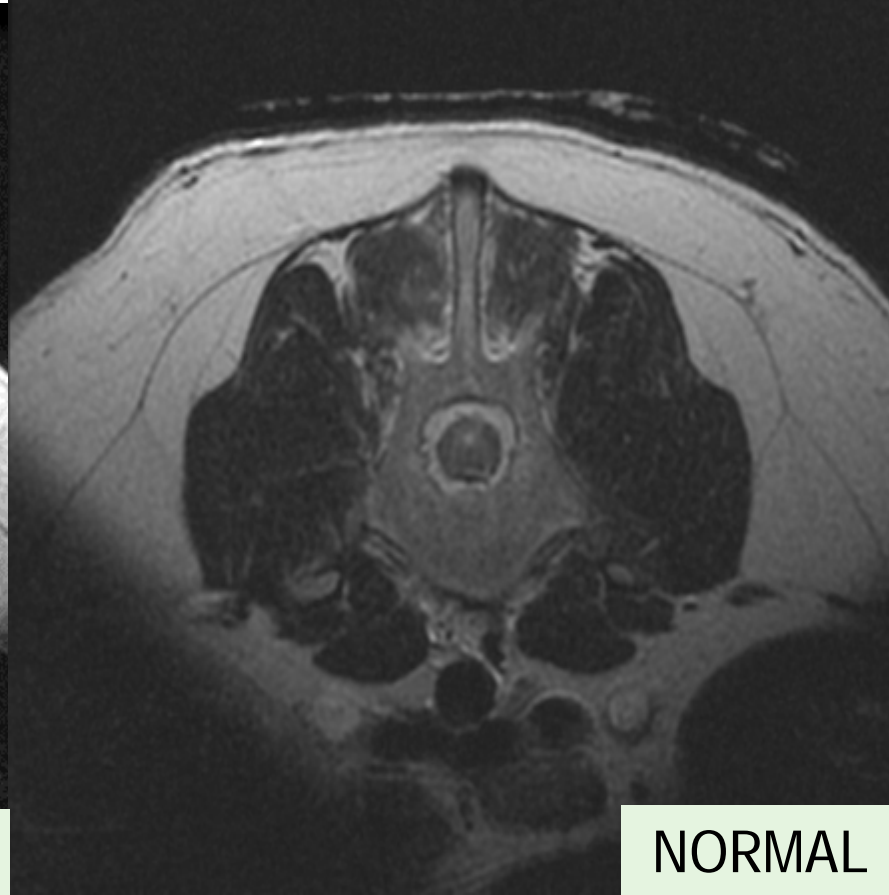
MRI



MRI



TESS



NORMAL

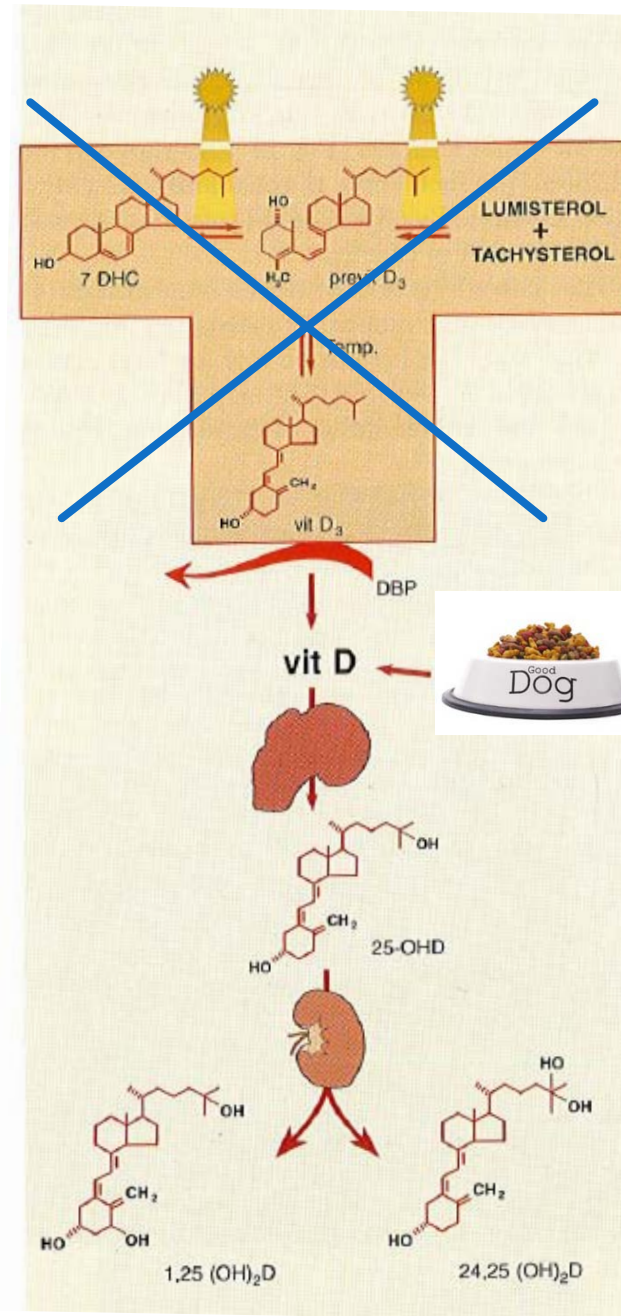
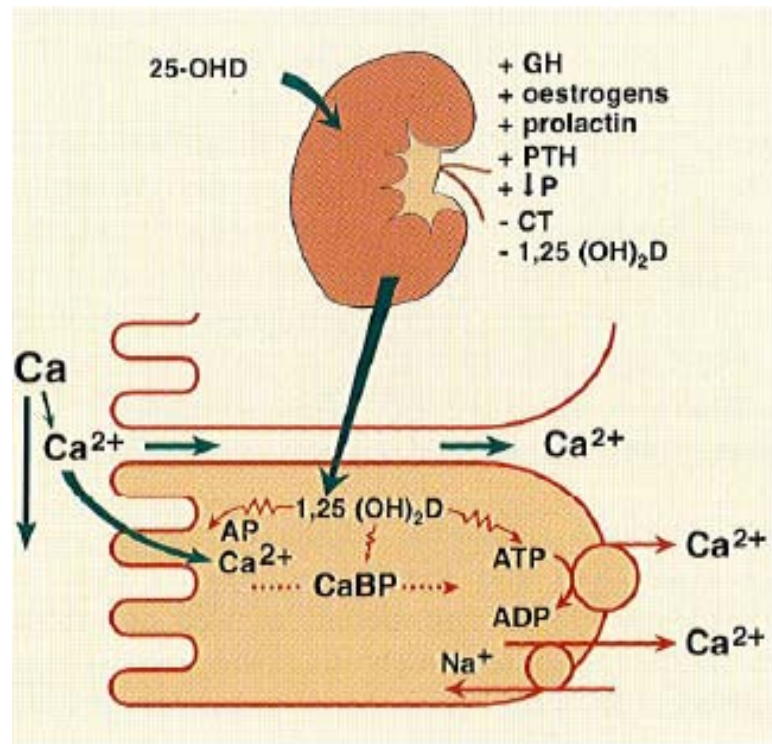
TESS, 6 MONTHS, FI, GIANT SCHNAUZER

- Lesion localised to T3-L3 segments
- MRI findings → acute fracture in L4
 - Contrast enhancement
 - Active bone remodelling OR
 - Secondary to diffuse osteopenia

**Primary DDx: Nutritional secondary
hyperparathyroidism**

**Secondary DDx: Genetic disease → osteogenesis
imperfecta**

NUTRITIONAL SECONDARY HYPERPARATHYROIDISM



Rijnberk, 1996

NUTRITIONAL SECONDARY HYPERPARATHYROIDISM

NUTRITIONAL SECONDARY HYPERPARATHYROIDISM OCCURRING IN A STRAIN OF GERMAN SHEPHERD PUPPIES

Kayo KAWAGUCHI, Ignacia Syjuco BRAGA III, Akemi TAKAHASHI,
Kenji OCHIAI and Chitoshi ITAKURA

Jpn. J. Vet. Res., 1993; 41(2-4): 89-96

Metabolic bone disease and hyperparathyroidism in an adult dog fed an unbalanced homemade diet

*Metabole botafwijkingen en hyperparathyroïdie bij een volwassen hond
na consumptie van een slecht uitgebalanceerd huishouddieet*

¹A. Verbrugghe, ²D. Paepe, ²L. Verhaert, ³J. Saunders, ⁴J. Fritz, ¹G.P.J. Janssens, ¹M. Hesta

Vlaams Diergeneeskundig Tijdschrift, 2011; 80: case report 61.

Influence of Calcium and Phosphorus Intake on the Apparent Digestibility of These Minerals in Growing Dogs^{1,2}

Britta Dobenecker³

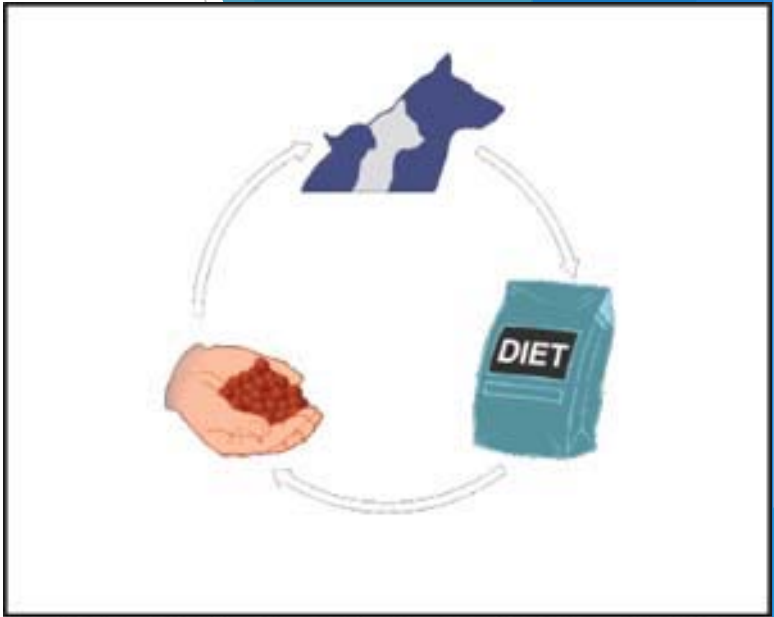
J. Nutr., 2002; 132: 1665S-1667S

DIET ANALYSIS - RECIPE

HOME MADE DIET RECIPE (BATCH FOR 2 WEEKS)

2 lbs. regular beef	2 red apples
2 cups grated carrots	3 eggs
2 cups green beans and broccoli	3-4 cups brown rice flour
2-3 tbsp. refined sunflower oil	1/2 cup oat bran

- 1/2 cup white organic rice, apples and carrots throughout the day
- 1 tsp. bone meal (manufacturer unknown)
- 1 capsule cod liver oil (manufacturer unknown)
- 4 meals a day



BALANCE IT (<https://secure.balanceit.com/>)

Total calories fed: 6797.8 kcal/day OR 338% of the calculated requirement

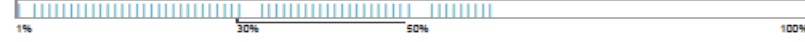
Protein calories: 14.7%



Fat calories: 25.1%



Carbohydrate calories: 60.2%



14.7% MF Protein 25.1% MF Fat 60.2% MF Carbohydrate

Calculated Energy Requirement Range 100% 6797.834 kcal Min kcal/day (50% MER):1006 Max kcal/day (150% MER):3019

Nutrients	% of Requirement	Amount (per Meal)	Requirement Range
[203] Protein	59.4%	37.331 g	(62.9 to [no max] g)
[511] Arginine	151.3%	2.677 g	(1.77 to [no max] g)
[512] Histidine	168.8%	1.051 g	(0.63 to [no max] g)
[503] Isoleucine	129.0%	1.664 g	(1.29 to [no max] g)
[504] Leucine	144.5%	2.977 g	(2.06 to [no max] g)
[505] Lysine	111.2%	2.446 g	(2.2 to [no max] g)
[1001013] Methionine-cystine	93.0%	1.405 g	(1.51 to [no max] g)
[1001017] Phenylalanine-tyrosine	114.1%	2.899 g	(2.54 to [no max] g)
[502] Threonine	86.3%	1.432 g	(1.66 to [no max] g)
[501] Tryptophan	49.3%	0.281 g	(0.57 to [no max] g)
[510] Valine	147.6%	2.022 g	(1.37 to [no max] g)
[204] Total lipid (fat)	123.3%	28.238 g	(22.9 to [no max] g)
[618] 18:2 undifferentiated	200.3%	5.809 g	(2.9 to [no max] g)
[205] Carbohydrate, by difference	100.0%	148.880 g	(0 to [no max] g)
[421] Choline, total	39.6%	134.389 mg	(339.653 to [no max] mg)
[435] Folate, DFE	127.0%	63.495 mcg_DFE	(50 to [no max] mcg_DFE)
[406] Niacin	344.0%	11.352 mg	(3.3 to [no max] mg)
[410] Pantothenic acid	124.4%	3.607 mg	(2.9 to [no max] mg)
[405] Riboflavin	67.9%	0.428 mg	(0.63 to [no max] mg)
[404] Thiamin	218.6%	0.634 mg	(0.29 to [no max] mg)
[320] Vitamin A, RAE	216.9%	930.051 mcg_RAE	(428.7 to 21428.7 mcg_RAE)
[418] Vitamin B-12	902.0%	0.054 mg	(0.006 to [no max] mg)
[415] Vitamin B-6	453.4%	1.315 mg	(0.29 to [no max] mg)
[323] Vitamin E (alpha-tocopherol)	33.7%	4.714 IU, Vit E	(14 to 286 IU, Vit E)
[301] Calcium, Ca	74.0%	2.146 g	(2.9 to 3.5 g)
[1000000] Chloride	0.0%	0.000 g	(1.29 to [no max] g)
[312] Copper, Cu	122.5%	2.573 mg	(2.1 to 71 mg)
[1000001] Iodine	0.0%	0.000 mg	(0.43 to 14 mg)
[303] Iron, Fe	32.5%	7.475 mg	(23 to 857 mg)
[304] Magnesium, Mg	153.6%	0.169 g	(0.11 to 0.86 g)
[315] Manganese, Mn	358.1%	5.014 mg	(1.4 to [no max] mg)
[305] Phosphorus, P	82.8%	1.905 g	(2.3 to 4.6 g)
[306] Potassium, K	52.5%	0.892 g	(1.7 to [no max] g)
[317] Selenium, Se	92.3%	0.028 mg	(0.03 to 0.57 mg)

DEFICIENCIES:

Protein, choline, B2, vit. E, Ca, Cl, I, Fe, P, Na, K, Se, Zn

[307] Sodium, Na

22.5% 0.194 g (0.86 to [no max] g)

[309] Zinc, Zn

37.5% 12.762 mg (34 to 286 mg)

[1000021] Ca:P ratio

118.6% 1.127 n/a (0.95 to 2.05 n/a)

[328] Vitamin D (D2 + D3)

155.2% 221.871 IU, Vit D (143 to 1429 IU, Vit D)

DIET ANALYSIS - LABORATORY

Nutrient Analysis (%)	Tess' Homemade Diet (as fed)	Tess' Homemade Diet (%DM)	NRC (2006) Recommended Allowance	AAFCO (2014) Min. Req. for growth
Moisture	54.07			
Protein (N X 6.25)	8.49	18.484	17.5 %DM	22%DM
Calcium	0.04	0.087	1.2 %DM	1 %DM
Phosphorus	0.17	0.370	1.0 %DM	0.8 %DM
Ca:P ratio		1:4	1.2:1	1.25:1
*Vitamin D (cholecalciferol)	Below Detection Limit	Below Detection Limit	55.2IU/100gDM	50IU/100gDM

VITAMIN D TOXICITY PROFILE (December 18, 2014)

Parameters	Results	Reference Range
Parathyroid hormone	4.6	0.5 - 5.8 pmol/L
25-Hydroxy vitamin D	8	60 - 215 nmol/L
Ionized calcium	1.5	1.25 - 1.45 mmol/L

DECEMBER 16,
2014

Parameters	Results	AHL Reference Range	Puppy Reference Range (4-6 months)
Ca	2.11	2.5 - 3 mmol/L	2.5 - 3.3 mmol/L
Alk Phos	473	22 - 143 U/L	126 - 438 U/L
CK	1058	40 - 255 U/L	40 - 192 U/L
Amylase	1238	299 - 947 U/L	≤1683

DECEMBER 16-17, 2014

Medications

- Hydromorphone
- Dexamedetomidine
- Fentanyl patch
- Meloxicam
- Tramadol
- Gabapentin
- Cephazolin
- Famotidine

DECEMBER 16-17, 2014

Diet while in Hospital

- Royal Canin Vet Diet GI High Energy (canned, UNKNOWN AMOUNTS)

Royal Canin Veterinary Diet Canine GASTROINTESTINAL HIGH ENERGY is formulated to meet the nutritional levels established by the AAFCO Dog Food Nutrient Profiles for maintenance. All Royal Canin Veterinary Diet Canine products guarantee 100% satisfaction with superior quality and consistency. If you have any questions or comments regarding these products, call Royal Canin USA Technical Services: 1-800-592-6687. For Canada: Your veterinary clinic is the best source of information for your pet, or contact us at www.royalcanin.ca.



Nutritional Support Plan....



GROWING LARGE BREED PUPPY KEY NUTRITIONAL FACTORS (I)

- Energy Requirements - 2.0-2.5 X RER
 - Prevention of obesity (Hand et al, 2010)
- Adequate Protein Levels - 23-31% DM
 - Arginine = essential AA for puppies (Nap et al, 1993)
- Fat - Min. of 8.5% DM
 - DHA + EPA 0.05% DM (DHA:EPA → 2:3) (NRC, 2006)
 - Conversion of polyunsaturated fatty acids to DHA → essential for growth (Bauer et al, 2006)²⁰

GROWING LARGE BREED PUPPY KEY NUTRITIONAL FACTORS (II)

- Calcium 0.8-1.4% DM (aim towards 1.2%)
- Phosphorus 0.7-1.2% DM
- Ca:P ratio 1.1:1-1.3:1

Nutritional Risks to Large-Breed Dogs: From Weaning to the Geriatric Years

Susan D. Lauten, PhD

Vet Clin Small Anim, 2006; 36: 1345-1359

ABSORPTION CONSIDERATIONS IN PUPPIES

Growth hormone modulates cholecalciferol metabolism with moderate effects on intestinal mineral absorption and specific effects on bone formation in growing dogs raised on balanced food

M.A. Tryfonidou^{a,*}, M.S. Holl^a, M.A. Oosterlaken-Dijksterhuis^a,
M. Vastenburg^b, W.E. van den Brom^a, H.A.W. Hazewinkel^a

Domestic Animal Endocrinology, 2003; 25: 155-174

Intestinal Calcium Absorption in Growing Dogs Is Influenced by Calcium Intake and Age but Not by Growth Rate¹

M. A. Tryfonidou,^{2*} J. van den Broek,† W. E. van den Brom* and H.A.W. Hazewinkel*

The Journal of Nutrition, 2002; 132: 3363-3368

ROYAL CANIN MAXI PUPPY

Nutrient Analysis	Maxi Puppy (%DM)	AAFCO (2014) Min. Req. for Growth (%DM)
Crude Protein	✓28.18	22
Crude Fat	✓15.03	8
Calcium	✓1.14	1
Phosphorus	✓0.85	0.8
Ca:P	✓1.3	1.25:1



Metabolizable Energy = 364.6 kcal/100g (346 kcal/cup)

Recommended amount: **388g** or 4 and 1/8 cups over 3-4 meals

DECEMBER 18, 2014

➤ Medications

- Fentanyl patch 100mcg/h (over 3 days)
- Tramadol 100mg, 1 capsule PO TID
- Gabapentin 100mg, 2 capsules PO TID
- Meloxicam 1.5mg/mL, measure to 20kg mark, PO QD
- Cephalexin 500mg, 1 tablet PO TID

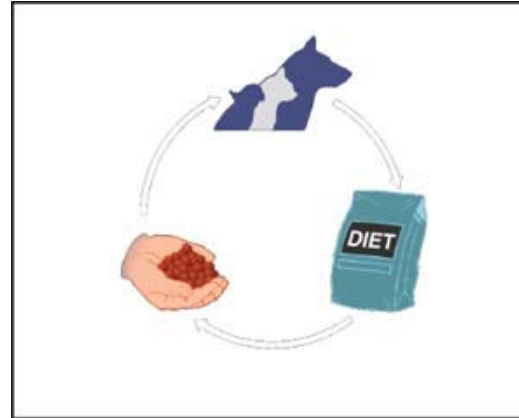
➤ Nutrition Support Plan

- Continue with Royal Canin Maxi Puppy
- Treats < 10% daily energy intake
- Adjustments according to weight, BCS, MCS and age

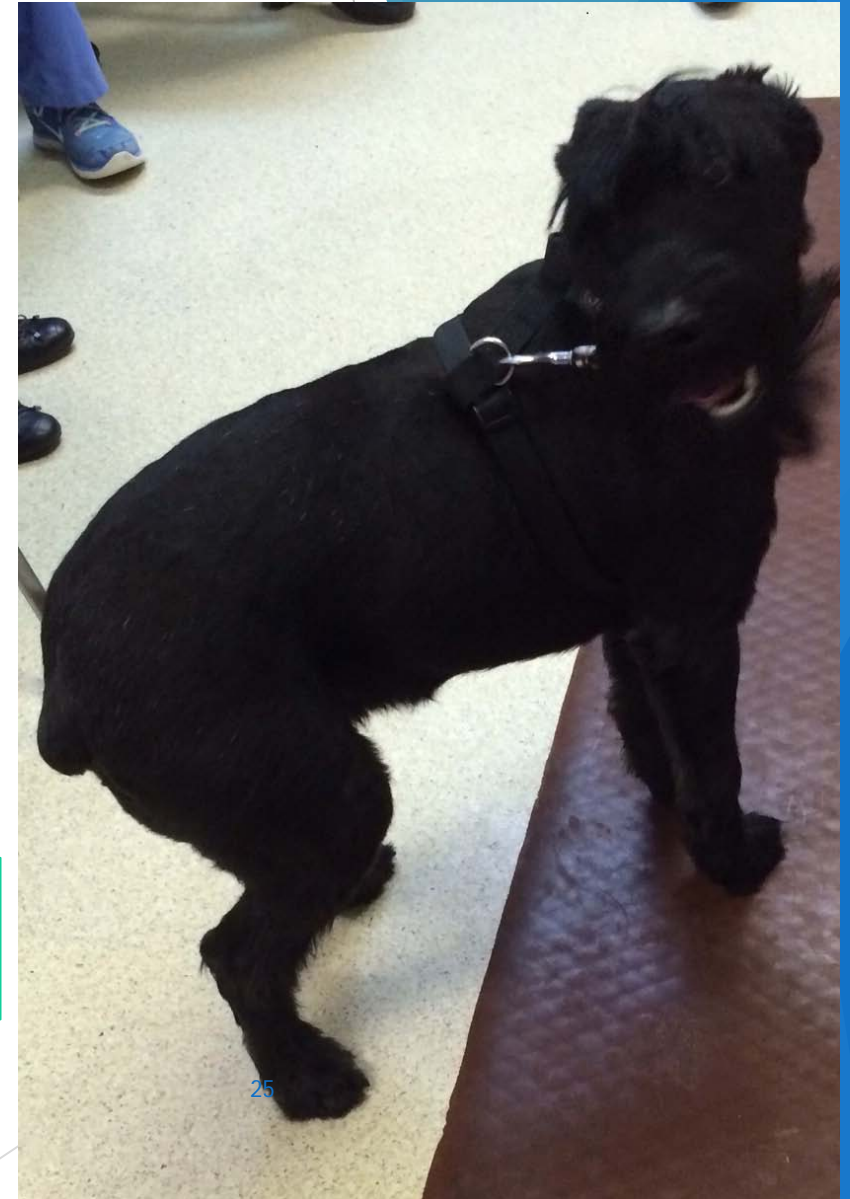


FEBRUARY 2, 2015

- Highly improved
- Residual ataxia
- Nutritional assessment:
 - Wt = 24kg
 - **BCS = 6/9**
 - MCS = mild muscle wasting
- Fed recommended RC Maxi Puppy AND
 - Apples and carrots
 - Table scrapes
 - Salmon skin rolls
 - Two knuckle bones a week



Treats > 10% daily
energy intake

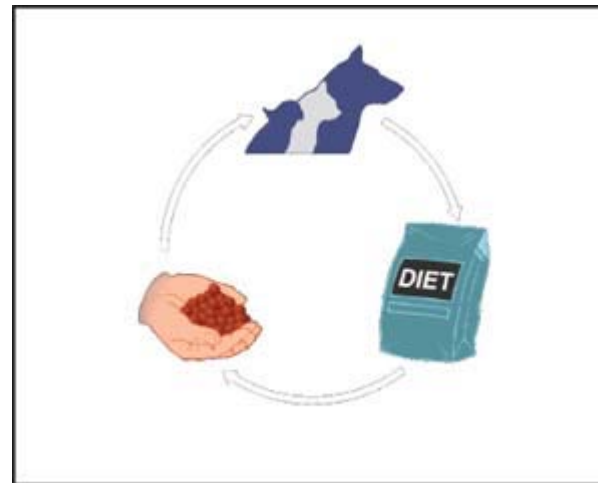


TAKE HOME MESSAGES

- COMPLETE AND BALANCED DIET!



- Follow large breed puppy requirements
- Diet history form



TAKE HOME MESSAGES

Handling Alternative Dietary Requests from Pet Owners

Jacqueline M. Parr, DVM, MS^{a,b,*},
Rebecca L. Remillard, PhD, DVM^{c,d,e}

Vet Clin Small Anim, 2014; 44: 667-688

Maintain empathy and understanding for owner - believe they are doing the BEST for their pet.

- Homemade diet (HMD):
 - **Nutrition consult!**
 - Quick assessment for a HMD recipe
 - Protein, carbohydrates, lipids, calcium, multivitamin and trace mineral source
 - Ca:P - especially in a large breed puppy
- Treats < 10% daily energy intake



SPECIAL THANKS

Dr. Adronie Verbrugghe

Dr. Jackie Parr

Dr. Andrew Barker

Dr. Georgina Stewart

Dr. Shawn MacKenzie

Dr. Alex Zuck-Linden

The ICU technicians

Phase 4 students

Nicole Weidner and Georgia Kritikos

REFERENCES

- Von Dehn, B. Pediatric Clinical Pathology. Vet Clin Small Anim, 2014; 44: 205-219.
- Rijnberk, A. Clinical Endocrinology of Dogs and Cats. Kluwer Academic Publishers, 1996. Chapters 9, 10: 167-195.
- Kawaguchi, K., Braga, I.S., Takahashi, A., Ochiai, K., Itakura, C. Nutritional secondary hyperparathyroidism occurring in a strain of German Shepherd puppies.
- Verbrugghe, A., Paepe, D., Verhaert, L., Saunders, J., Fritz, J., Janssens, G.P.J., Hesta, M. etabolic bone disease and hyperparathyroidism in an adult dog fed an unbalanced homemade diet. Vlaams Diergeneeskundig Tijdschrift, 2011; 80: case report 61.
- Dobenecker, B. Influence of calcium and phosphorus intake on the apparent digestibility of these minerals in growing dogs. J. Nutr., 2002; 132: 1665S-1667S.
- Hand, M.S., Thatcher, C.D., Remillard, R.L., Roudebush, P., Novotny, B.J. Small Animal Clinical Nutrition. Mark Morris Institute, 2010.
- Nap, R.C., Mol, J.A., Hazewinkel, H.A.W. Age-related plasma concentrations of growth hormone (GH) and insulin-like growth factor I (IGF-1) in great dane pups fed different dietary levels of protein. Domestic Animal Endocrinology, 1993; 10: 237-247.

REFERENCES

- Subcommittee on Dog and Cat Nutrition; Committee on Animal Nutrition; [Board on Agriculture and Natural Resources](#); [Division on Earth and Life Studies](#); [National Research Council](#). Nutrient requirements of Dogs and Cats. National Research Council of the National Academics, 2006. Chapter 5.
- Lauten, S.D. Nutritional risks to large-breed dogs: from weaning to the geriatric years. Vet Clin Small Anim, 2006; 361; 1345-1359.
- Tryfonidou, M.A. Growth hormone modulates cholecalciferol metabolism with moderate effects on intestinal mineral absorption and specific effects on bone formation in growing dogs raised on balanced food. Domestic Animal Endocrinology, 2003; 155-174.
- Tryfonidou, M.A., Van Den Broek, J., Van Den Brom, W.E., Hazewinkel, H.A.W. Intestinal calcium absorption in growing dogs is influenced by calcium intake and age but not by growth rate. J. Nutr., 2002; 132: 3363-3368.
- Parr, J.M., Remillard, R.L. Handling Alternative Dietary Requests from Pet Owners. Vet Clin Small Anim, 2014; 44: 667-688.

Iron overload disease in browser rhinoceroses in captivity.

Vandendriessche Veerle
ECVCN Residency Class 2015

Iron overload disease in browser rhinoceroses

- ✓ Introduction
- ✓ Iron metabolism
- ✓ Rhino anatomy and gastro-intestinal tract physiology
- ✓ Diet composition wild & captivity
- ✓ Past treatments applied
- ✓ Current/future research
- ✓ Discussion

Introduction

✓ Rhinoceros species:

- ☐ *Diceros bicornis*
- ☐ *Dicerorhinus sumatrensis*
- ☐ *Ceratotherium simum*
- ☐ *Rhinoceros unicornis*



Introduction

✓ Occurrence of IOD or captivity acquired hemosiderosis:

- ☐ Only in captive animals
- ☐ Only in the two browser species

☐ But also in



Introduction

- ✓ Diagnosis of IOD in the past = necropsy

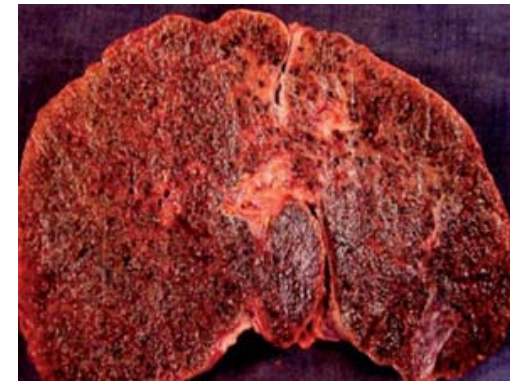
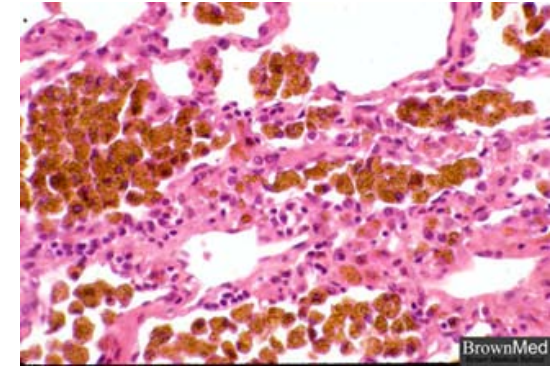
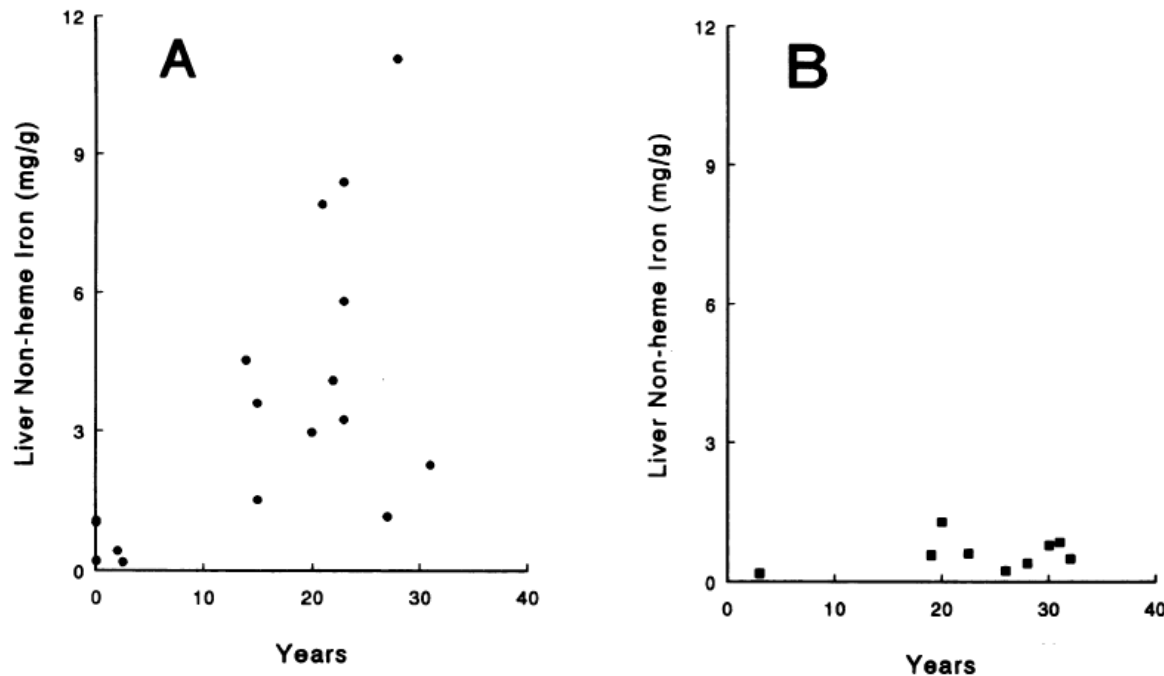


Figure 1. The relationship of liver nonheme iron to age or time in captivity in black (A) and white (B) rhinoceroses. ($N = 18$ for black rhinoceroses, $N = 9$ for white rhinoceroses).

Smith et al, 1995; Kock et al, 1992; Miller et al, 2012

Introduction

Species	No.	Iron ($\mu\text{g}/\text{dl}$)
Captive:		
Adult <i>D. bicornis</i>	69–70	227 ± 107
Juvenile <i>D. bicornis</i>	26–30	236 ± 135
<i>D. sumatrensis</i>	13–14	131 ± 47
<i>C. simum</i>	21–24	121 ± 43
<i>R. unicornis</i>	6–11	122 ± 31
Free-ranging in Southern Africa:		
<i>D. bicornis</i>	21–26	83 ± 32
<i>C. simum</i>	15–20	64 ± 11
Reference ranges:		
U.S. Equine		50–198
University of California, Los Angeles, Hematology Research Lab		65–165

Paglia & Tsu, 2012

Introduction

✓ Diagnosis of IOD in the present:

1. Compare ferritine to baseline values
2. MRI (visceral iron excess) or liver biopsy
3. Rule out aquired overload
4. Genetic origin

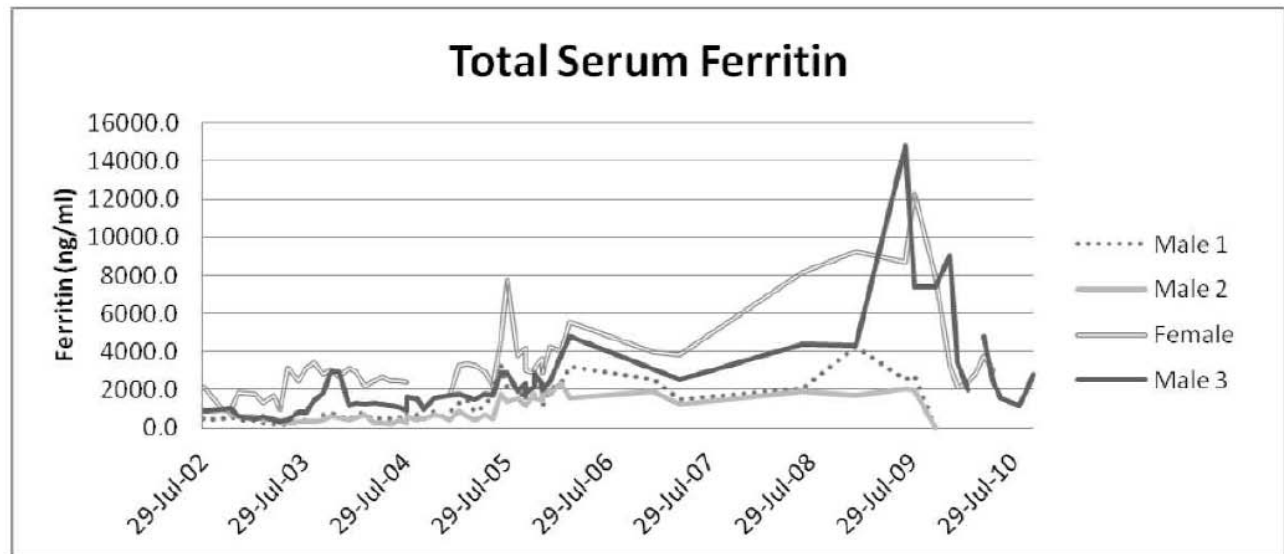
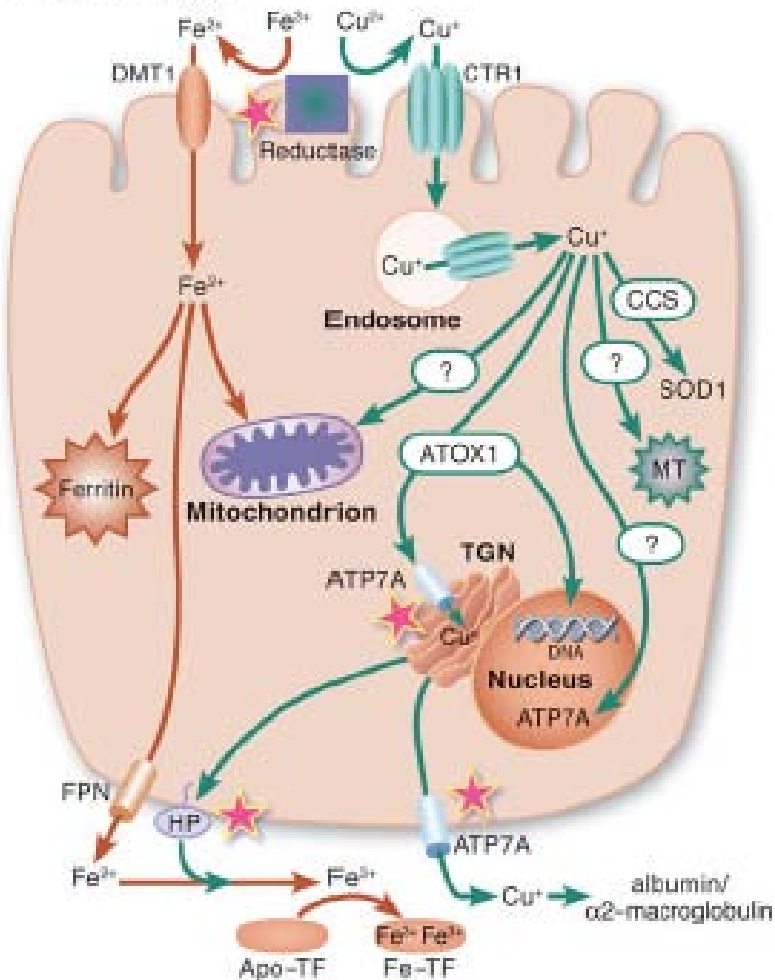


Figure 2. Total serum ferritin in 3:1 captive black rhinoceroses (*D. bicornis*) in a mixed-species savannah exhibit.

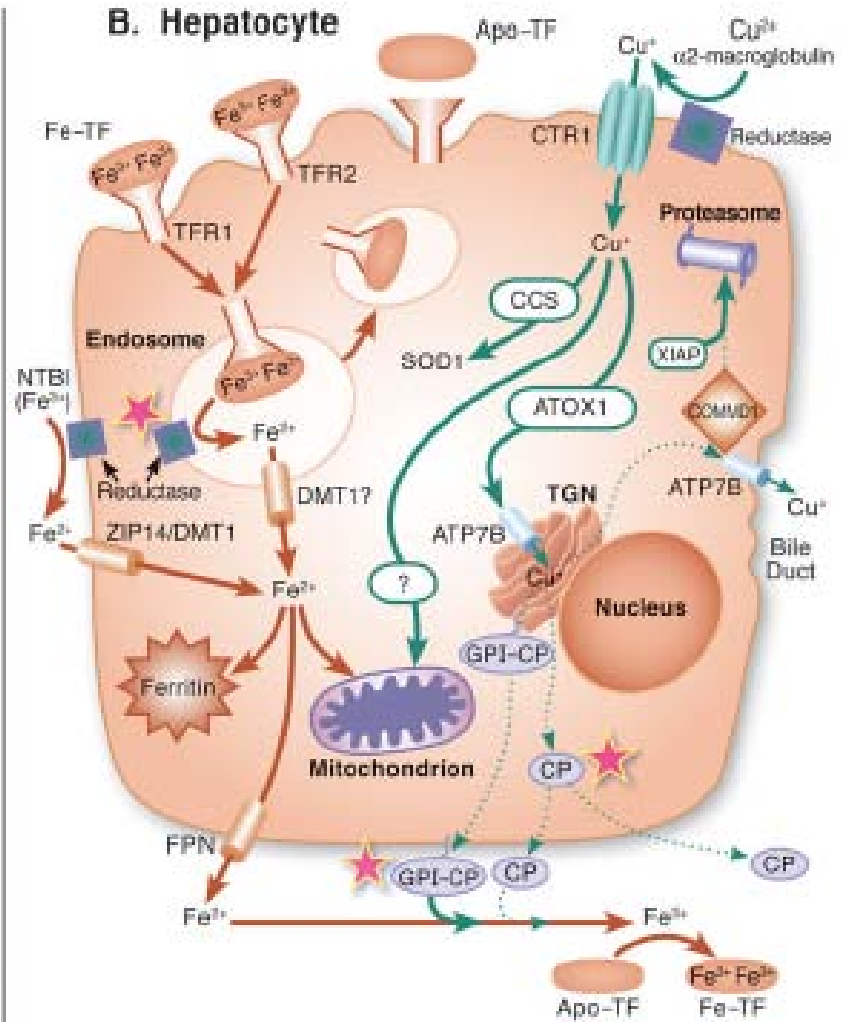
Mylniczenko et al, 2012

Iron metabolism

A. Enterocyte

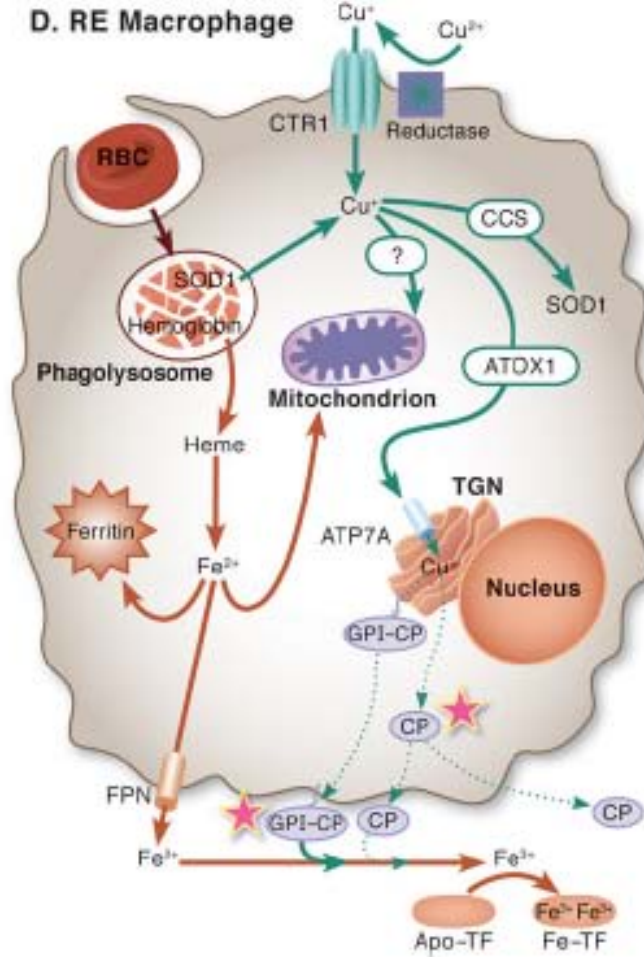
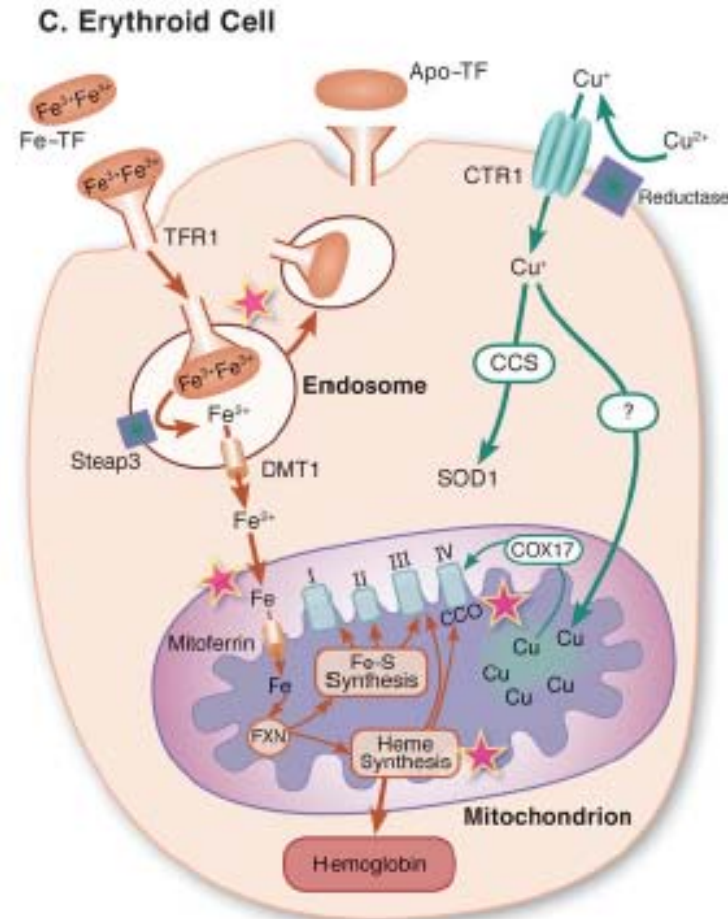


B. Hepatocyte



Collins et al, 2010

Iron metabolism



Collins et al, 2010

Rhino anatomy and digestibility characteristics

- ✓ Hindgut fermenter
- ✓ Species \neq retention time
- ✓ Species \neq digestibility
- ✓ \neq horses



Pony

(*Equus caballus*)

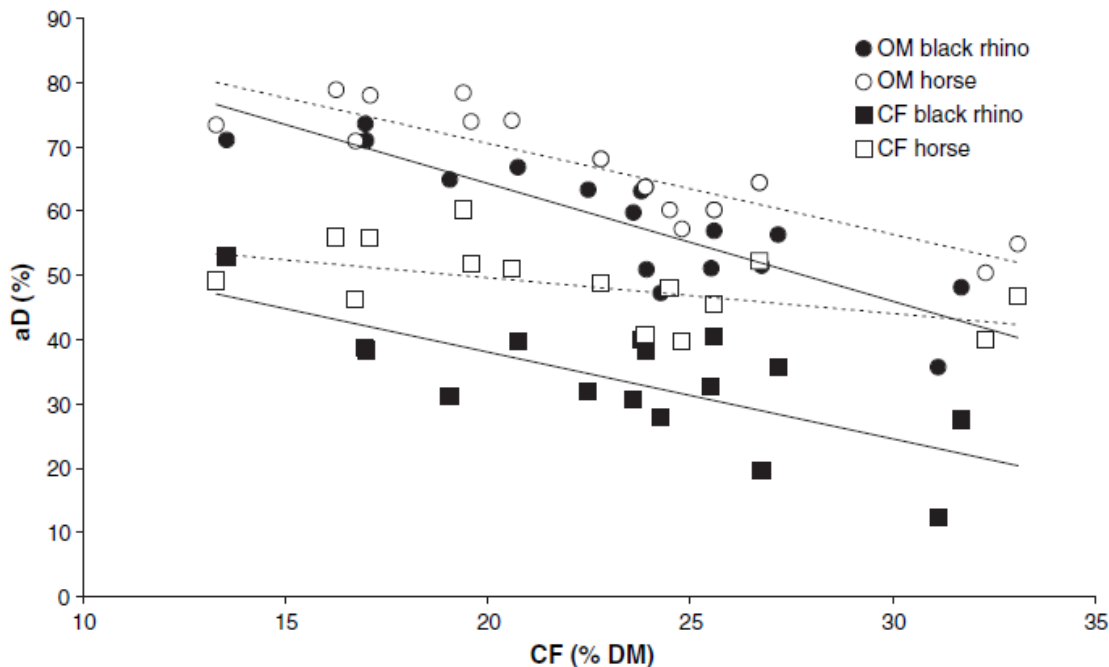
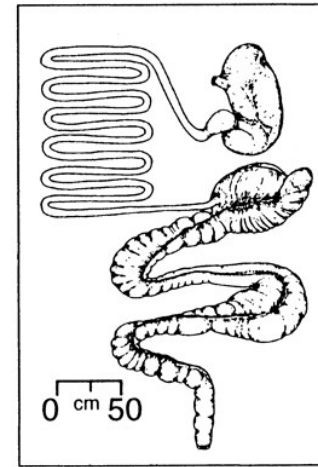
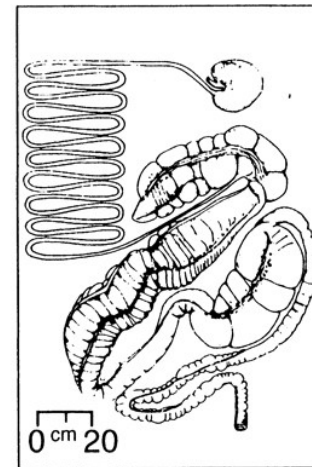
Body length: 164 cm



Rhinoceros

(*Diceros bicornis*)

Body length: 3.2 m



Clauss et al, 2006; Steuer et al, 2010

Rhino anatomy and digestibility characteristics

✓ Tannin Binding Salivatory Proteins (TBSP)

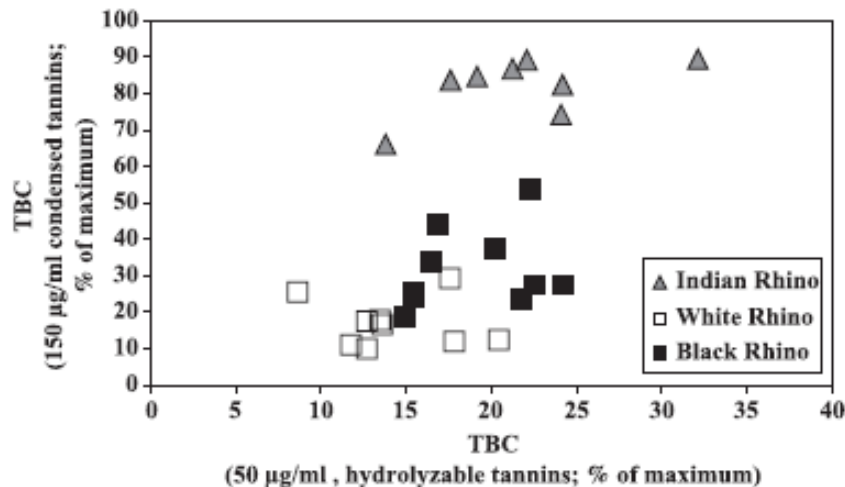


Fig. 1. Tannin-binding capacity (TBC) of salivary proteins of captive individuals of three rhinoceros species on regular zoo diets for tannic acid (a hydrolysable tannin) and quebracho (a source of condensed tannins).

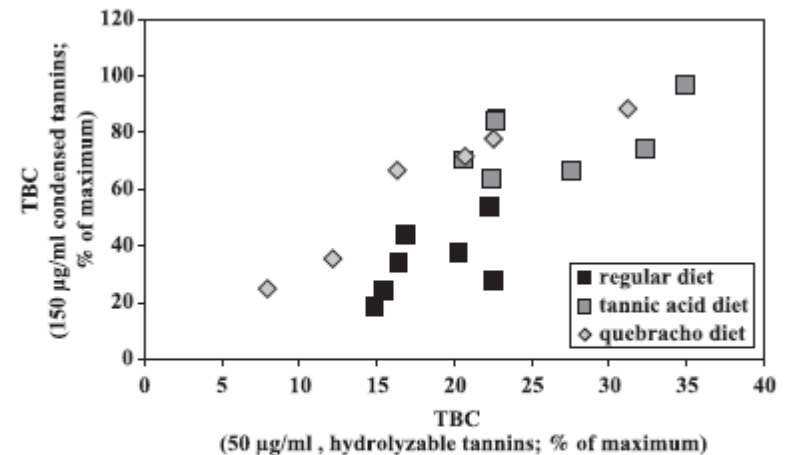


Fig. 2. Tannin-binding capacity (TBC) of salivary proteins of individual captive black rhinos on their regular zoo diet and on diets supplemented either with tannic acid or quebracho. TBC for tannic acid (a hydrolysable tannin) and quebracho (a source of condensed tannins).

Clauss et al, 2005

Diet composition wild black rhino's

Table 1 Diet composition (fresh matter) in free-ranging black rhinoceroses (*Diceros bicornis*)

Proportion of ingested diet (%)			
Shrubs and trees	Herbs	Grass	Source
87–95	5–13	0 (one observation)	Joubert and Eloff (1971)
54–81	18–41	0	Mukinya (1977)
81–94	6–19	0	Hall-Martin et al. (1982)
47–93	5–51	0	Oloo et al. (1994)
93–95	3–5	1	Atkinson (1995)
56–76	1–11	0–1	Pole (1995)
69	31	0	Hennig and Gindrig (2001)

Clauss et al, 2006

Diet composition wild black rhino's

Plant species^a

Biomass (%)

Bites (%)

- 1 *Grewia robusta*
- 2 *Coddia rudis*
- 3 *Phombago auriculata*
- 4 *Euclea undulata*
- 5 *Azima tetracantha*



van Lieverloo et al, 2009; Ghebremeskel et al, 1991; Dierenfeld et al, 1995

Laboratory of Animal Nutrition
veerle.vandendriessche@UGent.be

Diet composition wild black rhino's

Table 1. Seasonal variation of the iron content in the diet of three free-ranging black rhinoceros (*Diceros bicornis*) populations.

	Early dry season	Late dry season	Flushing period
Waterberg Plateau Park	61.2 ± 8.7 ^{aA}	49.5 ± 10.9 ^{bA}	50.7 ± 8.3 ^{bA}
Tswalu Kalahari Reserve	100.2 ± 14.8 ^{aB}	136.7 ± 47.0 ^{bB}	175.0 ± 31.5 ^{cB}
Great Fish River Reserve	76.4 ± 14.2 ^c	86.1 ± 19.0 ^c	84.2 ± 20.0 ^c

Fe (ppm) dry matter

Table 2. Seasonal variation of the condensed tannin content in the diet of three free-ranging black rhinoceros (*Diceros bicornis*) populations.

	Early dry season	Late dry season	Flushing period
Waterberg Plateau Park	4.3 ± 0.5 ^{aA}	4.3 ± 0.5 ^{bA}	3.4 ± 0.6 ^{cA}
Tswalu Kalahari Reserve	1.8 ± 0.7 ^{aB}	1.7 ± 0.7 ^{aB}	2.8 ± 1.6 ^{bAB}
Great Fish River Reserve	3.3 ± 1.6 ^{aC}	3.4 ± 1.5 ^{aA}	1.9 ± 1.7 ^{bB}

Helarey et al, 2012

Diet composition of captive black rhino's

Table 1. Measured consumption and iron content on a dry matter basis of diet items consumed by four black rhinoceroses at Disney's Animal Kingdom in July 2011 (current as of submission)

Maintenance items (fed daily)	Consumed (g/animal/day)	Fe (ppm) dry matter
Timothy hay	9,670	76
Disney's Animal Kingdom Wild Herbivore Pellet 5Z0X	6,810	306
Bermuda hay	4,280	180
Browse	~11,000	See values below
Training	~3,800	51 ± 15 ^a
Enrichment	~1,800	134 ± 35 ^a
Varieties of browse offered		
Willow (spring/summer months)	8,500	135
Banana (spring/summer months)	2,270	110
<i>Elaeocarpus</i> (winter only)	2,270	102
Ear leaf acacia (winter only)	7,500	72
Pine cones (1× a week in season)	640	251

^a Average "Training" iron value calculated based on analysis of carrots, apples, sweet potato, watermelon, oatmeal, and low-starch primate biscuit; Average "Enrichment" iron value calculated based on analysis of cucumber, carrot, romaine lettuce, green leaf lettuce, zucchini, endive, kale, and bean paste; Both are shown as averages plus or minus standard errors.

Mylniczenko et al, 2012; Clauss et al, 2012

Diet composition of captive black rhino's

MINERAL	FORAGE		TEMPERATE			MAINTENANCE RECOMMENDATION FOR HORSES ⁴
	BLACK RHINOCEROS ¹	WHITE RHINOCEROS ²	BROWSE ³	LUCERNE ³	GRASS ³	
mg/kg DM						
Fe	82 (12–215; <i>n</i> = 28)	177 (91–220; <i>n</i> = 6)	120 (64–191; <i>n</i> = 12)	180	129 (46–391; <i>n</i> = 10)	40–70
Mn	60 (1–269; <i>n</i> = 28)		92 (14–248; <i>n</i> = 12)	40	74 (37–147; <i>n</i> = 9)	40
Cu	5 (1–12; <i>n</i> = 28)	4 (3–6; <i>n</i> = 6)	11 (7–20; <i>n</i> = 12)	11	6 (4–9; <i>n</i> = 6)	10
Zn	14 (3–67; <i>n</i> = 28)	23 (16–35; <i>n</i> = 6)	53 (13–121; <i>n</i> = 12)	24	19 (15–23; <i>n</i> = 5)	40

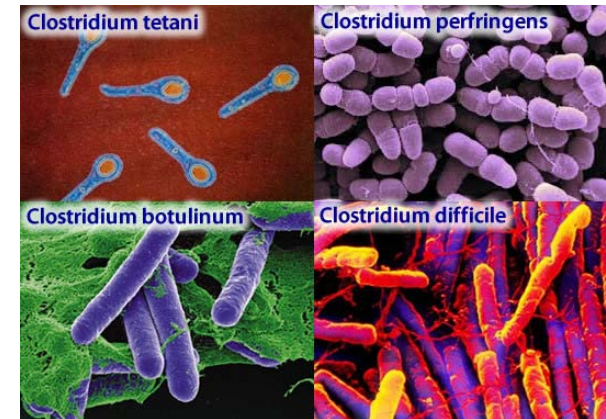
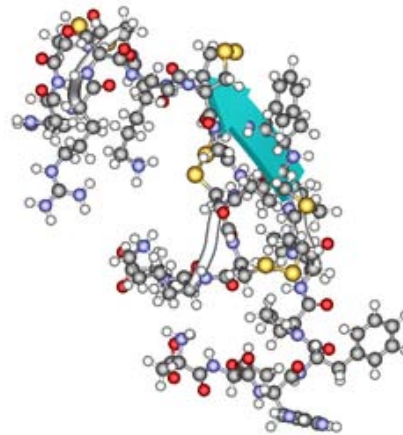
Past/current treatments

- ✓ Limit uptake of dietary iron to 300mg Fe/kg DM/day
 - ☐ Add more browse to their diet
 - ☐ Develop concentrates with lower Fe and Vit C content
 - ☐ Use hays with higher tannins or phenolics
 - ☐ White, ionized salt blocks
 - ☐ Analyse water source (< 0,3ppm Fe)
 - ☐ Routine analysis of all diet components
- ✓ Add iron chelators (mimosine)?
- ✓ Phlebotomy (effect on hepcidine)?

Clauss et al, 2012; Lanvin 2012

Current/future research

- ✓ Diet-related hemolysis?
- ✓ Role of hemolysin producing bacteria?
- ✓ Difference in iron excretion between wild and captive rhino's?
- ✓ Difference in hepcidine levels?
- ✓ ≠ intestinal bacterial species?
- ✓ Copper deficiency?
- ✓ Other minerals?
- ✓ Stress?
- ✓ Insulin resistance?
- ✓ Develop BCS



Nielsen et al, 2012; Ganz & Nemeth, 2012; Ganz et al, 2012

Conclusion

From a nutritionists point of view, there are still a lot of unknowns concerning the development of IOD in captive browser rhino's =>



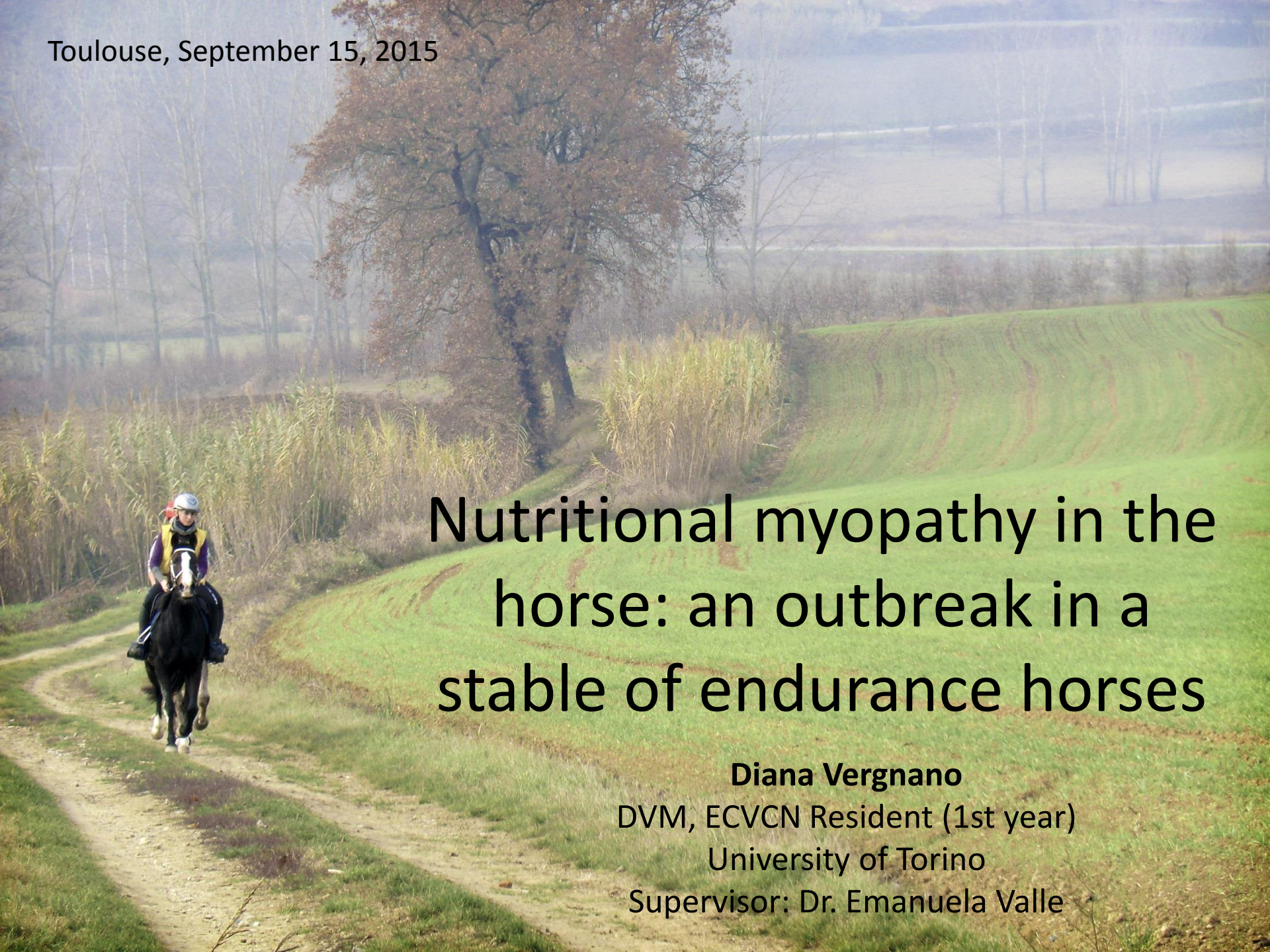
Thank you



Iron overload disease in browser rhinoceroses

- ✓ **Review of laboratory and necropsy evidence for Iron Storage Disease acquired by browser rhinoceroses.**
 - ✓ Donald E. Paglia and I-Hsien Tsu
 - ✓ Journal of Zoo and Wildlife Medicine 43 (3)
 - ✓ 2012

Toulouse, September 15, 2015

A person wearing a helmet and riding gear is riding a black horse on a dirt path. The path is surrounded by green grass and tall, dry grass. In the background, there are trees with autumn-colored leaves and a hazy landscape.

Nutritional myopathy in the horse: an outbreak in a stable of endurance horses

Diana Vergnano

DVM, ECVCN Resident (1st year)

University of Torino

Supervisor: Dr. Emanuela Valle

The nutritional consultant service received a phone call...

- **When:** March 2015, rainy period
- **Who:** veterinarian
- **Where:** endurance stable in Piedmont, Cuneo
- **Why:** suspected poisoning

Anamnesis

Horses involved: **two horses** of the same stable
with similar symptoms

Another horse showed similar symptoms in
autumn and died

Anamnesis

Horse 1: Duke

- Arabian horse, 12 years, gelding, BCS 4, 500 kg
- Sudden onset of clinical signs:
fasciculations, muscle tremors,
dysphagia, recumbency
- The day before participated in an Endurance competition

Anamnesis

Horse 2: Desdemona

- Pony breed, 15 years, female, BCS 5.5, 250 kg
- Clinical signs appeared one day after Duke's
- Symptoms: dysphagia, ptyalism, mucosal hyperhemia, muscle fasciculation

Anamnesis

Horse 2: Desdemona

Dysphagia: involvement of tongue, pharyngeal and masticatory muscles



Anamnesis



Anamnesis



Anamnesis

Feed composition

- First cut meadow hay, poor quality
- Concentrate: mixed flaked cereals



Roughage/Concentrate Ratio
70:30

Diagnosis – Laboratory findings

Hematological analysis:

Duke

↓ RBC: 5,94 (6,8-12,9)*
↓ HCT: 27,5 (30-53)
↓ HB: 10,4 (11-19))

} slight normochromic normocytic **anemia**
(normal leucocytes and platelets)

Desdemonia

↓ RBC: 5,6 (6,8-12,9)
↓ HCT: 25,8 (30-53)
↓ HB: 10,9 (11-19)
↓ Lym 850 (1500 – 7700)

} moderate normochromic normocytic **anemia**
moderate lymphopenia

*Lab reference values

Diagnosis – Laboratory findings

Biochemical analysis:

Duke

↓ PT: 5,3 (5,6-8 mg/dl) *

↑ Azotemia: 30,1 (10-25 mg/dl)

↓ Crea: 0,88 (1,2-1,9 mg/dl)

↑ CK: 558 (60-330 U/l)

↑ LDH: 1215 (300-720 U/l)

↑ AST: 717 (140-320 U/l)

↑ ALP: 579 (60-320 U/l)

↑ Bil: 3,65 (0,2-1,9 µmol/l)

↓ Ca: 8,1 (9-13 mg/dl)

↓ Na: 122 (133-150 mmol/l)

↓ Cl: 82 (97-109 mmol/l)

↓ K: 2,7 (3-5,3 mmol/l)

↓ Mg: 1,54 (1,6-2,9 mg/dl)

Desdemonia

↑ Azotemia: 45,3 (10-25 mg/dl)

↓ Crea: 1,1 (1,2-1,9 mg/dl)

↑ CK: 1651 (60-330 U/l)

↑ LDH: 1221 (300-720 U/l)

↑ AST: 906 (140-320 U/l)

↑ ALP: 1102 (60-320 U/l)

↑ Bil: 6,8 (0,2-1,9 µmol/l)

↓ Ca: 8,9 (9-13 mg/dl)



↓ Na: 128 (133-150 mmol/l)

↓ Cl: 94 (97-109 mmol/l)

Diagnosis: main findings

Principal localization of symptoms: **muscles**

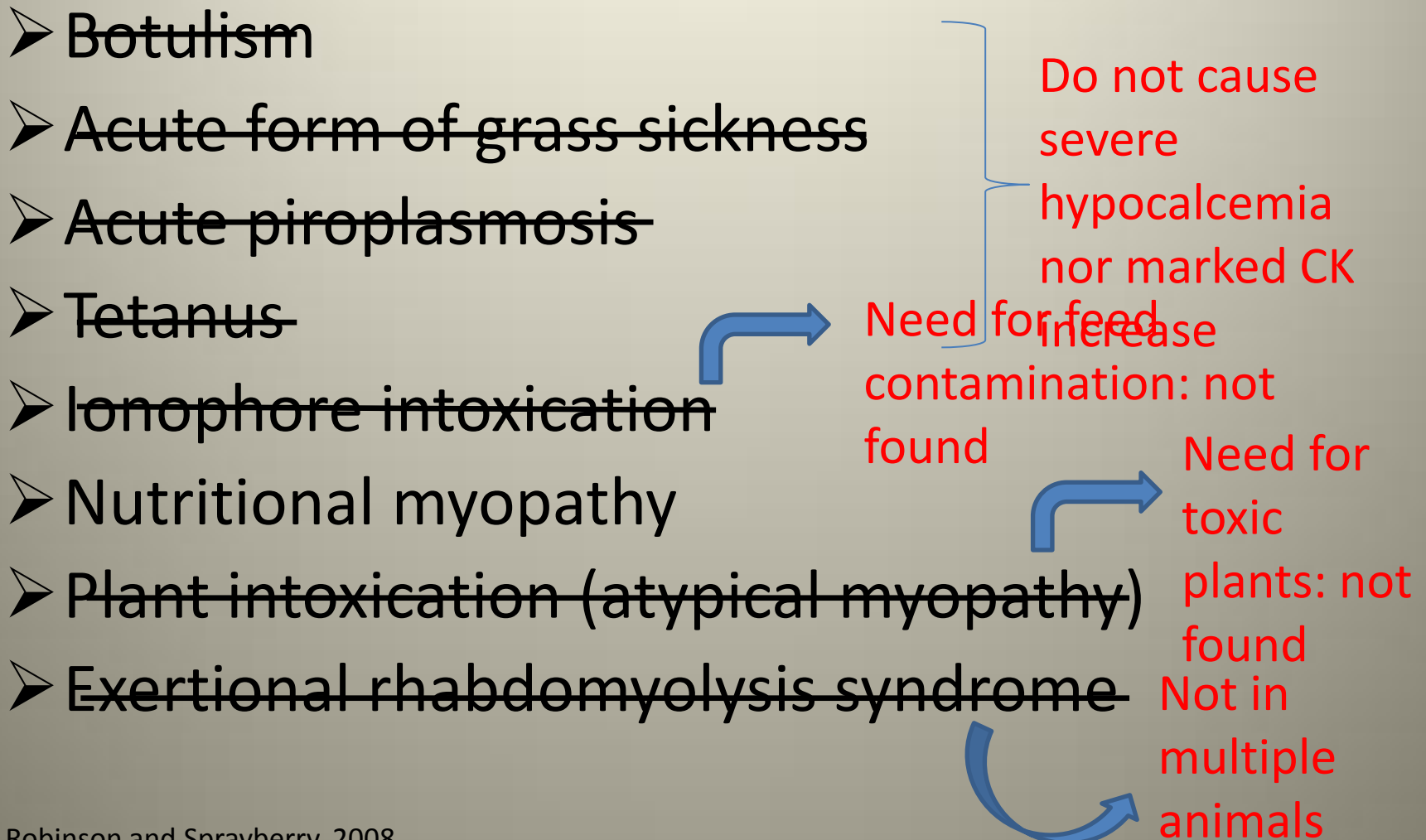
Hematological analysis: slight anemia

Biochemical analysis:  CK, LDH, AST
 Serum Calcium level

Differential Diagnosis

- Botulism
- Acute form of grass sickness
- Acute piroplasmosis
- Tetanus
- Ionophore intoxication
- Nutritional myopathy
- Plant intoxication (atypical myopathy)
- Exertional rhabdomyolysis syndrome

Differential Diagnosis: rule out of....



Differential Diagnosis: Feed Analysis

- Feed composition: vitamin E and Selenium content

Desdemona	Intakes	Requirements
Vit E	155,6 IU	250 IU
Se	0,26 mg	0,5 mg

- Piedmont: area of low selenium concentration in the soil

Differential Diagnosis: Vit E and Se

Test for serum Selenium and Vitamin E

Duke

Se: 26 (100-200 ug/l)*

Vit E: 0,8 (>1 mg/l)



Low Se

Low Vit E



Desdemona

Se: <10 (100-200 ug/l)

Vit E: 9,3 (>1 mg/l)



Low Se

Normal Vit E



Diagnosis

Nutritional Myopathy

Nutritional Myopathy

Nutritional myodegeneration

Deficiency of:

- Selenium
- Vit E (not always)

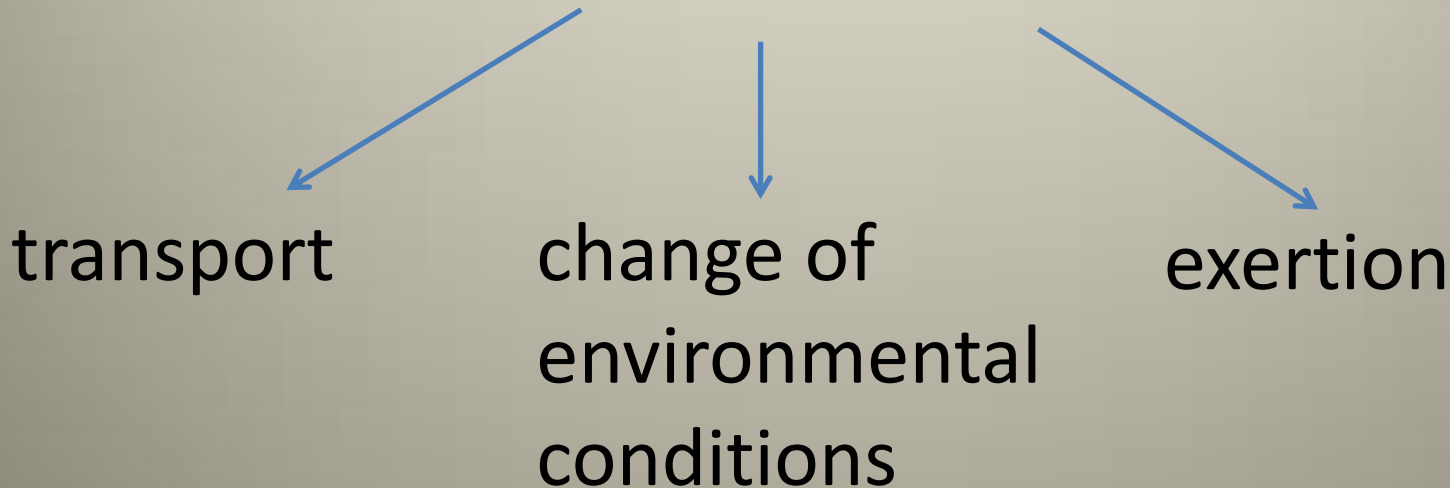
Poorly aerated, acid soils
Soils originated from volcanic rock
Biological antioxidants
Soils with a high content of iron or sulfur
prevent cellular damage from reactive oxygen species resulting from normal cellular metabolism

Poor quality hay
Rancid feed
Prolonged storage of grass/grains
Addition of fish or plant oils

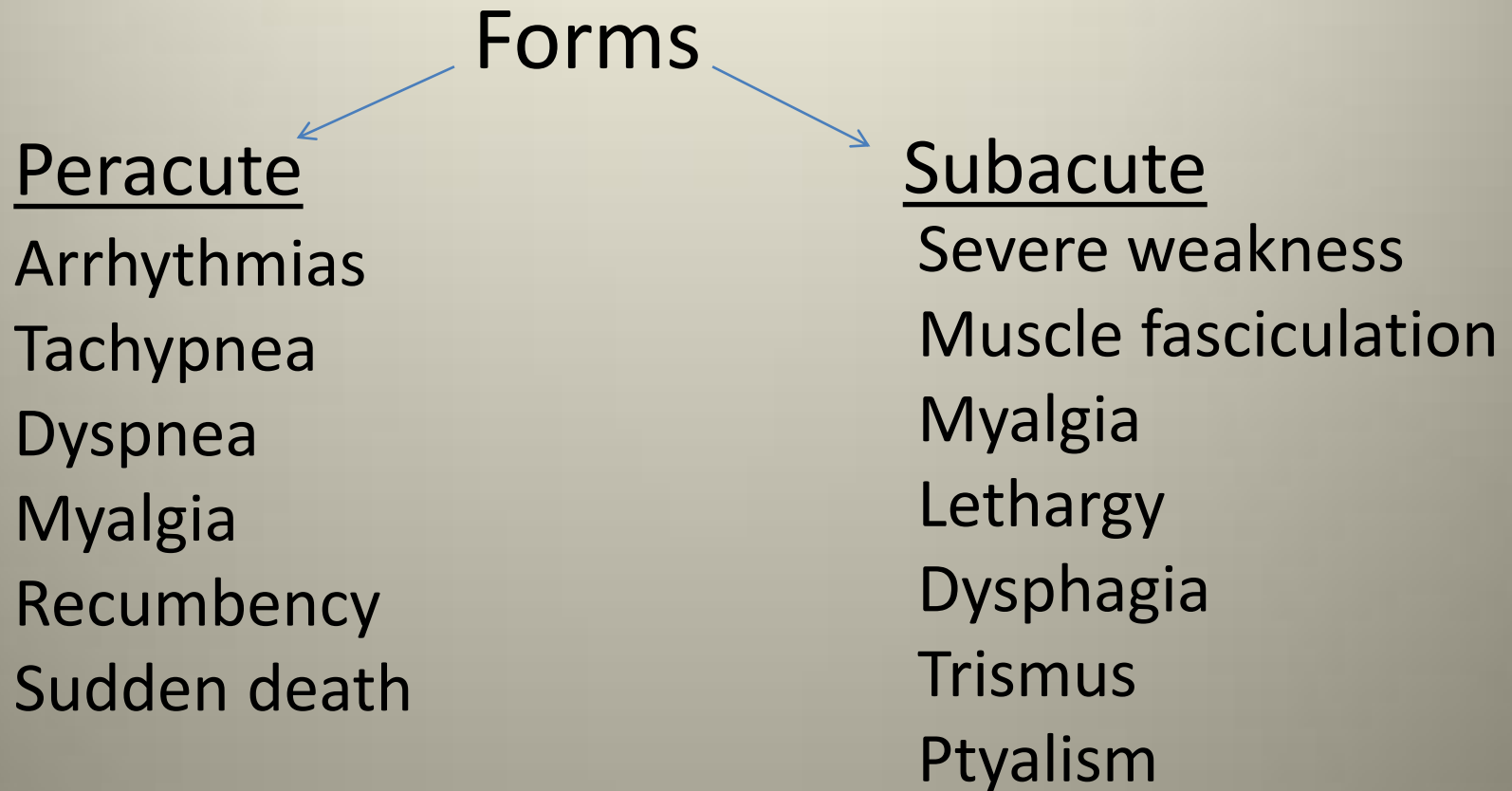
Nutritional Myopathy

Any age (from 2 months)

The onset of nutritional myodegeneration in adult horses probably requires some stress factors such



Nutritional Myopathy



Diagnosis

Nutritional Myopathy: Laboratory findings:

- Acute increase of CK and AST
- Severe hypocalcemia
- Hyperproteinemia
- Azotemia
- Hyponatremia
- Hypochloremia
- Hyperkalemia
- Hyperphosphatemia
- Respiratory Acidosis
- Myoglobinuria


Therapy

- No physical activity
- Supportive care: fluids
- Administration of selenium (1mg/day PO)
- Administration of vitamin E (5'000-10'000 IU/day PO) if deficient

Therapy

Which form of Selenium should be used?

PO administration better than IM

- Organic Source  probably more efficiently utilized (not confirmed to date)
- Inorganic Source: Sodium Selenite

Therapy

Which form of Vitamin E should be used?

α -tocopherol and α -tocopheryl acetate:
most biologically available forms

Vitamin E	RRR-form (natural)	All-rac-form (synthetic)
α -tocopherol	1.49 IU/mg	1.10 IU/mg
α -tocopheryl acetate	1.36 IU/mg	1.00 IU/mg

Therapy: new diet formulation

- Maintain roughage/concentrate ratio at max 70:30
- Use a better quality hay
- Allow access to pasture

For all the horses in the stable

Therapy: new diet formulation

- Introduction of a feed supplement

Additives per kg:

Vitamin E 100'000 mg (all-rac-alpha-tocopheryl acetate - 3a700)

Selenium 10,5 mg (organic form - 3b8.10)

Recommended dosage: 25-50 g



Therapy: new diet formulation

- Introduction of a feed balancer for all the stable

INGREDIENTS PER KG

Crude protein 9,9 %

Crude fiber 11,0 %

Crude Fat 8,0 %

Crude Hay 10,0 %

Calcium 1,3 %

Phosphorus 0,5 %

Vitamin E 400 IU

Selenium 0,7 mg

Recommended dosage:

150-300 g/100 kg BW



Therapy: new diet formulation

	Feed supplement 50 g	Feed balancer 1'000 g	Total
Vitamin E	5'000 IU	400 IU	5'400 IU
Selenium	0,52 mg	0,7 mg	1,22 mg



Follow up

- **Duke:** died prior to starting therapy
- **Desdemona:** started to recover after 2 weeks
- **Stable:** no more cases, periodic exams are fixed

References

- Robinson and Sprayberry, Current Therapy in Equine Medicine, ed 6, vol 3, 2008
- Lindberg, Feedstuffs for horses, Equine Applied and Clinical Nutrition, ed 1, 2013
- MacLeay, Disorders of Muscoskeletal System, Equine Internal Medicine, ed 3, 2009
- Ludvikova et al., Selenium and Vitamin E Status Correlated with Myopathies of Horses Reared in Farms in the Czech Republic, Acta Vet. Brno 74: 377–384, 2005
- Nutrient Requirements of Horses, ed 6, 2007
- Zeyner and Harris, Vitamins, Equine Applied and Clinical Nutrition, ed 1, 2013
- Aleman, A review of equine muscle disorders, Neuromuscular Disorders 18:277–287, 2008
- McGorum, Pirie, Keen, Nutritional Considerations in grass sickness, botulism equine motor neuron disease and equine degenerative myeloencephalopathy, Equine Applied and Clinical Nutrition, 2013
- Coenen, Macro and trace elements in equine nutrition, Equine Applied and Clinical Nutrition, 2013

Toulouse, September 15, 2015

Thank you!

Nutritional myopathy in the horse: an outbreak in a stable of endurance horses

Diana Vergnano

DVM, ECVCN Resident (1st year)

University of Torino

Supervisor: Dr. Emanuela Valle



Energy and nutrient costs of infectious diseases in animals



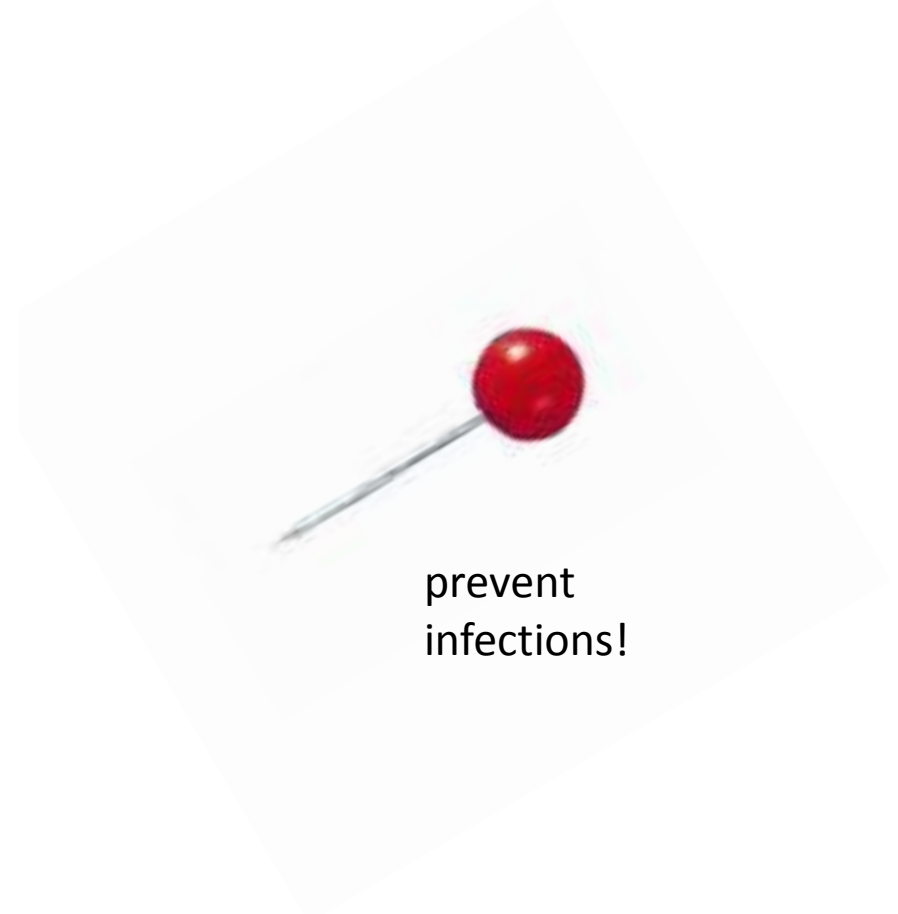
energy and nutrient costs of infections

Outline

- The way, infections affect energy and nutrient balance
- Quantifying of costs
- Practical examples
- One example for limiting the costs
- Conclusion



first off—there are two ways to optimize performance...



1. optimize feed +
environmental conditions

2. reduce energy and nutrient
costs through prevention

potential pathogens

fungi

protozoa

helminths

viruses

bacteria



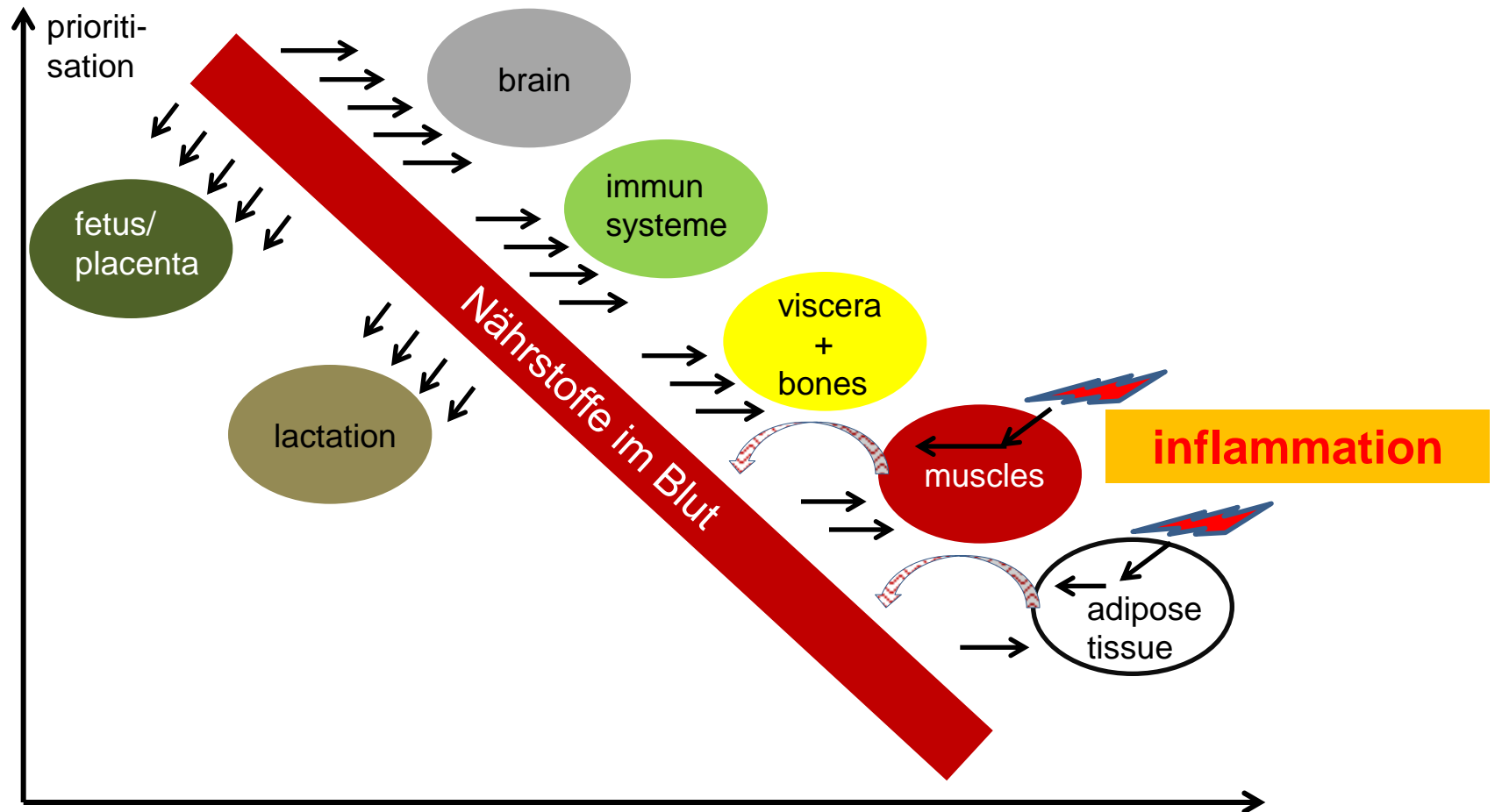
Kaspers 2014: Vertebrates need a fully functional immune system to survive

Players of the immune response...

Mechanisms of innate and acquired immunity (TIZARD 2013)

part	innate immune system	adaptive immune system
characterization	permanently ready for action	turned on by antigens
involved cells	Macrophages, dendritic cells, neutrophils, natural killer cells	T- and B-cells
evolutionary history	ancient	recent
onset	very fast (min to h)	slow (days to weeks)
specificity	rather low, common microbial structures	antigen-specific
power	potentially overwhelmed	rarely overwhelmed
memory	no	pronounced
efficiency	does not improve	improves with exposure

prioritization of supply



Ranking of the different organs with respect to their ability to utilize nutrients and nutrient release in case of infection/inflammation (modified after ELSASSER et al. 2007)

to think....

Which adaptive reactions are there?



Infections – adaptive reactions

HOST NUTRITIONAL RESPONSES TO INFECTION

1237

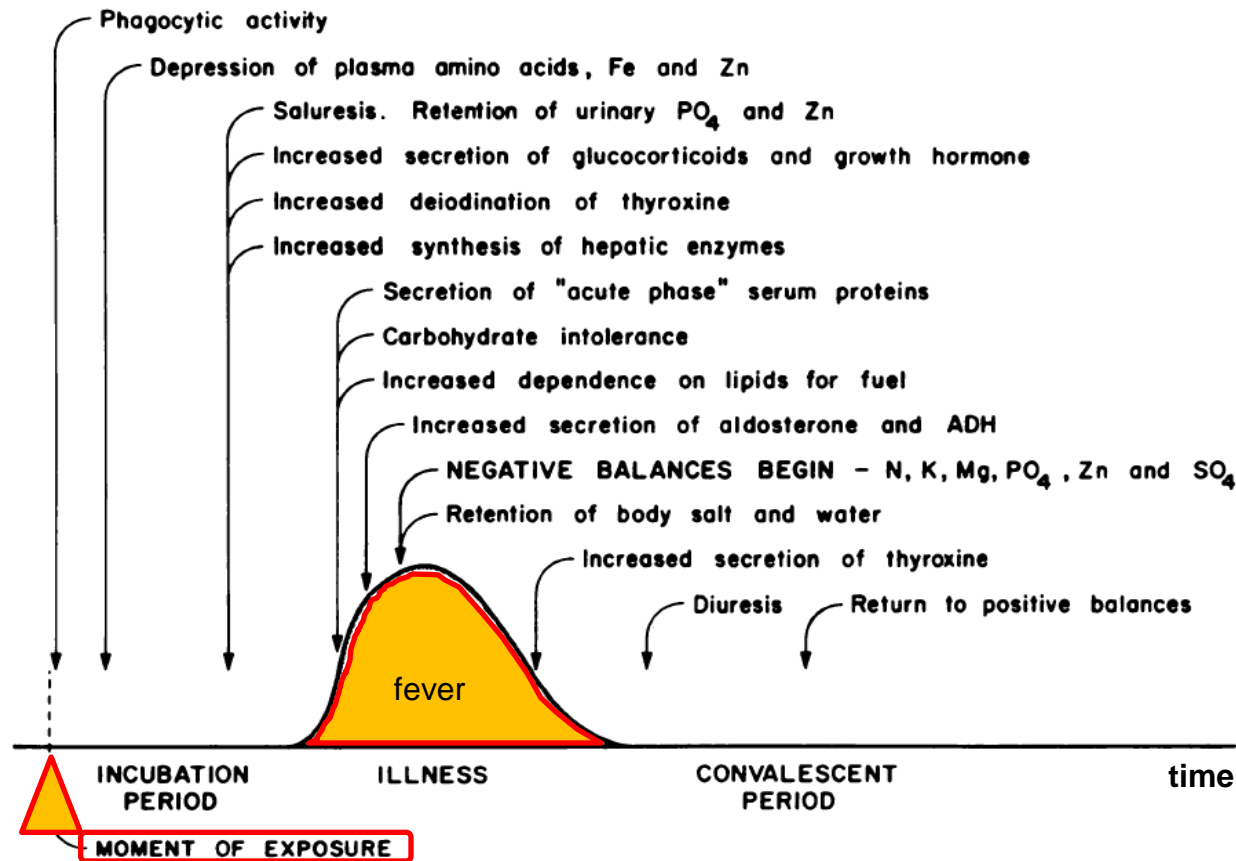
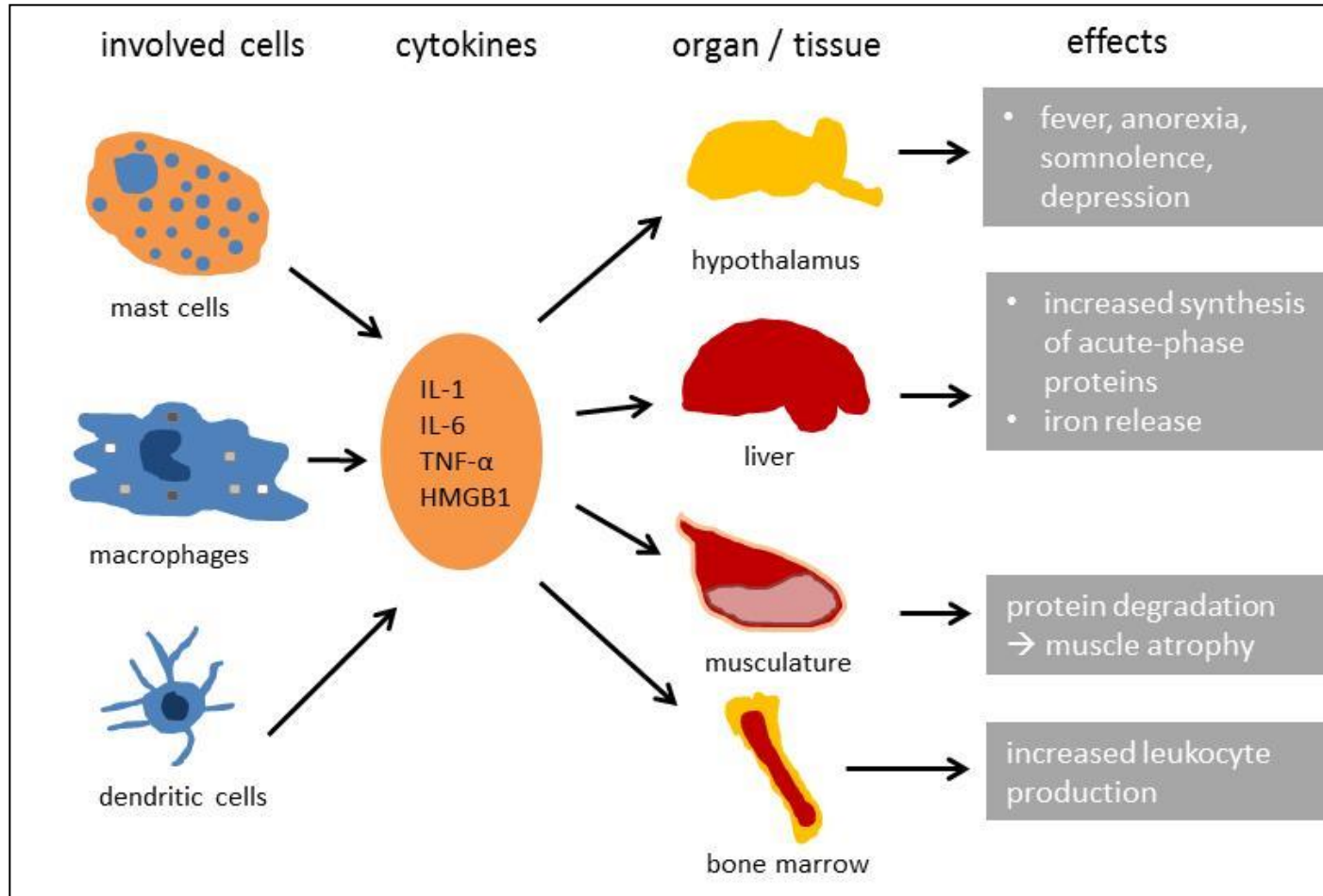


FIG. 1. Schematic representation of the sequence of nutritional responses that evolves during the course of a "typical" generalized febrile infectious illness (5).

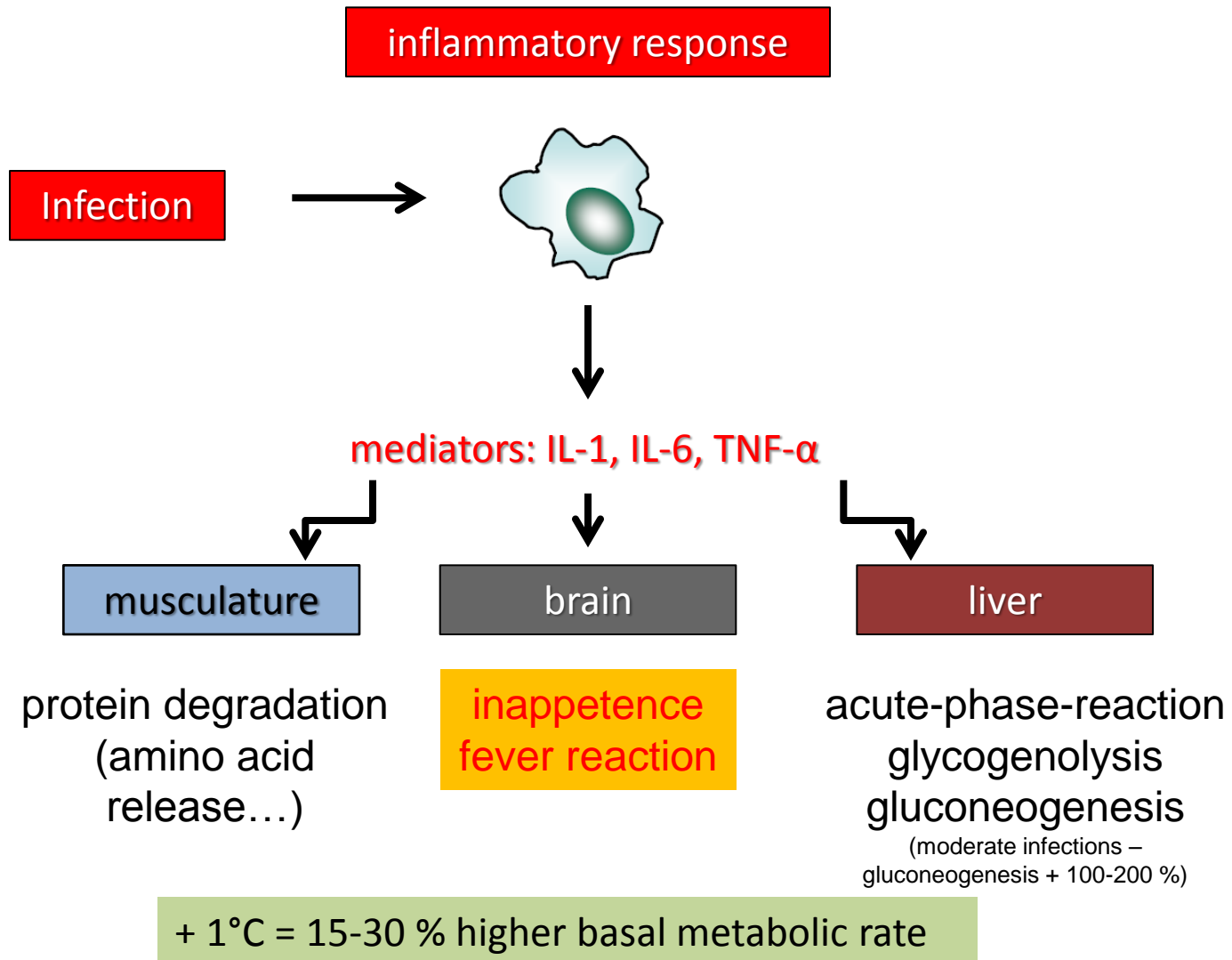
William R. Beisel,³ M.D., F.A.C.P. *The American Journal of Clinical Nutrition* 30: AUGUST 1977, pp. 1236–1247. Printed in U.S.A.

infection mechanisms



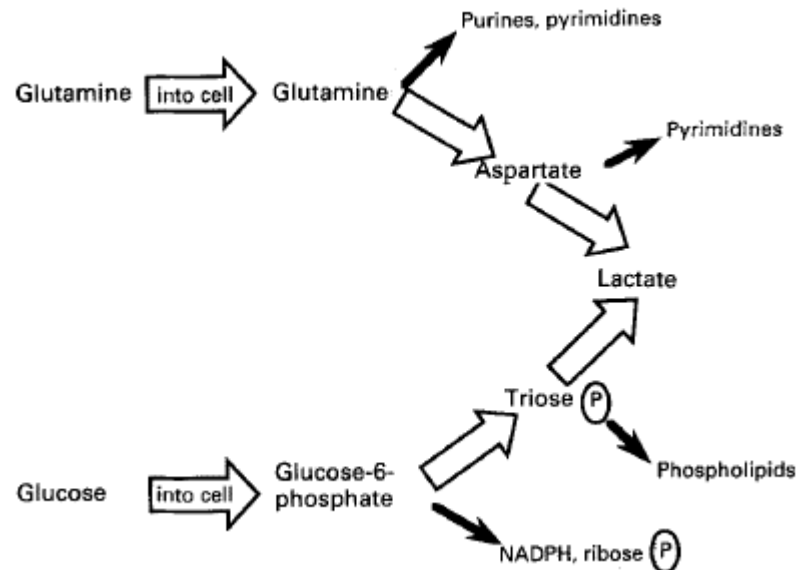
Typical reactions in the body or in tissues and organs to inflammatory stimuli. Systemic effects are based essentially on the effects due to release of the four major cytokines by sentinel cells, mast cells, macrophages and dendritic cells (modified from Le Floch et al. 2004, Tizard, 2013). The major sickness-inducing cytokines are IL-1, IL-6, TNF- α and the high-mobility group box protein 1 (HMGB1); from Visscher (2014).

infection mechanisms



What cells of the immune system need...

- glutamine
- glucose
- possibly using of ketone bodies

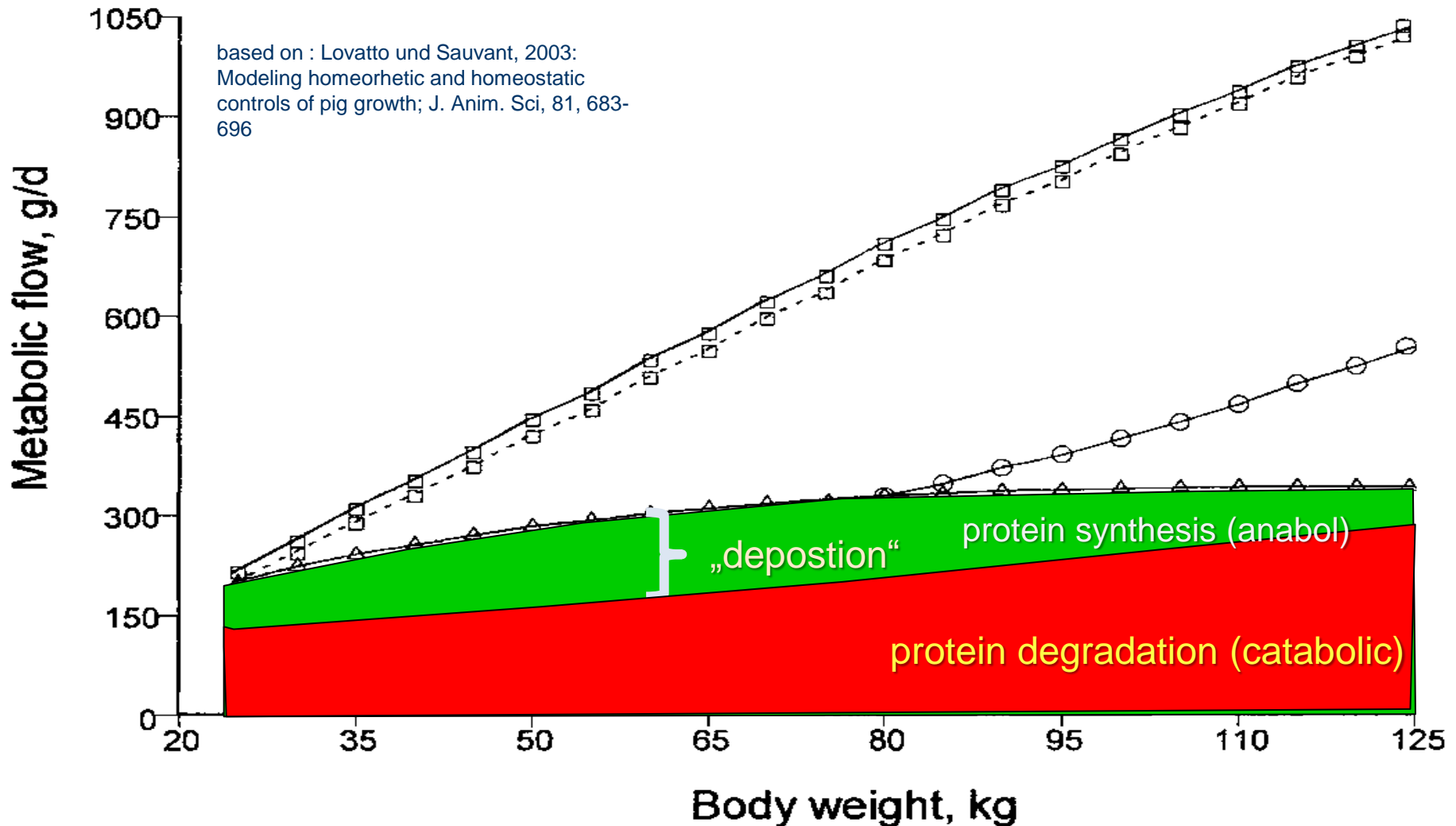


catabolic metabolism....

an unfavourable way of providing of nutrients

- The amino acid pattern of muscle protein breakdown differs from the current requirement to combat infection
- the negative nitrogen balance is the inevitable consequence of this catabolic response to provide amino acids for the defense
- The extent of these adverse metabolic response increases depending on the severity of the infection

growth....



Simulated metabolic fluxes of protein and lipids for the growth of pigs. Anabolic and catabolic nutrient flows are characterized by solid and dotted lines; \square = visceral proteins, Δ = body protein, o = fats

How to analyze?

- The immune system is not restricted in an allocated organ
- The immune system cells migrate throughout the body
- The immune system consists out of many different components
- The immune system changes its functional states
- The components of the immune system do compete for the same resources energy and amino acids
- You can not measure the "immunocompetence"

based on Kaspers 2014

How to analyze?

In vitro

**Stimulation of individual components
of the immune system**

Analysis of energy needs

Analysis of nutrient requirements



Extrapolating to the whole body

Klasing 1998

- The mass of all constituents and products of the immune system (cells and proteins) is less than 5 % of body mass in chickens
- Leucopoiesis during an immune response accounts for less than 1 % (lysine requirement) of daily weight gain of a growing chicken

→ Costs are minimal compared with growth and egg production

calculation of energy and nutrient costs...

Example lysine

I.G. Colditz / Livestock Production Science 75 (2002) 257–268

261

Utilisation of lysine for maintenance of the immune system and during an immune response in chickens (adapted from Klasing and Calvert, 1999)

Process	Maintenance		LPS challenged	
	Production mg/kg/day	Cost μmol lys/kg/day	Production mg/kg/day	Cost μmol lys/kg/day
Leucopoiesis	650	45.5	1300	90.9
Ig synthesis	114	65.6	121	69.6
Acute phase proteins	~ 0	~ 0	710	386
Total for immunity	764	111	2131	546
% for immunity		1.17		6.71

calculation of energy and nutrient costs...

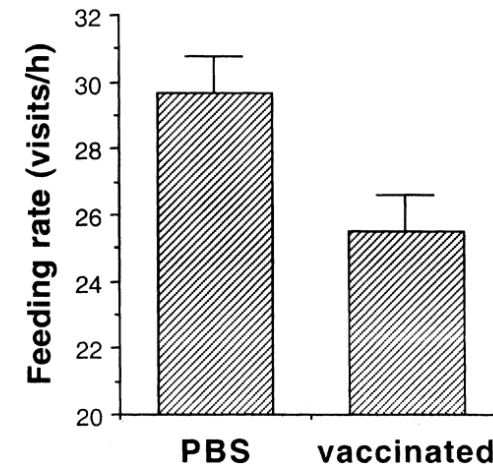
How to analyze?

In vivo

stimulation of the immune system

Analysis of the effect on other characteristics: basal metabolism, growth, litter size, **behavior**, performance, synthesis

protein-Antigen



Raberg et al. Ecology Letters 2000; 3, 382-386

based on Kaspers 2014

In vivo costs of a stimulation of the immune system...

Effect of stimulation of the immune system (adaptive) on the basal metabolic rate (modified by Scanes and Braun 2013)

species	changes in energy maintenance requirements (in %)*	Quelle
House sparrow (<i>Passer domesticus</i>)	+ 29	MARTIN et al. (2003)
Great tit (<i>Parus major</i>)	+ 9	OTS et al. (2001)
Blue tit (<i>Parus caeruleus</i>)	+ 8 bis 13 (n.s.)	SVENSSON et al. (1998)
Common quail (<i>Corturnix corturnix</i>)	-~7	BOUGHTON et al. (2007)

* following phytohemagglutinin challenge

In vivo costs of a stimulation of the immune system...

Estimated energy costs (percentage increase in the basal metabolic rate relative to the control) of vertebrate animals for the immune response after different treatments (modified after Lochmiller and Deerenberg 2000); from Visscher (2014)

species	immuno-stimulation through	costs (in %)	source
human	sepsis and injury	57	CLARK et al. (1996)
	sepsis	30	KREYMANN et al. (1993)
	sepsis	30	CARLSON et al. (1997)
	typhoid vaccination	16	COOPER et al. (1992)
	sickle cell disease	15	BOREL et al. (1998)
rat	inflammation (due turpentine-injection)	28	COOPER et al. (1994)
	IL-1 infusion	18	TOCCOBRADLEY et al. (1987)
mouse	KLH challenge ^a	30	DEMAS et al. (1997)
sheep	endotoxins	28	FEWELL et al. (1991)
	endotoxins	10-49	BARACOS et al. (1987)
duck	endotoxins	23	MARAIS et al. (2011)

vaccination: +16 %

sepsis: + 57 %↑

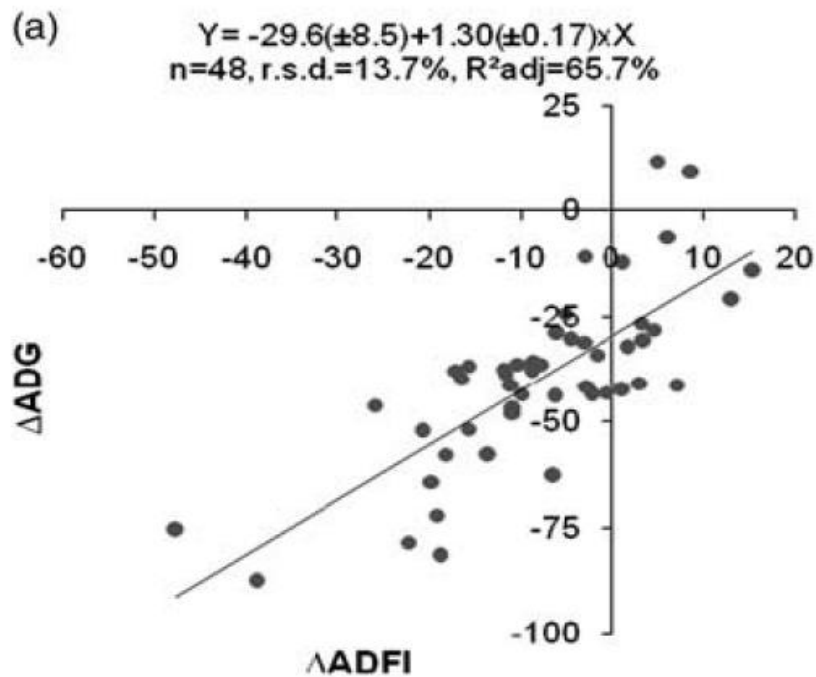
In vivo costs of a stimulation of the immune system...

Estimated changes (percentage change compared to the control) in feed intake (FI), average daily gain (ADG), nitrogen excretion in the urine (N), protein degradation rate (PAR), protein synthesis rate (PSR) and total body protein content (BPC) in vertebrates under the influence of immuno-stimulation (modified after Lochmiller and Deerenberg 2000); from Visscher (2014)

species	interventionEingriff	parameter	change (in %)	source
swine	PRRS ^a -vaccination + LPS	FI	-15	SPURLOCK et al. (1997)
		ADG	-21	
poultry	HVT ^b -vaccination	FI	-3	LEE u. REID (1977)
	SRBC ^c	FI	0	HENKEN and BRANDSMA(1982)
		ADG	0	
	SRBC	ADG	-13	KLASING et al. (1987)
	endotoxins	ADG	-18	
human	sickle cell disease	PAR	+32	BOREL et al. (1998)
		PSR	+38	
	sepsis	N- (Harn)	+160	CARLSON et al. (1997)
	sepsis and injury	BPC	-12	CLARK et al. (1996)
rat	sepsis	PAR	+40	HOBLER et al. (1998)

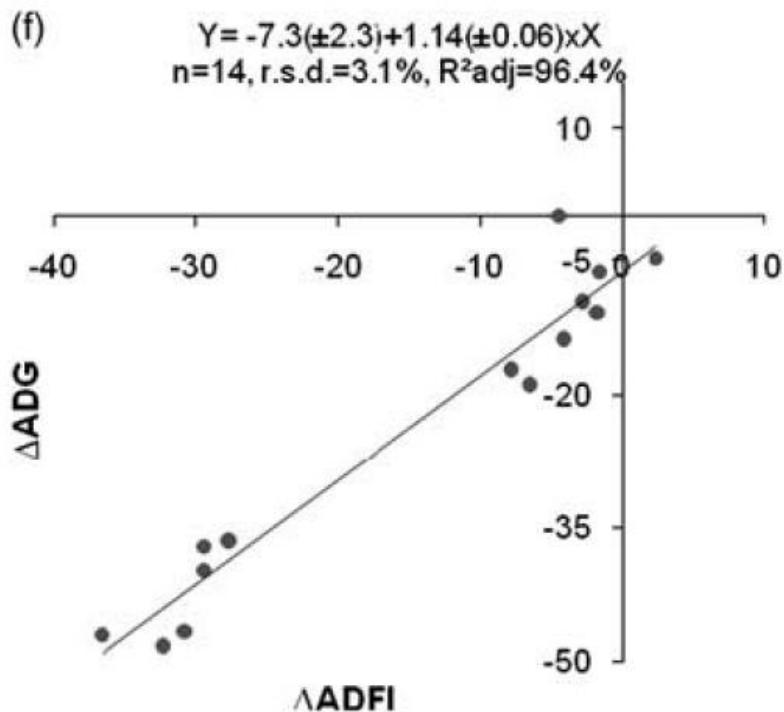
feed intake -15 % body weight -13 % protein catabolism +40 %

^a endotoxin + five times the recommended dose of a PRRSV-Vaccine; ^b Herpes Virus of Turkey; ^c sheep red blood cells



Pastorelli et al. 2011

Relationship between the change in feed intake (ΔADFI) and growth (ΔADG) of pigs challenged with digestive bacterial infections (a). Responses are expressed as results of the challenged pigs relative to that of a control group. The lines represent the linear or the quadratic model adjustments. Estimated parameters differed from zero ($P, 0.05$).



Relationship between the change in feed intake (ΔADFI) and growth (ΔADG) of pigs challenged with respiratory diseases (f). Responses are expressed as results of the challenged pigs relative to that of a control group. The lines represent the linear or the quadratic model adjustments. Estimated parameters differed from zero ($P, 0.05$).

In vivo costs of a stimulation of the immune system...

Costs of an immune response

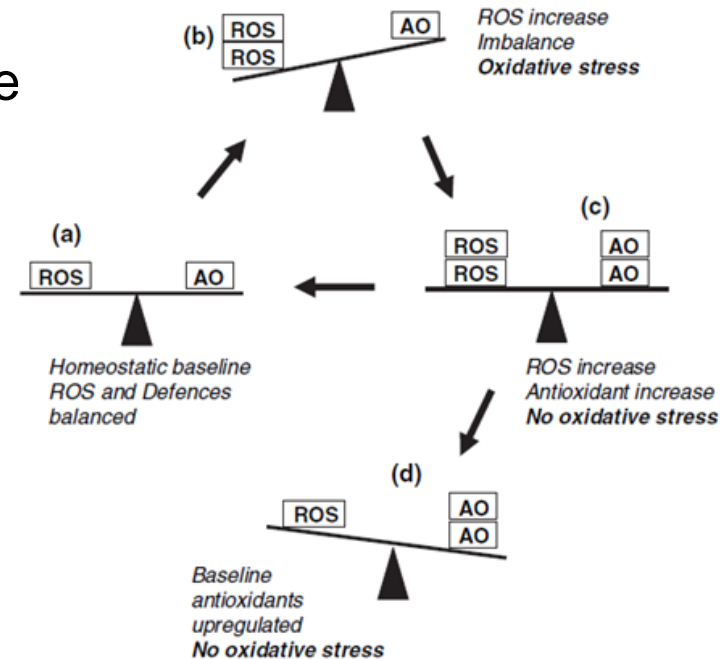
- **Energy costs** - changes in metabolic rate after immunological stimulation (acute phase reaction, leukocyte proliferation, antibody production)
- **Synthesis costs** - Acute phase reaction requires the greatest amount of nutrients (including AS for gluconeogenesis; carotenoids, Se, Vit E.)
- **Preventing autoimmune reactions** - high stress can cause cell death and muscle damage - the body comes into contact with self-antigens - autoimmune response - prevention by secretion of stress hormones in order to suppress the immune system

based on Hasselquist und Nilsson 2012

In vivo costs of a stimulation of the immune system...

Costs of an immune response

- not only costs due to *activation* of the immune system, but also as a result of the by-products of an immune response overcoming
 - oxidative stress - high amounts of reactive O₂ compounds due to macrophage activity, inflammation and fever
 - with short-term and long-term consequences
 - these could be very important !!



based on Hasselquist und Nilsson 2012 and Monaghan et al. 2009

In vivo costs of a stimulation of the immune system...

Costs of an immune response

- Vaccination can reduce the production of reactive oxygen species?
→ positive effect on - for example - inflammatory lung changes

VIRAL IMMUNOLOGY
Volume 24, Number 6, 2011
© Mary Ann Liebert, Inc.
Pp. 475–482
DOI: 10.1089/vim.2011.0040

Intranasal Delivery of an Adjuvanted Modified Live Porcine Reproductive and Respiratory Syndrome Virus Vaccine Reduces ROS Production

Basavaraj Binjawadagi,¹ Varun Dwivedi,¹ Cordelia Manickam,¹
Jordi B. Torrelles,² and Gourapura J. Renukaradhya¹

based on Binjawadagi et al. 2011

In vivo costs of a stimulation of the immune system...

2120 • The Journal of Neuroscience, February 5, 2014 • 34(6):2120–2129

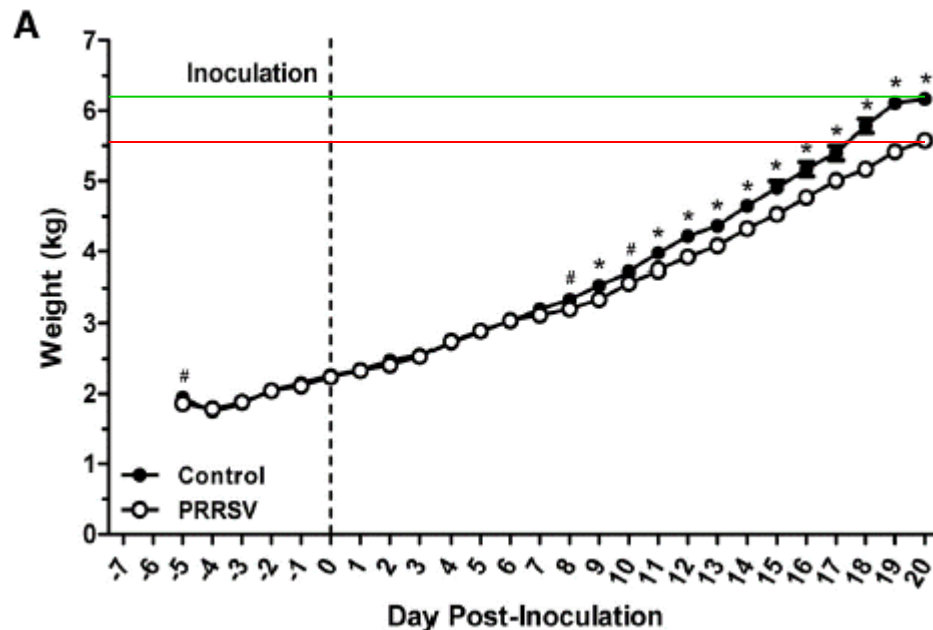
early infections

Behavioral/Cognitive

Respiratory Viral Infection in Neonatal Piglets Causes Marked Microglia Activation in the Hippocampus and Deficits in Spatial Learning

Monica R. P. Elmore,^{1,2} Michael D. Burton,^{1,2} Matthew S. Conrad,^{2,3} Jennifer L. Rytch,² William G. Van Alstine,⁴ and Rodney W. Johnson^{1,2,3}

¹Department of Animal Sciences, ²Integrative Immunology and Behavior Program, and ³Neuroscience Program, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801, and ⁴Department of Comparative Pathobiology, Purdue University, West Lafayette, Indiana 47907



$\Delta=0,6$ kg body mass

based on Elmore et al. 2014

In vivo costs of a stimulation of the immune system...

Early infections

- per kg weight gain a piglet needs 4.1 liters of milk
→ i.e. $\Delta 0.6$ kg bw corresponds to 2.46 l sow's milk
- one kg milk contains 5 MJ ME
→ i.e. the piglet has a 12.3 MJ ME lower nutrient turn over
 - by a lower feed intake
 - by increased costs (energy / nutrient costs and oxidative stress)
 - due to effects in the sow?

2120 • The Journal of Neuroscience, February 5, 2014 • 34(6):2120–2129

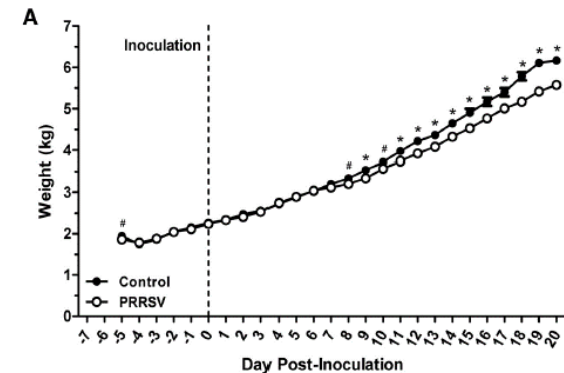
Behavioral/Cognitive

Respiratory Viral Infection in Neonatal Piglets Causes Marked Microglia Activation in the Hippocampus and Deficits in Spatial Learning

Monica R. P. Elmore,^{1,2} Michael D. Burton,^{1,2} Matthew S. Conrad,^{2,3} Jennifer L. Ryttych,² William G. Van Alstine,⁴ and Rodney W. Johnson^{1,2,3}

¹Department of Animal Sciences, ²Integrative Immunology and Behavior Program, and ³Neuroscience Program, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801, and ⁴Department of Comparative Pathobiology, Purdue University, West Lafayette, Indiana 47907

$\Delta = 0.6$ kg body mass



based on Elmore et al. 2014

Energy and protein supply - consequences

Houdijk et al. 2012

Dissecting effects of metabolizable protein and energy nutrition on resistance to parasites.

Host and Ref. ^a		Metabolizable energy (MJ/kg ^{0.75} /day)		Metabolizable protein (g/kg ^{0.75} /day)	FEC (epg)	Worm burden (total)
Growing lambs						
Bown et al. (1991) ^b	Low	0.61	Low	5.5	1,299,000	39,300
	High	0.70	Low	5.5	2,851,000	45,700
	Low	0.69	High	10.0	2,017,000	17,800
Kahn et al. (2001) ^c	Low	0.50	Low	3.90	2000	12,320
	Low	0.50	High	5.41	1850	11,333
	High	0.58	Low	3.47	850	7313
	High	0.62	High	5.85	2200	9770
Twin-rearing ewes	Low	1.28	Low	10.80	2000	11,474
	Low	1.37	High	14.35	260	3397
Donaldson et al. (1998)	High	1.43	Low	10.31	2500	16,253
	High	1.48	High	12.30	250	3738
Pregnant ewes	High	0.54	High	3.87	25	–
Houdijk et al. (2001c)	Low	0.38	High	3.61	25	–
	Low	0.38	Low	2.26	100	–
Lactating rats	Low	0.81	Low	10.07	1228	160
Sakkas et al. (2009)	Low	0.80	High	14.72	357	121
	High	1.06	Low	10.07	1454	218
	High	1.04	High	14.33	333	153

^a The data in this table are derived from the original data presented in the references given.

^b FEC data given as eggs per day.

^c Personal communications.

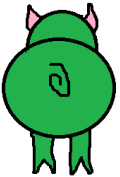
one example to limit the costs...

Infections in a different light...



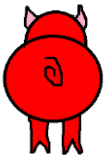
Material and Methods

Group / treatment classification



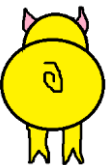
VAC- CF-

Not vaccinated, without clinical findings



VAC- CF+

Not vaccinated, faeces PCR positive,
with clinical findings (soft to liquid faeces)



VAC+ CF-

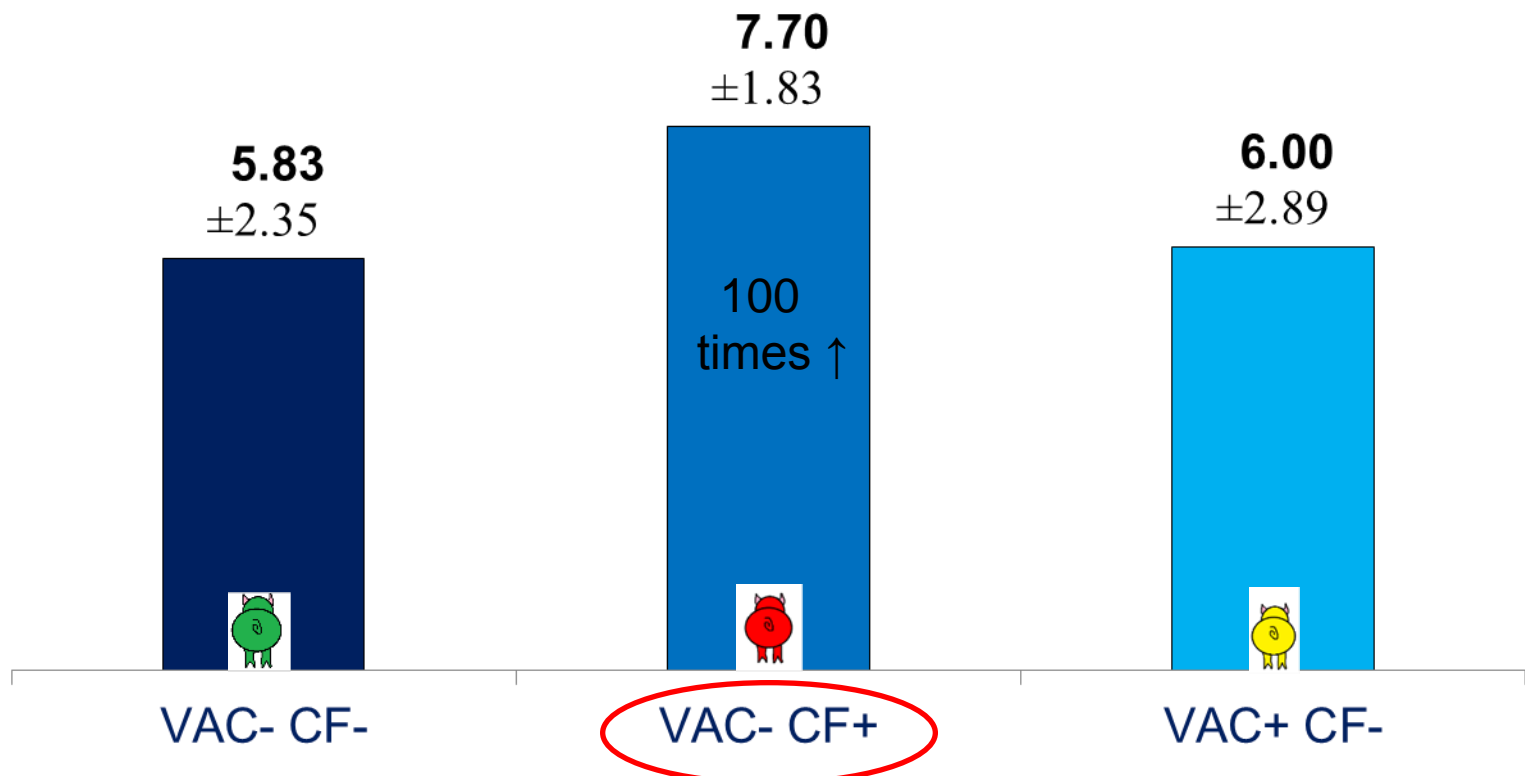
Vaccinated (Enterisol® Ileitis), without clinical findings

Results (1)

Shedding of *Lawsonia intracellularis* via faeces in pigs

Faecal shedding of *L.i.* during the digestibility trial,
detected by quantitative PCR

Lg genome equivalents (GE)/g faeces



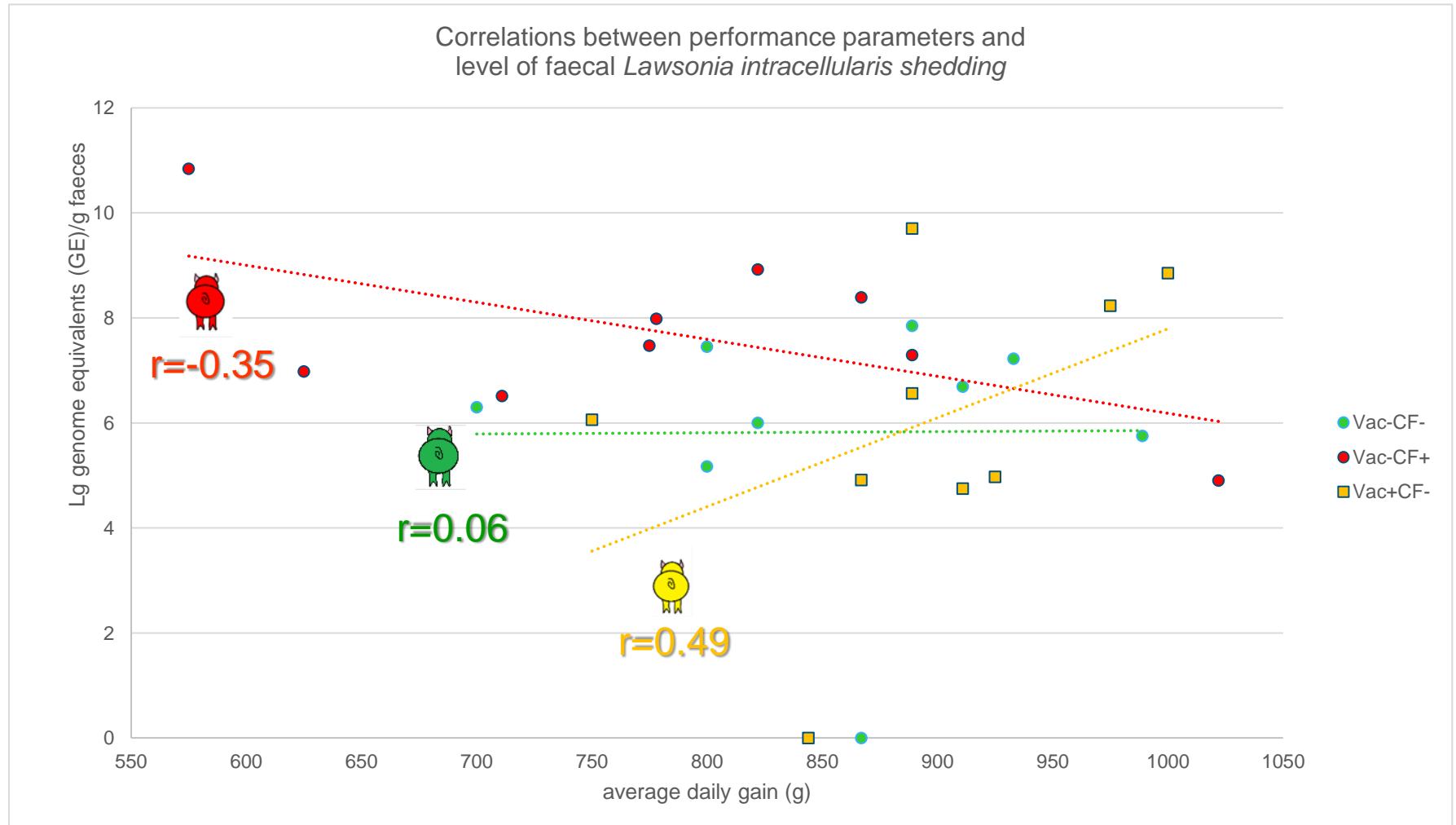
Results (2)

Correlations



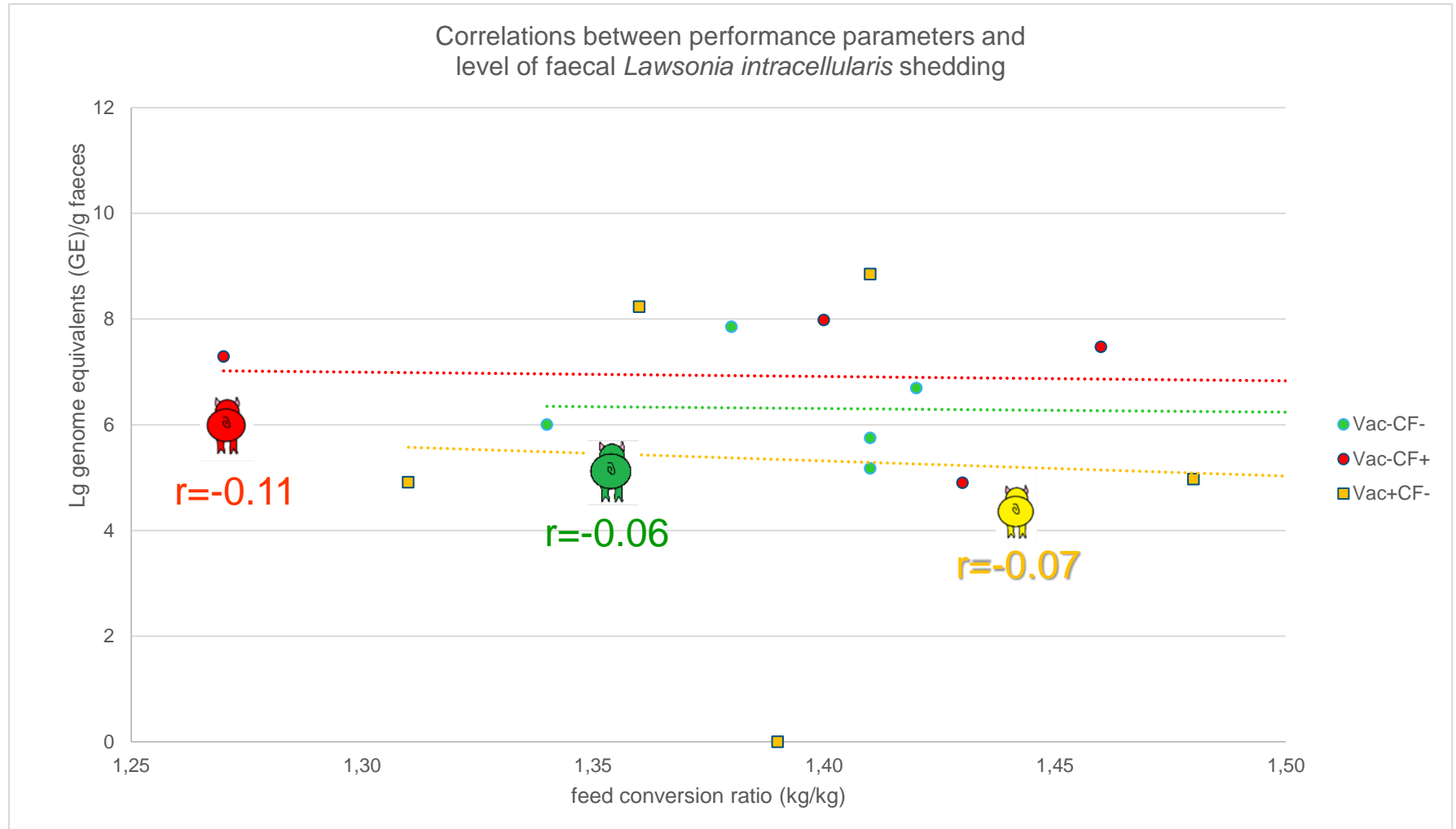
Results (3)

Correlations



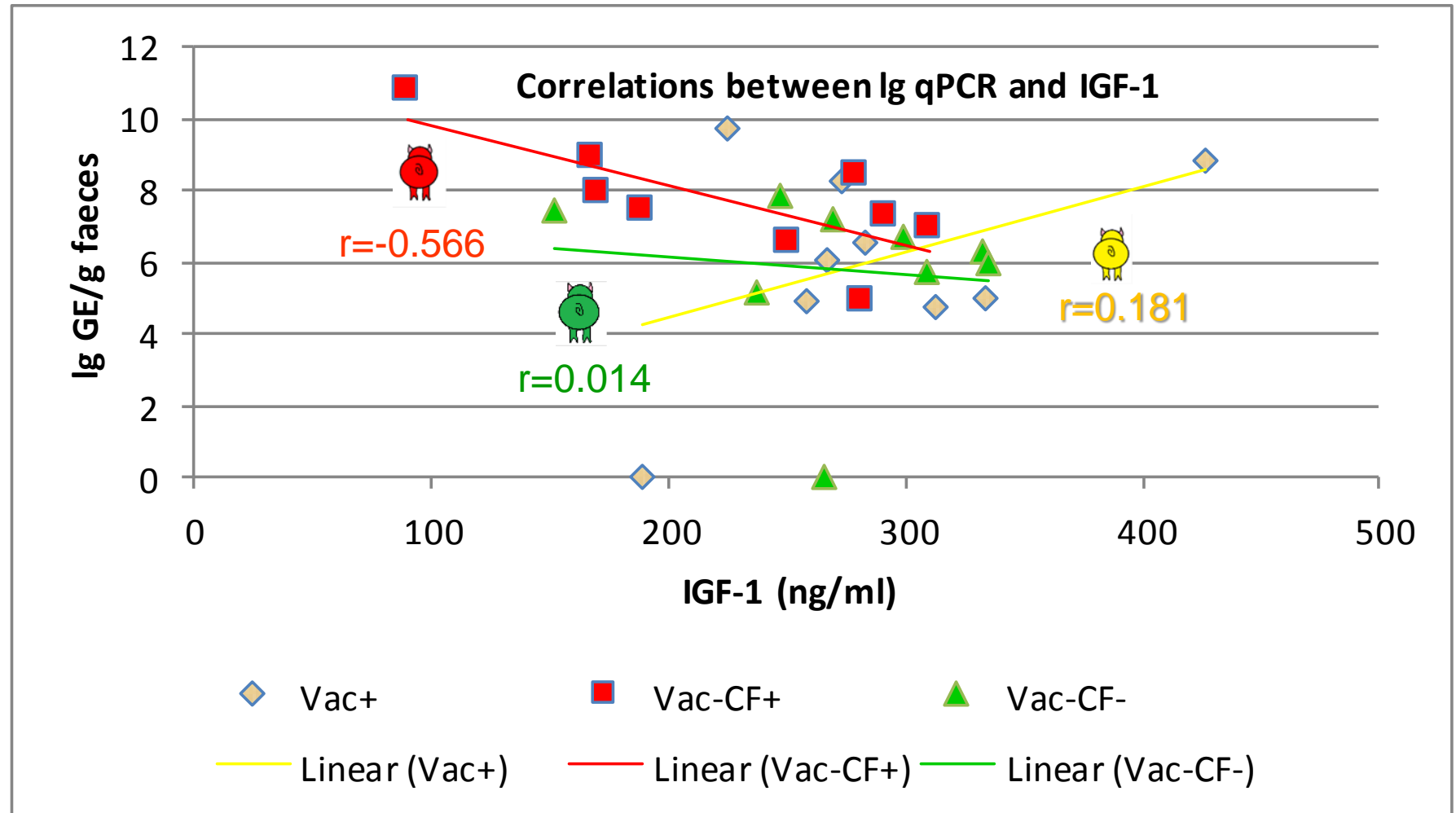
Results (4)

Correlations



Results (5)

Correlations



Results (6)

Explanation

7.2.2 Post-inflammatory metabolic responses: Plasma IGF-1 and IGF-1 mRNA remained reduced 8 weeks post-infection, long after reduced food intake and other acute-phase responses to infection had resolved (Elsasser et al, 1995). This suggests that the regulation of appetite and body weights are separable events and that disease can uncouple the normally tight association between appetite and growth. The delay in IGF-1 recovery from infection relative to recovery of appetite probably explains the stunting that is often observed with severe disease.

What we are learning...

- Effects of immunological challenges with all its consequences as well as the effectiveness of countermeasures can be assessed in growing animal easiest on growth
- Under similar conditions, breeding for maximum performance means breeding to “efficient costs” for immune function (not too much - not too little)

Questions?





Nutritional management of right dorsal colitis in horses: a case report

Wendy Wambacq, Resident ECVCN

Laboratory of Animal Nutrition, Ghent University, Belgium



RDC in Equids

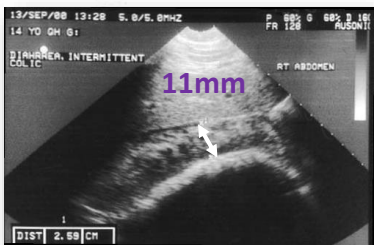
(Andrews and Robertson, 1988; Karcher *et al.*, 1990; Simmons *et al.*, 1990; Cohen *et al.*, 1995; Bueno *et al.*, 2000)



Case report



KWPN, 8y old, Mc
BCS 3/9
Estimated id. BW 630kg



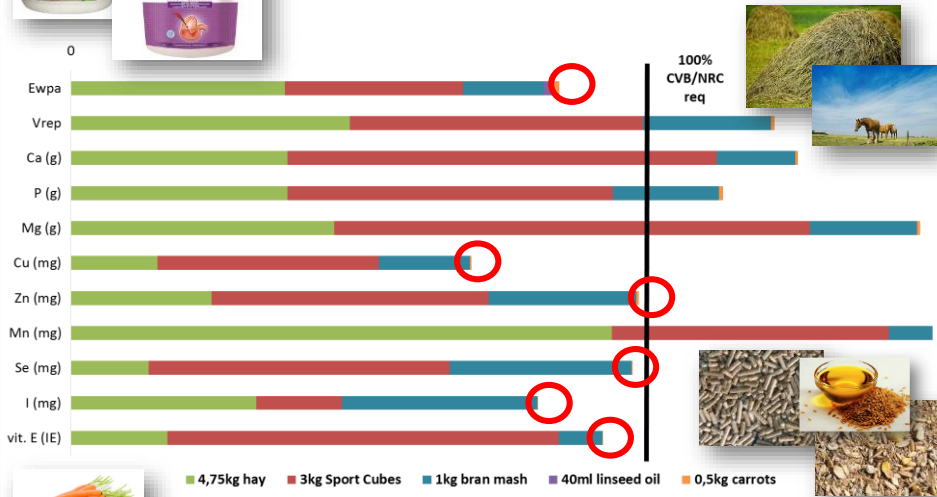
(Cohen, 2002)



Laboratory of Animal Nutrition
wendy.wambacq@UGent.be



Current diet



Laboratory of Animal Nutrition
wendy.wambacq@UGent.be

CF 24,5%DM
CP 11,3%DM

CFAT 4,3%DM
Sugar+starch 18,1%DM



Nutritional management of RDC



Low-bulk diet
(Cohen *et al.*, 1995)



psyllium
(Fettman, 1992; Bugaut and Bentejac, 1993; Argenzio, 1994; Fahey, 1994; Inan *et al.*, 2000, Cohen, 2010)



oil
(Schepp *et al.*, 1988; Cargile and Merritt, 1989; Henry *et al.*, 1990; McCann and Carrick, 1998)



Sugar and starch <1gr/kgBW/meal



Avoid dehydration



Multiple small meals



KEEP CALM AND HAPPY 6 MONTHS
(Cohen, 2010)

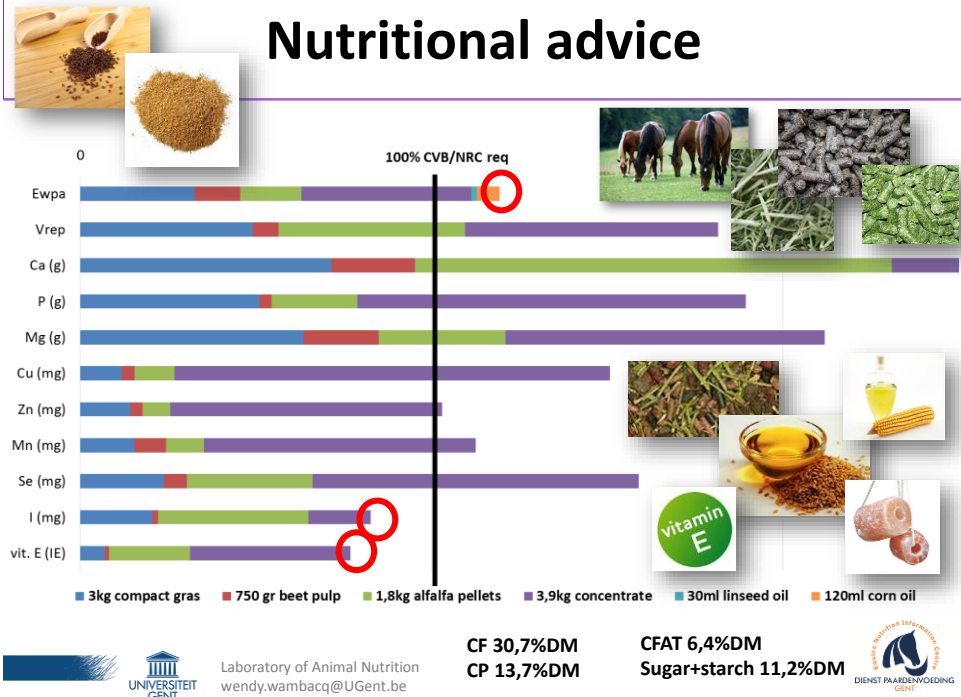


Laboratory of Animal Nutrition
wendy.wambacq@UGent.be



DIENT PAARDENVOEDING
GENT

Nutritional advice



Concentrates: high fiber, low sugar and starch



Sugar and starch: 8%



10%



11%



10,5%



12,1%



9,4%



17%



x%



x%



Laboratory of Animal Nutrition
wendy.wambacq@UGent.be



Dienst Paardenvoeding
Gent

Follow-up

One month later...





Laboratory of Animal Nutrition
wendy.wambacq@UGent.be



Dienst Paardenvoeding
Gent

Thanks to...



Dr. Marie-Thérèse Picavet, DVM, DECEIM

Horse's owner



Thank you for your attention!

wendy.wambacq@ugent.be



Laboratory of Animal Nutrition
wendy.wambacq@UGent.be

