Utrecht University

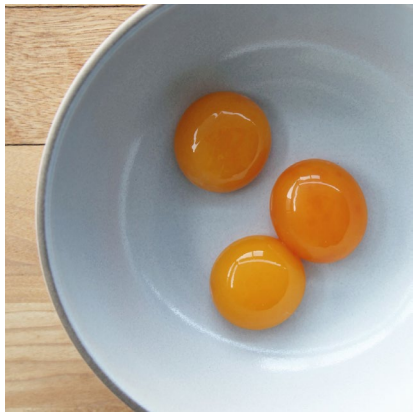
Veterinary Medicine

10 May 2023

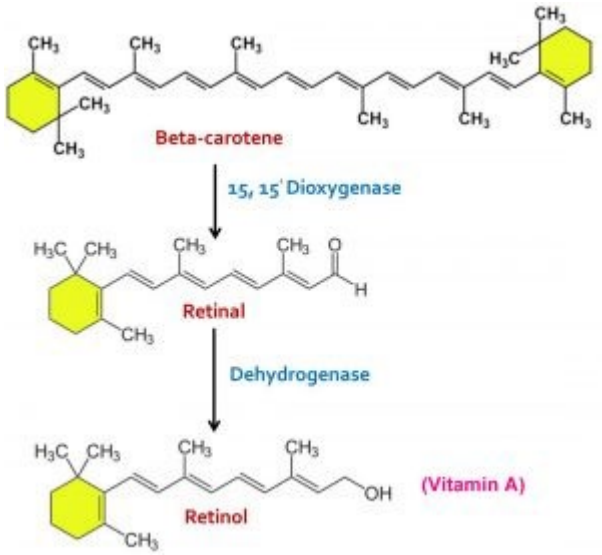
# *Vitamins A and E: what do we know for optimal use?*

**Dr. Ronald Jan Corbee**
DVM, PhD, Dipl. ECVCN

# Vitamin A sources

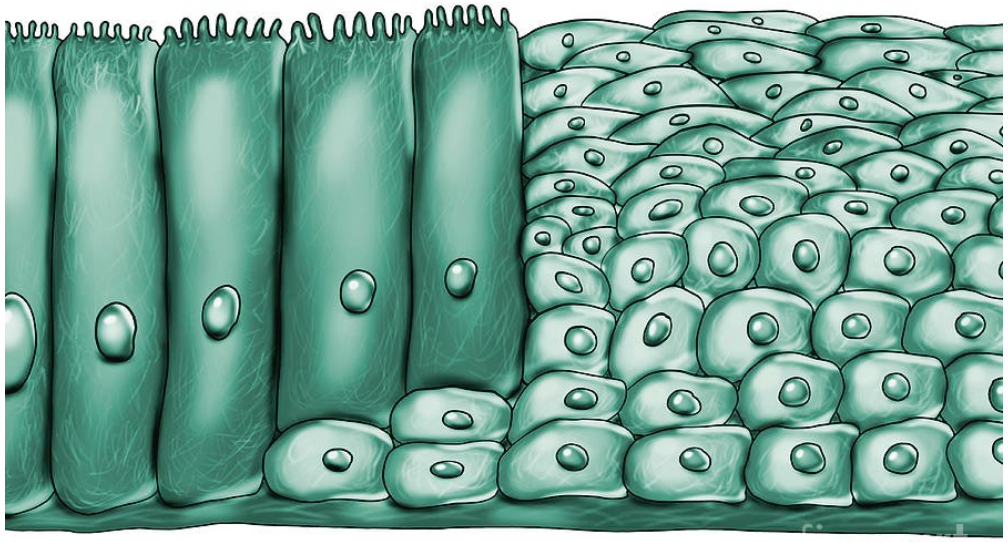



# Vitamin A synthesis

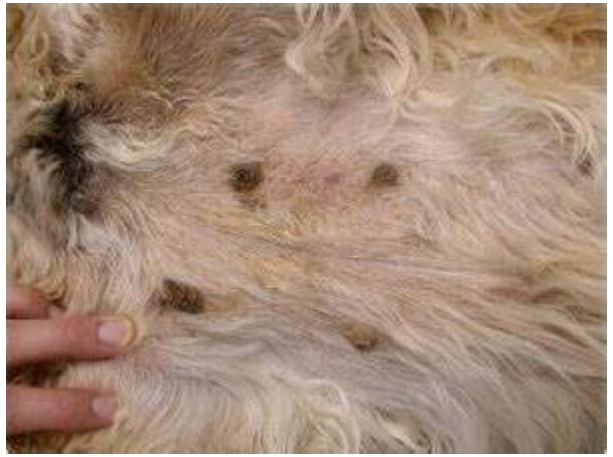


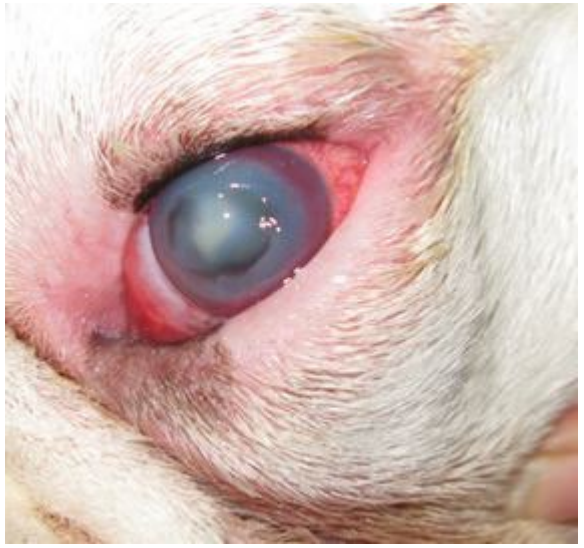

# Vitamin A functions

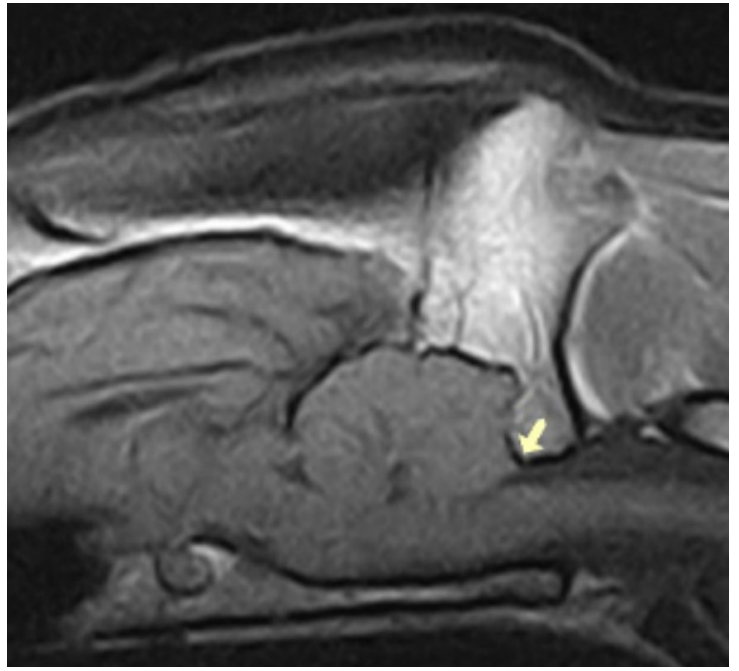
Vision
Growth
Cellular differentiation
Morphogenesis
Immune function



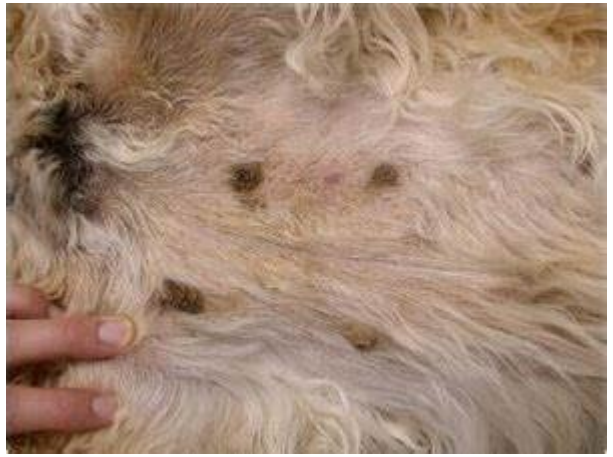
# Vitamin A minimum/deficiency

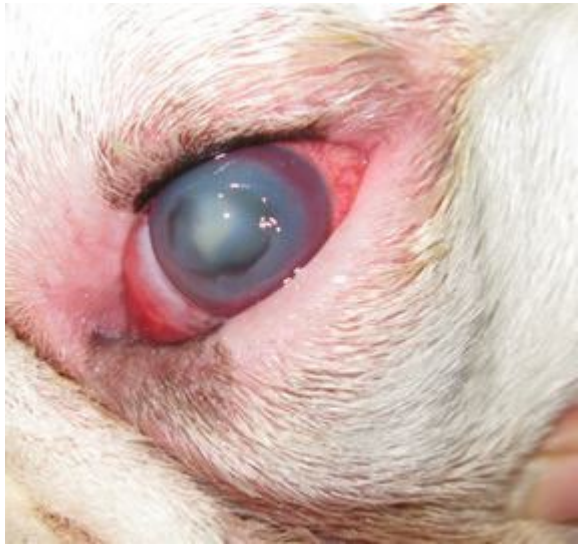




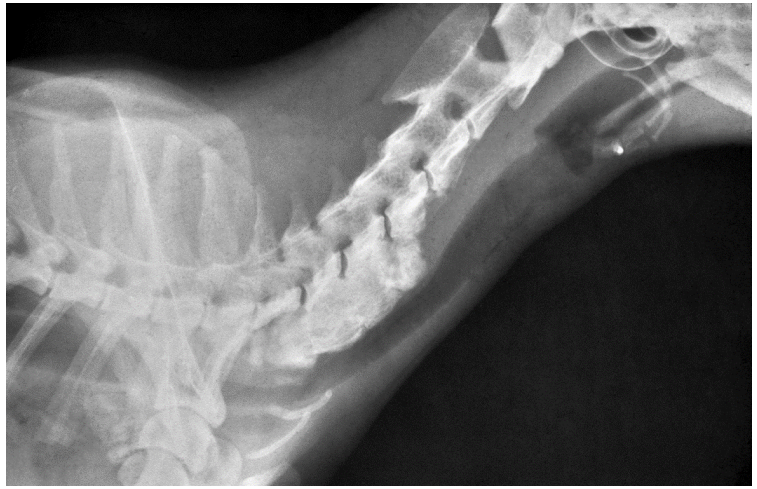



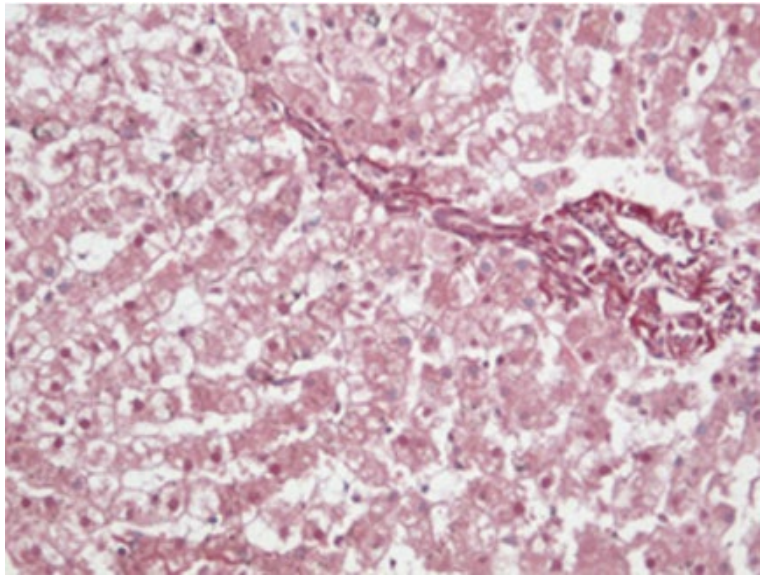
# Vitamin A maximum/excess

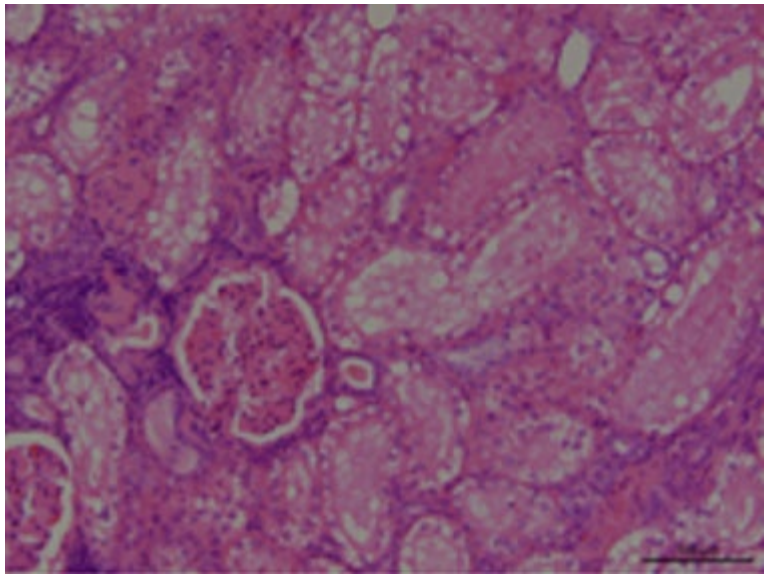





# Vitamin A maximum/excess







# Vitamin A maximum/excess

The Veterinary Journal 202 (2014) 503–509

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

## Skeletal and hepatic changes induced by chronic vitamin A supplementation in cats

R.J. Corbee [a,*], M.A. Tryfonidou [a], G.C.M. Grinwis [b], B. Schotanus [a], M.R. Molenaar [c], G. Voorhout [a], A.B. Vaandrager [c], H.C.M. Heuven [a], H.A.W. Hazewinkel [a]

Journal of Feline Medicine and Surgery
Volume 16, Issue 3, March 2014, Pages 243-248

https://doi-org.proxy.library.uu.nl/10.1177/1098612X13516121

*Case Reports*

## Hypervitaminosis A-induced hepatic fibrosis in a cat

**Juliana M Guerra [1,2], Alexandre G T Daniel [3], Thiago P A Aloia [1], Adriana de Siqueira [1], André R Fukushima [1], Denise M N Simões [4], Archivaldo Reche-Júior [4], and Bruno Cogliati [1]**

# Vitamin A future directions/optimal use

- NRC AI 303 RA 379 SUL 3750 RE/1000kcal puppy/lactation
- NRC SUL 16000 RE/1000kcal adult
- NRC AI 200 RA 250 SUL 20000 RE/1000kcal kitten
- NRC AI 400 RA 500 SUL 25000 RE/1000kcal lactation
- NRC SUL 25000 RE/1000kcal adult

- FEDIAF 375-30000 RE per 1000kcal dog
- FEDIAF 250-33000 RE per 1000kcal cat

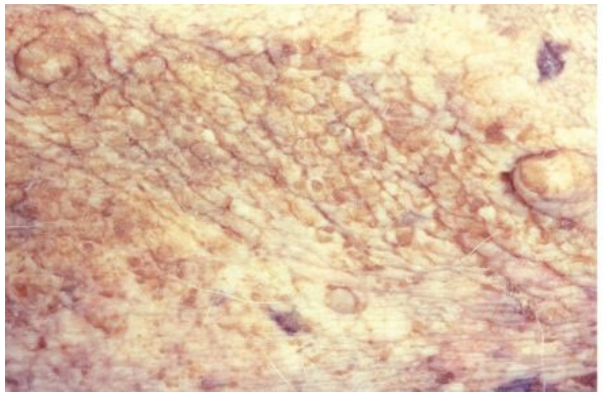
*British Journal of Nutrition* (2012), **108**, 1800–1809 doi:10.1017/S0007114512000128

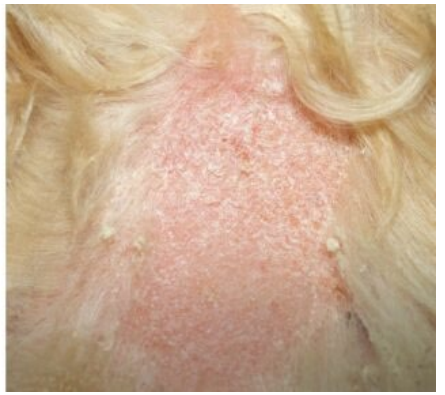

**Safety evaluation of vitamin A in growing dogs**

Penelope J. Morris[1]*, Carina Salt[1], Jens Raila[2], Thomas Brenten[3], Barbara Kohn[4], Florian J. Schweigert[2] and Jürgen Zentek[5]

# Vitamin A responsive dermatosis

- Other causes of seborrhea/hyperkeratosis should be ruled out first
- 10000 IU per day for 5-8 weeks (per os)
- Continue with 400 IU per kg per day or
- Single injection of 6000 IU per kg every 2 months
- Severe systemic effects if given for wrong indication

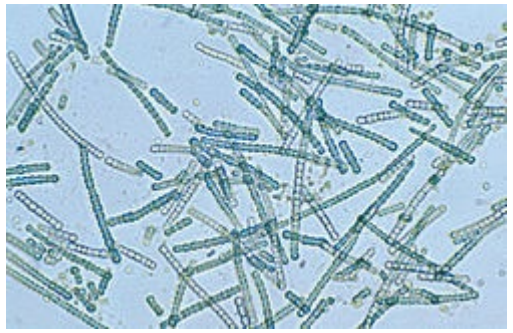




# Vitamin A in eyedrops / eye ointment

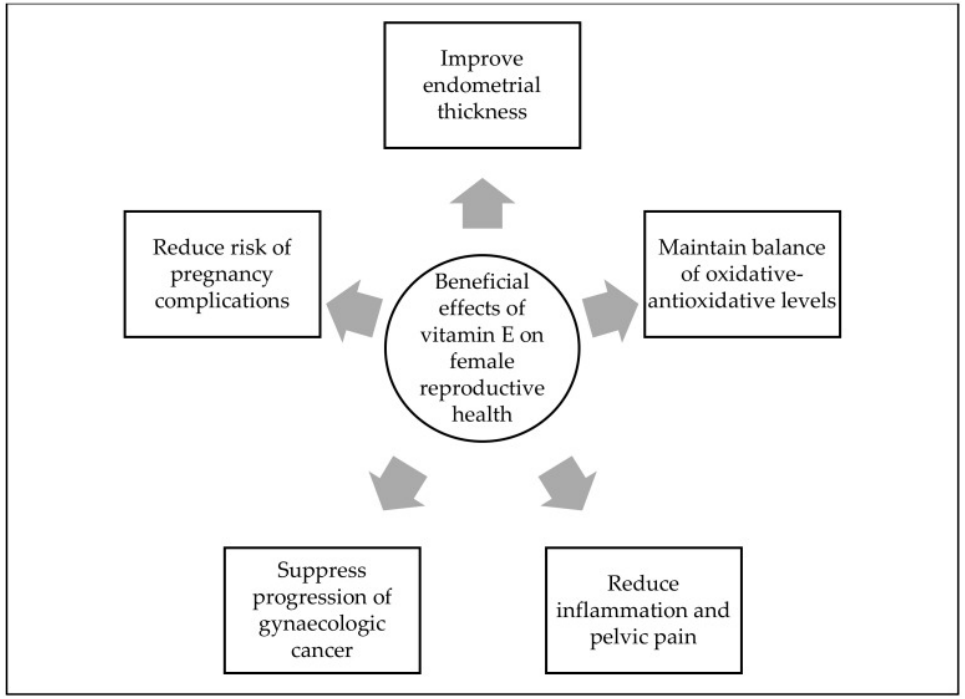
- Natural component of tear layer on the eyes
- Lubrication
- Prevention of water loss from the cornea because of fatty layer
- No systemic effects

# Vitamin E sources



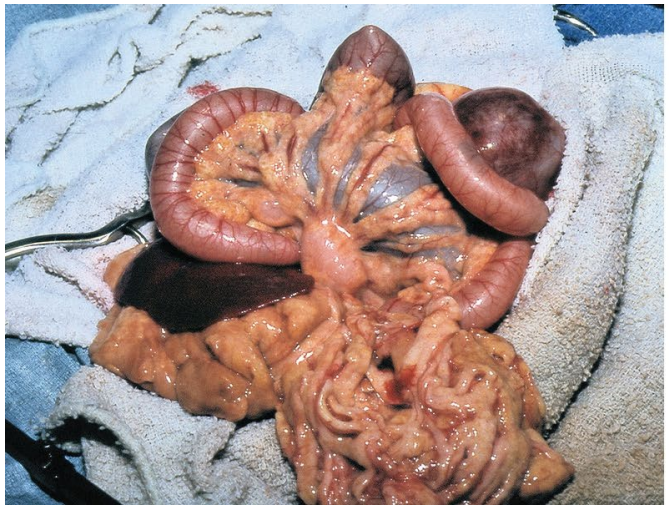
# Vitamin E functions

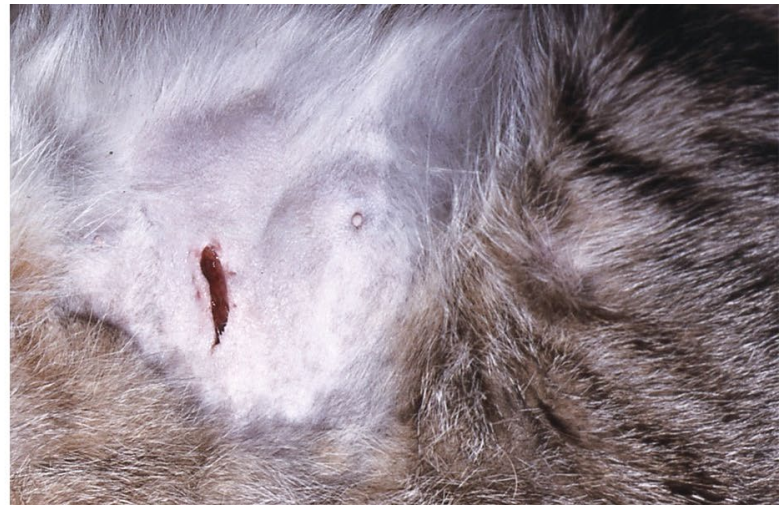
Antioxidant
Protection of PUFAs in cellular membranes
Role in cell signalling
Needed for reproduction
Immune function



# Vitamin E minimum/deficiency

- Muscle weakness / myopathy
- Steatitis
- Anorexia
- Sterility
- Dermatosis
- Immune deficiency
- Ataxia (in people)





# Vitamin E maximum/excess

- For fat soluble vitamin relatively nontoxic
- Interference with vitamin A, D and K absorption

# Vitamin E future directions/optimal use

- NRC AI 6.0 RA 7.5 IU/1000kcal dog
- NRC AI 7.5 RA 9.4 kitten (7.8 lactation 9.8 adult) cat

- FEDIAF minimum12.5 dog
- FEDIAF minimum 9.5 cat

# Vitamin E requirements

- Much still unknown
- Increased need when more fat and more PUFAs are in the diet, as well as with a higher degree of peroxidation
- Also dependent on selenium and other antioxidants
- Use in PUFA supplements to prevent oxidation

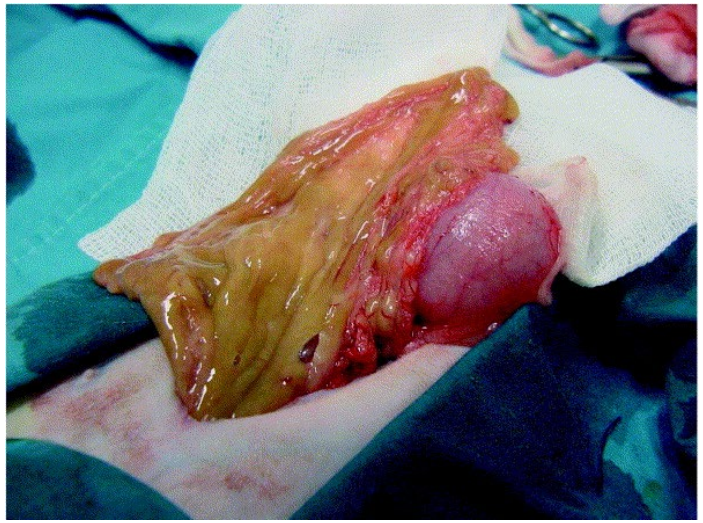
# Vitamin E in steatitis in cats

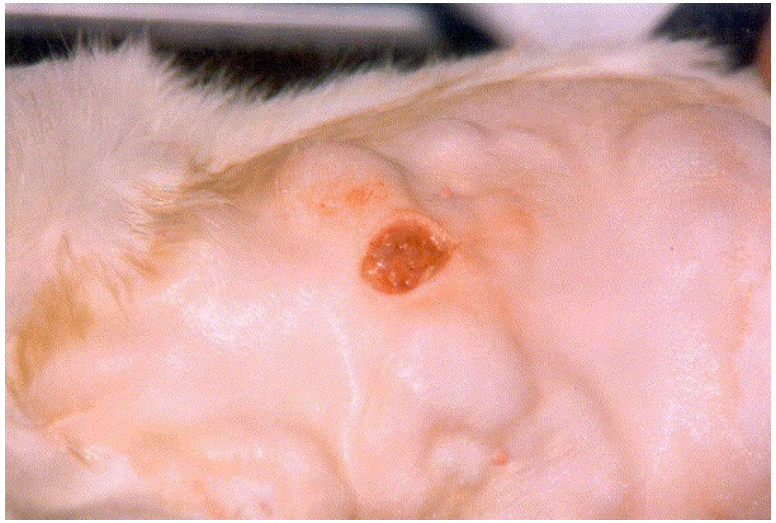
Journal of Feline Medicine & Surgery
Volume 5, Issue 5, October 2003, Pages 271-277

Feline pansteatitis revisited: hazards of unbalanced home-made diets

M.M.R.E Niza, C.L Vilela, L.M.A Ferreira

- 25-75 IU every 12h or 50mg/kg SID PO 30-45 days
- Change diet
- Corticosteroids and symptomatic treatment if needed





# Vitamin E in other diseases

- Dermatological disease
- Cardiac disease
- Osteoarthritis (400 IU per dog per day)
- Chronic kidney disease (5 IU per kg body weight per day)
- Hepatic disease (10-15IU per kg body weight per day)
- Immune disorders (225mg per kg diet)
- Cancer/frailty (15-20 IU per 100kcal)

TABLE 8-3 Recovery of Vitamins and Carotenoids Added to Extruded Petfoods and Percentage Loss on Storage

| Active | Chemical Form | Product Form | % Recovery After Processing | | | Storage Loss (% per month) |
|---|---|---|---|---|---|---|
| | | | Typical | Low | High | |
| Retinol | Retinyl acetate | Cross-linked beadlet | 81 | 63 | 90 | 6 |
| | | Beadlet | 65 | 40 | 80 | 30 |
| Cholecalciferol | Cholecalciferol | Spray-dried beadlet | 85 | 75 | 90 | 4 |
| Vitamin E | all-*rac*-α-Tocopheryl acetate | Adsorbate | 45 | 30 | 85 | 1 |
| | | Spray-dried beadlet | 45 | 30 | 85 | 1 |
| | *RRR*-α-Tocopherol | Oil | 40 | 10 | 60 | 10 |
| Vitamin K | Menadione sodium bisulfite complex | Crystalline powder | 45 | 20 | 65 | 17 |
| | Menadione nicotinamide bisulfite | Crystalline powder | 56 | 40 | 75 | 11 |
| | Menadione dimethylpyrimidinol bisulfite | Crystalline powder | 50 | 30 | 70 | 12 |
| Thiamin | Thiamin mononitrate | Crystalline powder | 90 | 30 | 95 | 4 |
| | Thiami hydrochloride | Crystalline powder | 80 | 50 | 85 | 4 |
| Riboflavin | Riboflavin | Spray-dried beadlet | 82 | 70 | 90 | 3 |
| Pyridoxine | Pyridoxine hydrochloride | Crystalline powder | 75 | 70 | 90 | 3 |
| D-Pantothenic Acid | D-Calcium pantothenate | Crystalline powder | 85 | 75 | 95 | 2 |
| Niacin | Nicotinic acid | Crystalline powder | 80 | 64 | 90 | 2 |
| Biotin | Biotin | Spray-dried beadlet | 88 | 60 | 95 | 2 |
| Folic Acid | Folic acid | Spray-dried beadlet | 90 | 65 | 95 | <1 |
| Vitamin C | Ascorbyl-2-polyphosphate | Spray-dried beadlet | 96 | 85 | 100 | <1 |
| | Ascorbic acid | Crystalline powder | 40 | 0 | 60 | 37 |
| Lutein | Lutein | Spray-dried beadlet | 72 | 50 | 80 | 2 |
| Lycopene | Lycopene | Spray-dried beadlet | 64 | 40 | 75 | 2 |
| β-Carotene | beta-Carotene | Beadlet | 34 | 20 | 50 | 2 |

SOURCE: Information supplied by J. W. Wilson, Roche Vitamins Inc.

# Future directions:

# Example of research project looking at SUL and nutrient interactions

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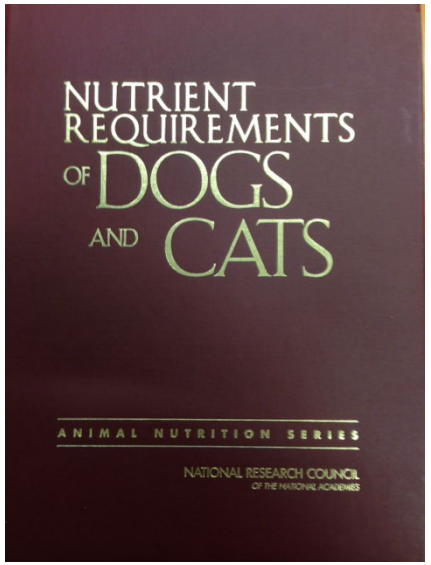
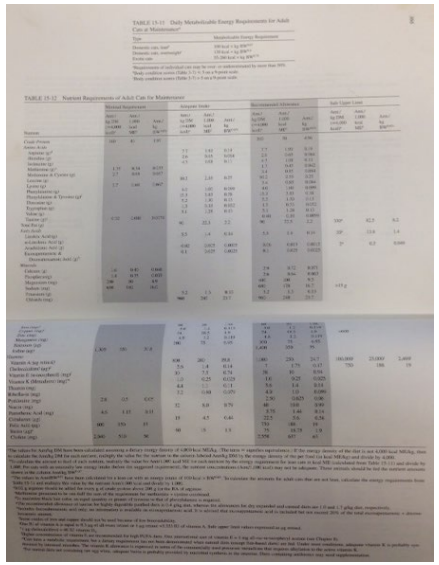
[a] Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands
[b] Department of Pathobiology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands
[c] Department of Biochemistry and Cell Biology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands

# Introduction

- Nutrition is about balance
- Currently deficiencies are rare
- Toxicities are more likely and often safe upper limits of nutrients are not determined



# Introduction

- In cats, the safe upper limit for vitamin A is based on 1 study, which stated that 3/15 adult cats that were exposed to 306.000ug retinol per kg diet during 2-3 years developed skeletal lesions of the cervical vertebrae (Freytag et al. 2003)

- The safe upper limit for adult was set at 100.000ug retinol per kg diet which equals 333.333IU per kg, which is 26.500IU per day for an average cat

# Introduction

## VITAMINS

### Vitamin A

**Vitamin A (Adult cats)** The FEDIAF maximum is based on the study reported by Seawright et al. in kittens. [a]

The FEDIAF maximum of 40 000 IU/100g DM is about 50% of the maximum NOAEL reported by Seawright et al. [a] in kittens from 6 to 8 weeks of age fed for 41 weeks. Since kittens are at least equally vulnerable as adults to hypervitaminosis A, this level should also be safe for adult cats.

**Vitamin A (Growth and reproduction)** Seawright et al. [a] reported no adverse effects in kittens from 6 to 8 weeks of age fed for 41 weeks on a vitamin A intake of 50,000 IU/kg BW corresponding to about 90,000 IU per 100g DM. Therefore, FEDIAF's maximum of 40,000 IU/100g DM can be considered safe for growing kittens.

Freytag et al. [b] reported that feeding a food with 100,000 IU/100g DM to pregnant queens caused fatal malformations in kittens. The next lowest value of 2000 IU/100g DM caused no adverse effects. From these data NRC 2006 recommended not to exceed 33,330 IU/100g DM in feeding stuffs intended for reproduction. [c]

In view of these data, FEDIAF recommends a maximum vitamin A level of 33,330 IU/100g DM for products designed for reproducing queens.

[a] *Seawright AA, English PB, Gartner RJW. Hypervitaminosis A and deforming cervical spondylosis of the cat. J. Comp. Path.1967; 77: 29-39.*

[a] *Seawright AA, English PB, Gartner RJW. Hypervitaminosis A and deforming cervical spondylosis of the cat. J. Comp. Path.1967; 77: 29-39.*

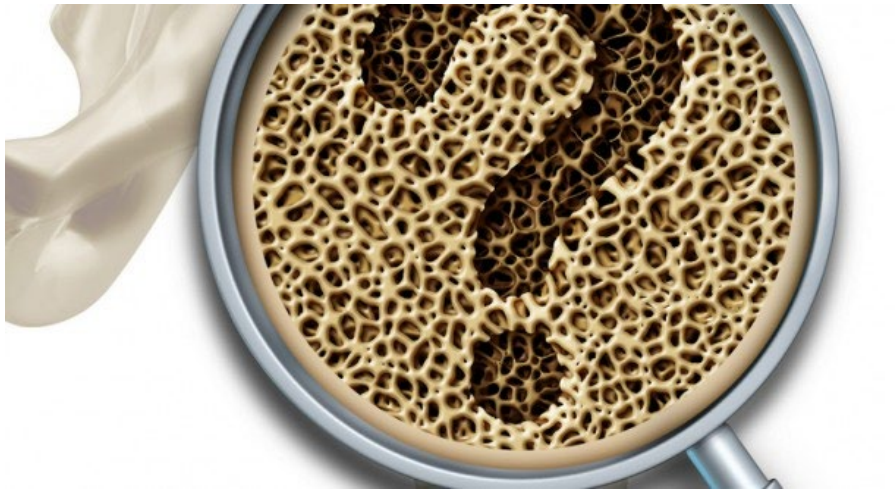
[b] *Freytag TL, Liu SM, Rogers AR, Morris JG. Teratogenic effects of chronic ingestion of high levels of vitamin A in cats. J. Anim Phys and Anim Nutr. 2003; 87: 42-51.*

[c] *NRC Chapter 8. Vitamins - Hypervitaminosis A. In: Nutrient Requirements of Dogs and Cats. The National Academic Press, Washington, DC. 2006: p. 200.*

# Introduction

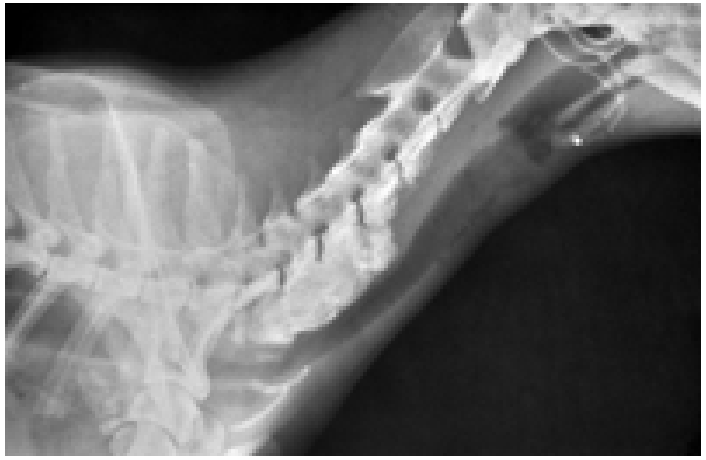
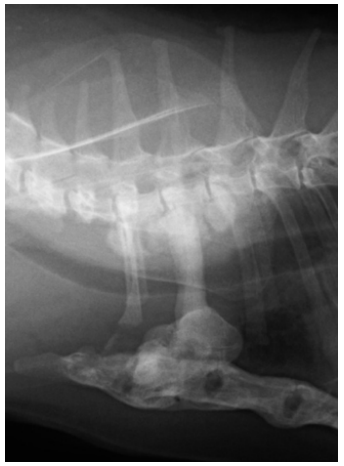
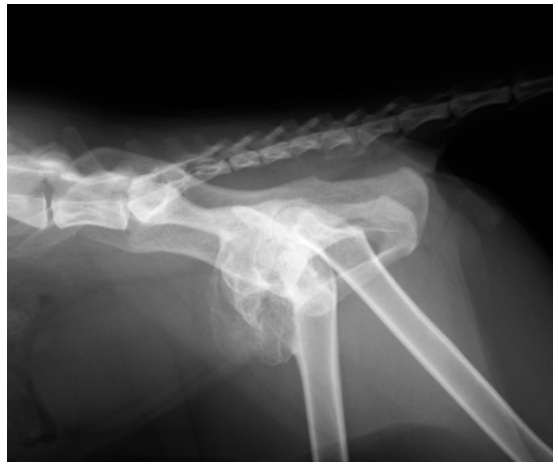
- In rats and humans, hypervitaminosis A is associated with osteoporosis
(Lind et al. 2012, Hu et al. 2010)

- In cats, hypervitaminosis A is associated with osteoporosis (Clark 1970, 1973), but also with hyperostosis / new bone formation
(Franch et al. 2000)



# Introduction

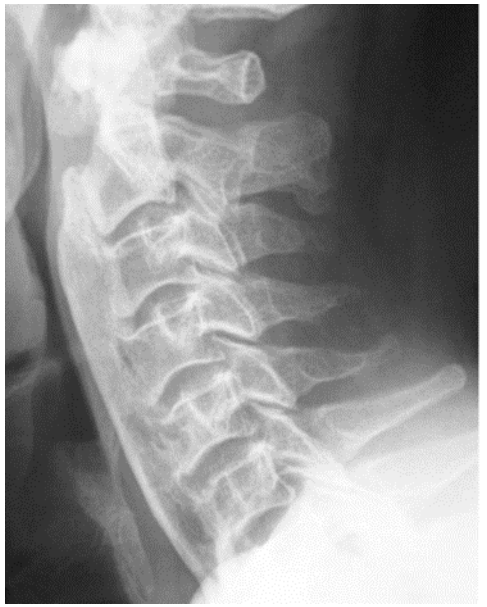
- The fusion of vertebrae, as well as massive new bone formations around joints are typical for hypervitaminosis A, as is reported in case reports (Polizopoulou et al. 2005)
- Most of the reported cases describe chronic consumption of liver
- Liver contains more vitamin A and more vitamin D compared to other foods (Becker 2013)

# Introduction

- Paleopathologic evaluation of monks (on a diet predominantly consisting of salmon) of the St Servaas church in Maastricht revealed similar pathology (Waldron et al. 2008)

- Case reports in humans associated with supplements or consumption of cod liver oil (Wendling et al. 2009)



# Interactions between A and D

- Circulating retinol results in lower 1,25 -DHCC (Ørnsrud et al. 2013)
- Vitamin A stimulates 24-hydroxylase (Allegretto et al. 1995)
- 24,25-DHCC :
- Inhibition of 1-α-hydroxylase
- Inhibition of PTH
- Stimulation of synthesis and growth of cartilage
- Stimulation of mineralization of osteoid (DeLuca 1982, Van Leeuwen et al. 2001)

# Introduction

- Hypervitaminosis A is characterized by liver fibrosis in humans (Waldron et al. 2008) but not in cats (Freytag et al. 2003)

- Vitamin A is stored in hepatic stellate cells (HSCs) in both humans ( Shirakami et al. 2012) and cats (Seawright et al. 1967)

- HSCs can be activated by vitamin A, and over-accumulation can lead to leakage of vitamin A into liver parenchyma, both causing fibrosis (Shirakami et al. 2012)

# Clinical study

- The aim of this study was to determine whether vitamin D supplementation influences the effects of high vitamin A intake on new bone formation in adult cats

- The second aim was to determine whether high vitamin A intake in cats causes liver pathology and, if so, whether the current SUL for the dietary intake of vitamin A for healthy adult cats is safe

# Materials and methods

- 24 cats divided in 4 groups

Daily intake average cat

| | Control | HA | HAMD | HAHD | Safe upper limit according to NRC 2006 |
|---|---|---|---|---|---|
| **Vitamin A (IU)** | 257 | 26,953 | 26,953 | 26,953 | 26,500 |
| **Vitamin D (IU)** | 31 | 31 | 156 | 2,022 | 2,385 |

Intake from raw beef liver 33.796IU vitamin A and 98IU vitamin D per day

- After 0, 6, 12, 18 (and 24) months evaluation:
- Blood, Rx, FPA, Eye examination
- Liver biopsies at baseline and 18 months
- At end point euthanasia and pathology

Approved by ethical committee under number DEC 2011.III.01.008

# Statistics

- Kolomogorov-Smirnov test: normal distribution

- Between groups t-test or Mann-Whitney U-test
- Between time points multivariate analysis
- R-statistics software (R i386 3.0.1)
- The best model fit was used
- $P<0.05$ in univariate analysis
- $P<0.01$ in multivariate analysis, to correct for multiple testing
- $P<0.10$ tendency in univariate analysis

# Results

- 2 cats withdrawn due to DM (HAED) and due to primary lung tumor (HA)
- Supplements were accepted well
- No abnormalities at clinical examination during the 18 month period in the other cats

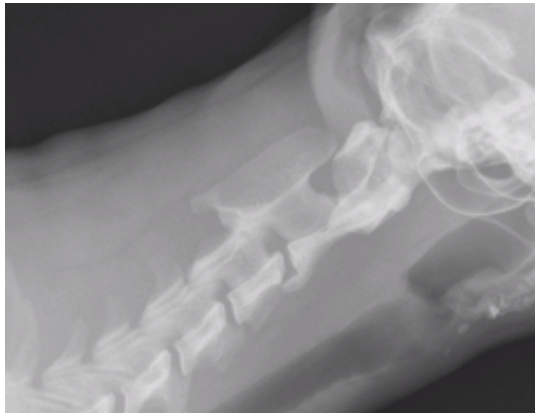
# Blood work

| | | 0 | 6 | 12 | 18 |
|---|---|---|---|---|---|
| C | 25OHD | 121.5±33.7 | 121.5±45.7$^{A}$ | 128.7±48.2$^{A}$ | 135.8±50.0$^{A}$ |
| HA | | 168.7±30.5 | 162.5±63.6$^{A}$ | 126.8±48.2$^{A}$ | 135.0±53.9$^{A}$ |
| HAED | | 108.8±27.6 | 140.8±50.33$^{A}$ | 175.2±31.9$^{B}$ | 207.2±41.9$^{B}$ |
| HAHD | | 128.5±51.4 | 357±181.6$^{B}$ | 626.8±136.8$^{C}$ | 656.0±95.7$^{C}$ |
| C | RE | 1093±723 | 733±432 | 231±134 | 1102±310 |
| HA | | 3190±1262 | 2113±1106 | 905±605 | 3101±1551 |
| HAED | | 1825±566 | 1932±1144 | 1198±646 | 2969±608 |
| HAHD | | 1507±1021 | 1682±1286 | 1139±404 | 4775±3966 |
| C | Retinol | 562±83 | 645±145$^{A}$ | 759±94$^{A}$ | 762±124$^{A}$ |
| HA | | 736±59 | 1061±431$^{B}$ | 1115±254$^{B}$ | 1422±352$^{B}$ |
| HAED | | 697±216 | 1055±233$^{B}$ | 1456±384$^{B}$ | 1261±223$^{B}$ |
| HAHD | | 807±157 | 1106±216$^{B}$ | 1252±213$^{B}$ | 1593±317$^{B}$ |

Ca, P, Albumin not significantly different
Case reports had values comparable with HAED group

# Rx, FPA, Eye examination

- No severe abnormalities as was seen in case reports
- Some OA and vertebral exostosis developed



- Cats already suffering from OA had more severe OA during supplementation, but not in C group
- No abnormalities on FPA and eye examination

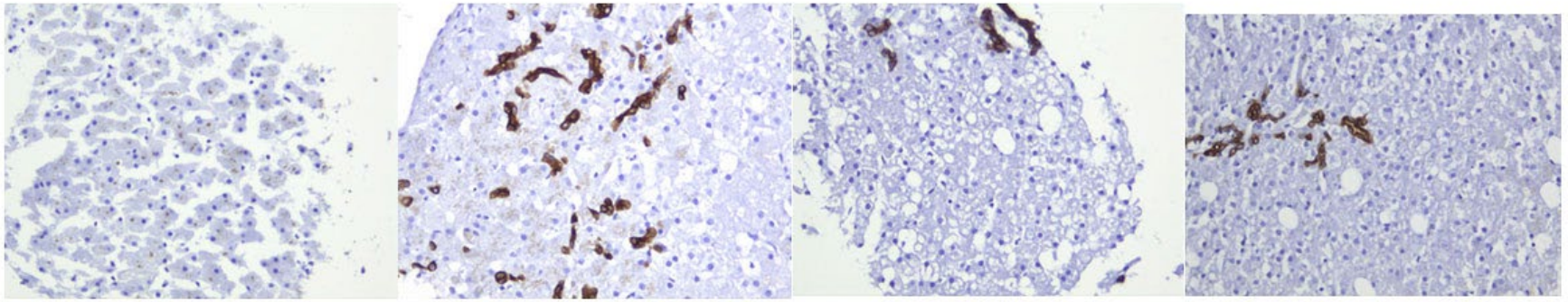
# Liver biopsies

- HE for plain histology
- Cytokeratin 19 for demonstrating active cells
- Ki67 protein as proliferation marker
- Picrosirius red staining for collagen
- Alpha-smooth muscle actin as marker for differentiation of smooth muscle cells

# Liver biopsies

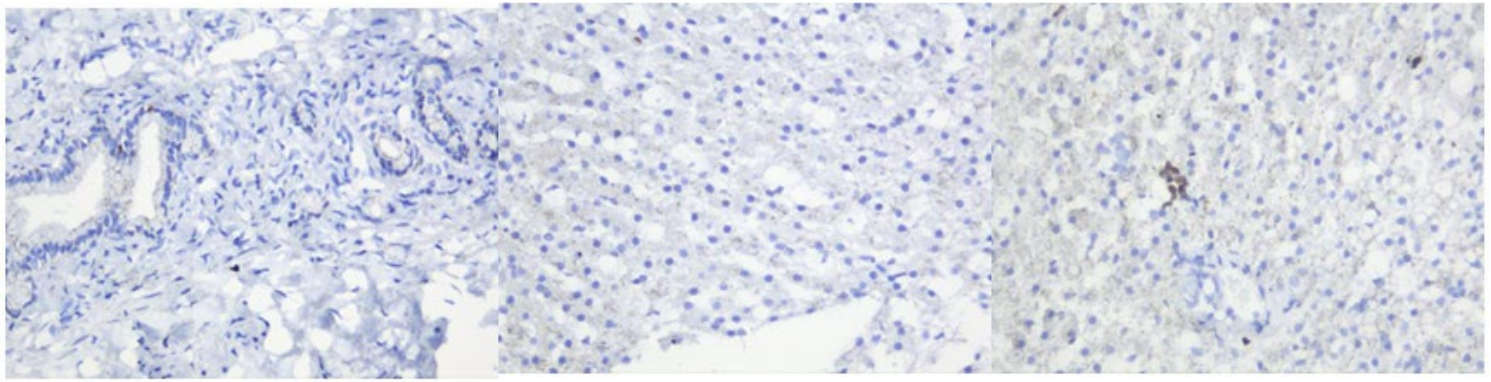
K19

C HA HAED HAHD



Ki67

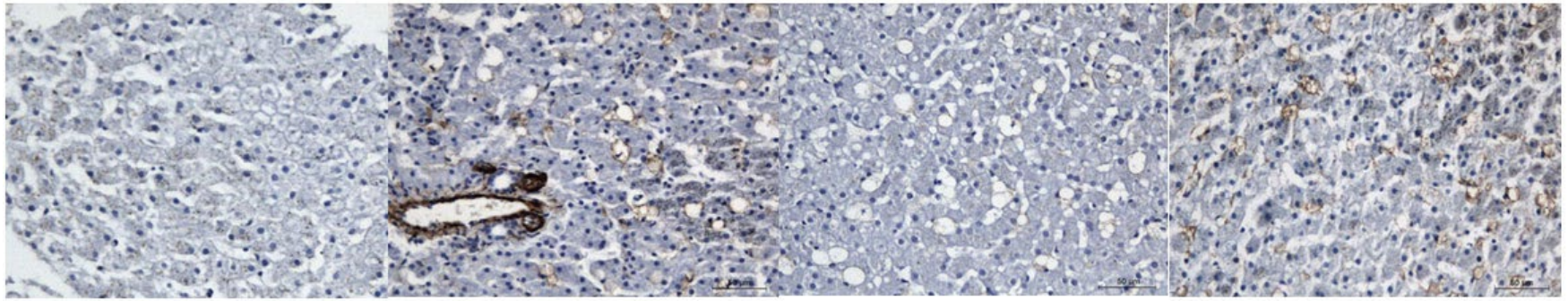
Positive stain in DR Negative Positive



# Liver biopsies

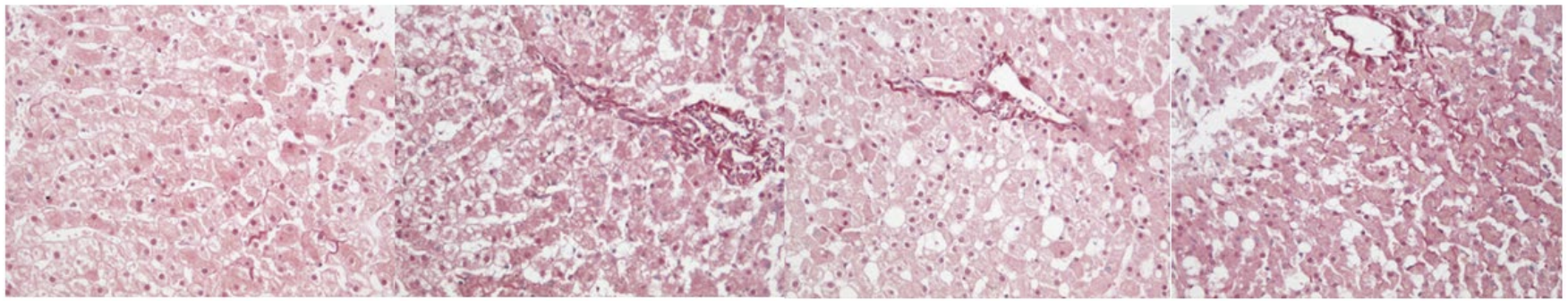
SMA

C HA HAED HAHD



Picrosirus red

C HA HAED HAHD



# Liver biopsies

- HA group had most severe abnormalities, followed by HAHD group
- All supplemented groups had signs of liver fibrosis, which was not seen in the C group
- HAMD group had K19, Ki67 and SMA comparable to C group

| | K19 | α-SMA por | α-SMA par | Ki67 hep | Ki67 HSC | SR par | Hypertrophic HSC |
|---|---|---|---|---|---|---|---|
| C | $1.42\pm0.58^{A,B}$ | $1.33\pm0.52^{A}$ | $1.00\pm0.63^{A}$ | $3.50\pm3.67$ | $0.67\pm0.82$ | $1.17\pm0.75^{A}$ | $0.94\pm0.90^{A}$ |
| HA | $1.90\pm0.42^{B}$ | $2.50\pm0.35^{B}$ | $2.40\pm0.89^{B}$ | $19.0\pm29.9$ | $1.00\pm1.73$ | $1.60\pm1.14^{B}$ | $20.0\pm9.22^{B}$ |
| HAMD | $1.20\pm0.45^{A}$ | $1.60\pm0.55^{A,B}$ | $1.60\pm0.55^{A,B}$ | $3.60\pm2.30$ | $0.00\pm0.00$ | $2.00\pm1.00^{B}$ | $2.00\pm5.28^{B}$ |
| HAHD | $1.92\pm0.49^{B}$ | $1.75\pm0.61^{B}$ | $2.00\pm0.84^{B}$ | $7.00\pm9.38$ | $1.33\pm2.42$ | $2.00\pm0.89^{B}$ | $22.2\pm8.92^{B}$ |

C = Control group; HA = High vitamin A group; HAMD = High vitamin A, moderate vitamin D group; HAHD = High vitamin A, high vitamin D group; 0 = Baseline; 18 = After 18 months of supplementation. K19 = Cytokeratin 19; α-SMA = α-Smooth muscle actin; por = Portal area; par = Parenchymal area; hep = Hepatocytes; HSC = Hepatic stellate cell; SR = Picrosirius red. Total number of K19 positive cells per microscopic field; percentage of α-SMA expression, total number of Ki67 positive cells per microscopic field; percentage of picrosirius red staining; total number of hypertrophic hepatic stellate cells per high power field; $^{A}$ = significantly different from $^{B}$ ($p<0.05$)

# Discussion

-> Some extra vitamin D to hypervitaminosis A is protective for activation of hepatic stellate cells by vitamin A

-> Too much vitamin D is no longer protective

# Discussion

- Mild skeletal pathology
- No abnormal gait (FPA)

- Early signs of liver fibrosis
- No signs of liver failure

- Dosage? Duration?

- Other aspects of raw liver causing skeletal lesions?

# Discussion

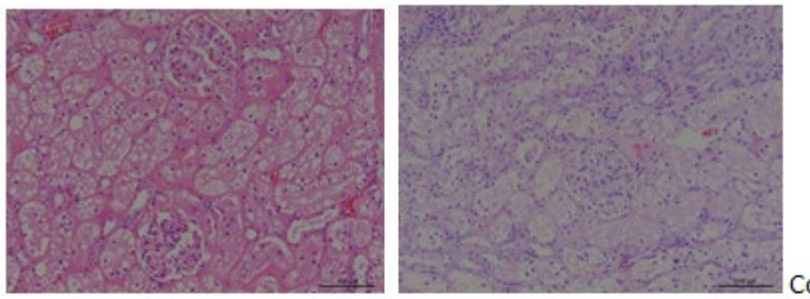
- Activation of bone metabolism by low Ca content of liver?
- Activation of bone metabolism in study of Freytag et al. 2003 because of gestation/lactation?

# Extension of the project

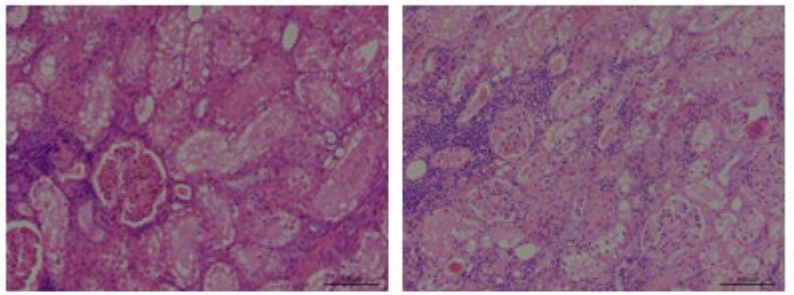
- Complete diet replaced by home -made  chicken-based diet with low Ca-content
- After 6 months Blood, Rx, FPA, eye examination
- Pathology after the study

# Extension of the project

- No differences, except slightly further aggravation of OA
- Of the 24 cats, 6 were previously euthanized due to clinical signs of renal failure
  (3 in HAHD, 2 in HA, and 1 in HAED, none in C group)

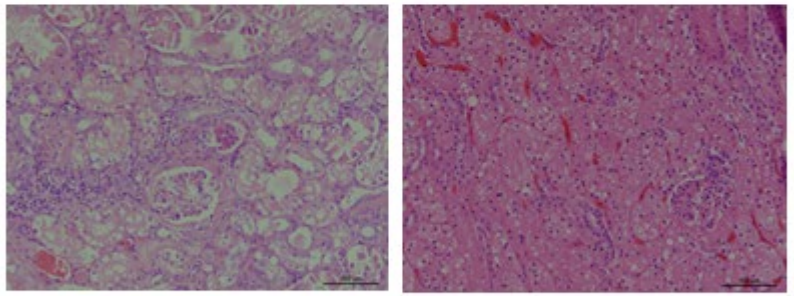


Control



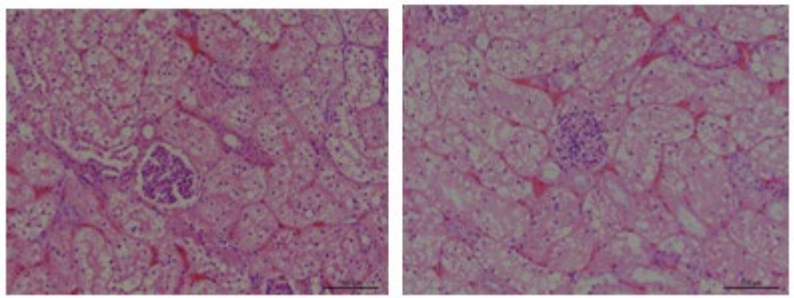
HA

More sclerosis
More inflammation



HAED

More inflammation



HAHD

More sclerosis

ANOVA

Sclerosis p = 0,029

Inflammation p = 0,047

# Histology of kidney hypervitaminosis A

- Chronic vitamin A supplementation evokes renal lesions in cats (i.e. inflammation and fibrosis) (Scoring according to McLeland et al. 2015)

- Similar effects of vitamin D supplementation on (early signs of) fibrosis

# Conclusion

- Current maximum allowance is too high because of mild skeletal pathology, kidney pathology, and early signs of liver fibrosis
- No influence of calcium and vitamin D on skeletal pathology based on this study
- Extra vitamin D can be protective for liver and kidney pathology, however too much vitamin D is no longer protective

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Guest Editorial

# Refining the hypothesis of a complete diet

Commercial diets are relatively recent phenomena for companion animals. Since the last century, there has been a vast amount of research into the dietary requirements of dogs and cats to define a nutritionally complete diet. There have been some major advances, such as the discovery of cats' absolute requirement for taurine and the effect of taurine deficiency (Pion et al., 1987). There is no doubt that these complete diets comprise one factor which has contributed to the increasing lifespan of dogs and cats. To define diets that are adequate to feed to healthy dogs and cats for (potentially) 20 years or more is no small task; to define such a diet for animals with disease processes causing metabolic disturbances adds a further layer of complexity. Despite this, specific commercial diets have been demonstrated to have profound therapeutic impacts on mortality, for example in cats with chronic renal failure (Hoffmann et al., 2009). As with all science, these definitions (or hypotheses) should undergo constant revision as more is learned. The recent paper by R.J. Corbee of Utrecht University and his colleagues, published recently in *The Veterinary Journal* (Corbee et al., 2014), provides some fascinating insights into further refining the hypothesis of a complete feline diet and the complex interplay between nutrients.

The first finding by Corbee et al. (2014) was that cats fed close to the upper safe limit of vitamin A developed hepatic fibrosis and new bone formation in the form of osteophytes and osteoarthritis. As the authors suggest, it would appear that the upper safe limit for vitamin A may be too high. This finding is all the more interesting as these changes occurred over only an 18 month period; it begs the question of whether the upper safe limit should be even lower for a diet consumed over the lifetime of a cat. Osteoarthritis is extremely common in domestic cats, with a radiographic prevalence of up to 92% in geriatric cats (Lascelles et al., 2010). Although this is commonly thought to be a primary disease process, it could in fact be cryptogenic. Any mechanism that reduces osteoarthritis would also have a profound impact on improving feline welfare. It would be ironic if the little fact that every veterinary student learns and keeps during their whole career that 'a liver diet causing hypervitaminosis A and new bone formation in cats' had any role to play in reducing the prevalence of osteoarthritis.

The other finding that was equally striking from the study of Corbee et al. (2014) was that vitamin D appeared to have a protective effect against vitamin A-induced hepatic fibrosis. This occurred only in the group moderately supplemented with vitamin D and not in the high supplementation group, suggesting an optimal dose of vitamin D, which perhaps hints at the complexity of designing a 'balanced' diet. This anti-fibrotic effect is not without precedent; there is increasing evidence that vitamin D directly modulates fibrosis by reducing transforming growth factor-β and epithelial to mesenchymal transformation in both renal and pulmonary fibrosis. There is also some evidence that vitamin D has a role in hepatic fibrosis. The hepatic stellate cell is a key player in the production of extracellular matrix and fibrosis formation. Hepatic stellate cells have been shown to express vitamin D receptors and, experimentally, vitamin D supplementation upregulates their vitamin D receptor expression, inhibiting proliferation and reducing the level of experimentally-induced fibrosis in rats (Abramovitch et al., 2011). This could be the effect demonstrated by Corbee et al. (2014). Chronic liver disease is prevalent in both dogs and cats and the production of extracellular matrix and fibrosis is commonly the end result.

The ability to modulate fibrosis would be of great benefit to small animal patients and the potential role of vitamin D will be followed with great interest. Aside from its role in calcium homeostasis, it is increasingly recognised that vitamin D has a complex role in the immune system. In the current veterinary literature, vitamin D is implicated by correlation in an increasing number of disease processes such as atopic dermatitis, inflammatory bowel disease, mast cell tumours and mycobacterial infections (Gow et al., 2011; Wakshlag et al., 2011; Kovalik et al., 2012; Lalor et al., 2012; Kraus et al., 2014). While these results are very interesting, further prospective studies (such as those being performed in human medicine) are required to demonstrate causation and also to establish whether vitamin D supplementation affects disease pathogenesis and morbidity in animals.

The research performed by Corbee et al. (2014) provides important data on vitamins A and D in cats and might also contain further signposts to the veterinary profession in the journey to further refine balanced diets and improve treatments for the animals in our care.

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