

HIPERLIPIDEMIA

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Definição de Hiperlipidemia

• Hipertrigliceridemia e/ou hipercolesterolemia

• Em jejum de + de 10h

• Avaliar sempre em jejum de 12-16h

Limites de Normalidade:

	Cão	Gato
Triglicerídeos (mg/dL)	50-150	20-110
Colesterol (mg/dL)	125-270	95-130



• Lipemia

- Tg > 250-400 mg/dL
- ↑ Col não causa lipemia

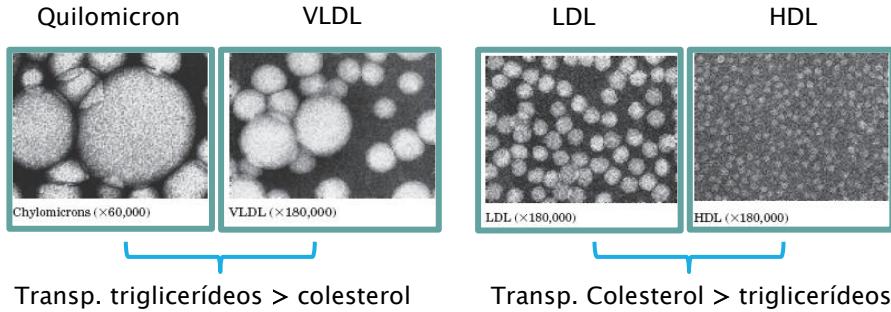
• Dislipidemia

- termo mais amplo para descrever qualquer anormalidade em lipídios e/ou lipoproteínas



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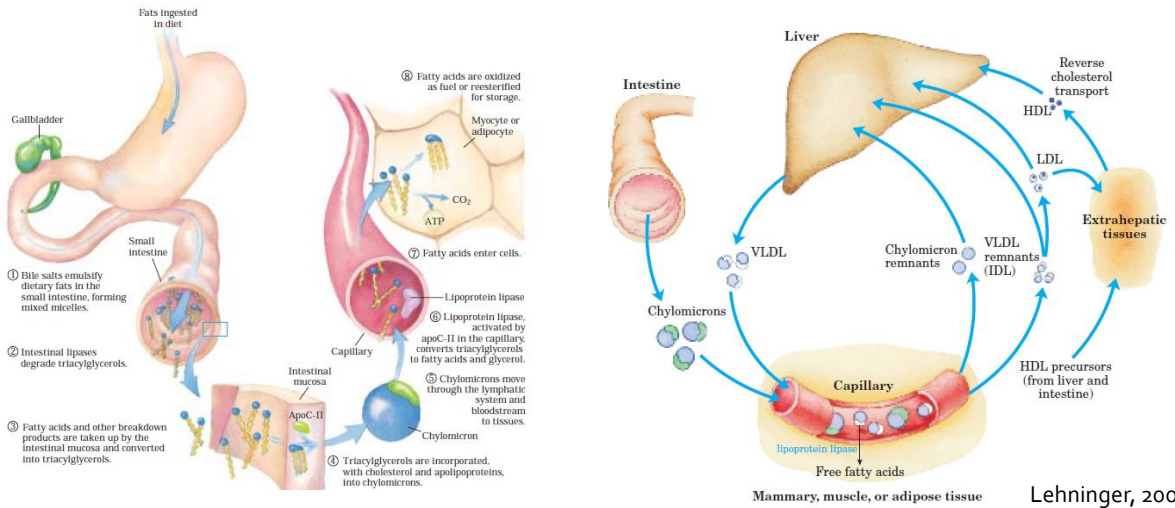
TRANSPORTE DE LIPÍDEOS NO PLASMA (LIPOPROTEÍNAS)



Lipoprotein	Density (g/mL)	Composition (wt %)				
		Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95-1.006	10	18	7	12	50
LDL	1.006-1.063	23	20	8	37	10
HDL	1.063-1.210	55	24	2	15	4

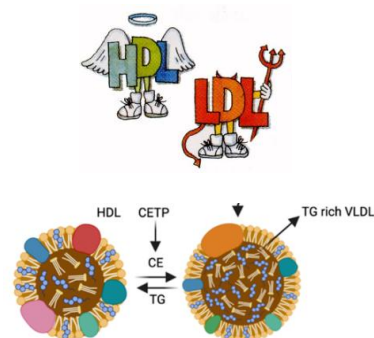
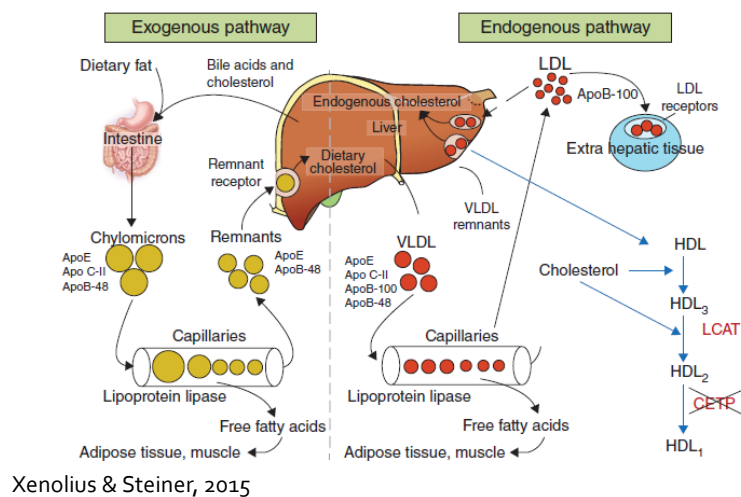
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Transporte de Lipídeos no Sangue



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Cães e Gatos são espécies "HDL-positivas"



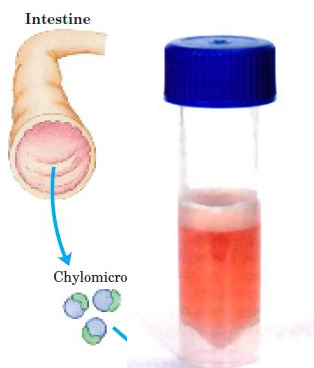
LCAT – Lecitina-colesterol Aciltransferase

CETP – Ptn Tranferidora de Ésteres de Colesterol ausente em cães e gatos

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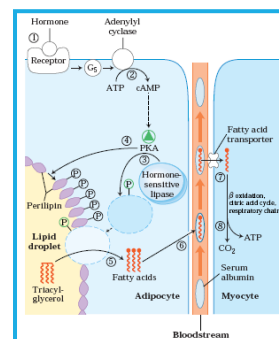
Etiopatogenia da Hiperlipidemia

• Hiperlipidemia FISIOLÓGICA



• Hiperlipidemia SECUNDÁRIA

- **Diabetes Mellitus**
- **Hipercortisolismo**
- **Hipotireoidismo**
- Alt. Hormônios sexuais
- **Colestase**, Insuf. Hepática
- Pancreatite
- Nefropatia perdedora Proteína
- Parvovirose, Leishmaniose
- **Obesidade / Alimentar**
- **Induzida por drogas**
 - Corticoides
 - Ciclosporina
 - Fenobarbital)



Lehninger, 2004

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Etioptogenia da Hiperlipidemia

- Hiperlipidemia PRIMÁRIA

- Hiperlipidemia Familiar Schnauzer (TG>COL)



- Hiperlipidemia Idiopática (Doberman, Rottweiler, Beagle, Pastor Shetland, Briard, Collie – COL>TG)



- Hiperlipidemia Idiopática / hiperquilomicrominemia Felina (TG>COL)

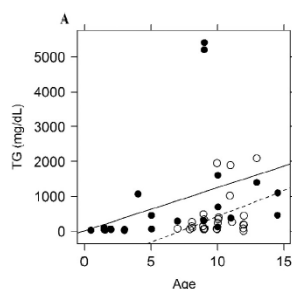
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Etioptogenia da Hiperlipidemia

- A prevalência e magnitude das hiperlipidemias primárias e secundárias é maior com a idade, assim como o perfil de lipidograma pode ser afetado pela idade
- Até 40% Schnauzers > 6 anos c/ HTG
- Até 75% Schnauzers > 10 anos c/ HTG
- Respostas variáveis a diferentes ttos...



Proteinuria and lipoprotein lipase activity in Miniature Schnauzer dogs with and without hypertriglyceridemia
E. Fornace¹*, J.A. Jager¹, V.J. Parker¹, K.W. Hirschfeld¹, S.E. Johnson¹, S.J. Mundel¹,
J.R. de Boer¹, K.C. Sterling¹, J.D. Brunzell¹



Kawasumi et al. BMC Veterinary Research 2016, 16:57
<http://www.biomedcentral.com/1746-6148/16/57>



RESEARCH ARTICLE Open Access

Age effects on plasma cholesterol and triglyceride profiles and metabolite concentrations in dogs

Koh Kawasumi¹, Nanae Kashiwado¹, Yuki Okada¹, Masaki Sawamura², Yasuhiro Sasaki³, Eiji Iwazaki¹, Nobuko Mori¹, Ichiro Yamamoto¹ and Toshiro Arai¹

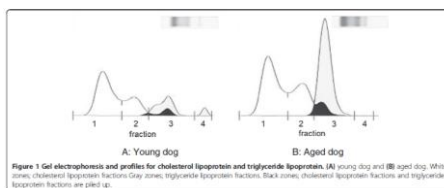


Figure 1 Gel electrophoresis and profiles for cholesterol lipoprotein and triglyceride lipoprotein. (A) young dog and (B) aged dog. White lines, cholesterol lipoprotein fractions; grey lines, triglyceride lipoprotein fractions. Black lines, cholesterol lipoprotein fractions and triglyceride lipoprotein fractions are piled up.

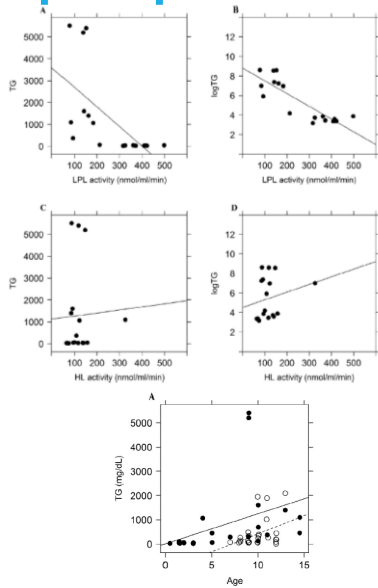
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Etioopatogenia da Hiperlipidemia

➤ Mecanismos Propostos:

- Maior Produção de VLDL?
- **Atividade reduzida da lipase lipoproteica**
- Defeito receptor hepático → clearance <
- Mutações apoproteínas?
- Baixa atividade lipase hepática?

➤ A prevalência, magnitude e perfil da hiperlipidemia piora com a idade



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STANDARD ARTICLE

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American College of Veterinary Internal Medicine

Clustering analysis of lipoprotein profiles to identify subtypes of hypertriglyceridemia in Miniature Schnauzers

Nicole M. Tate¹ | Punyamanee Yamkate² | Panagiotis G. Xenoulis^{2,3} |
Jörg M. Steiner² | Erica L. Behling-Kelly⁴ | Aaron K. Rendahl¹ |
Yu-An Wu² | Eva Furrow¹

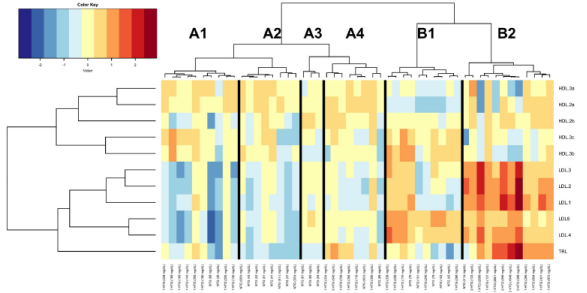
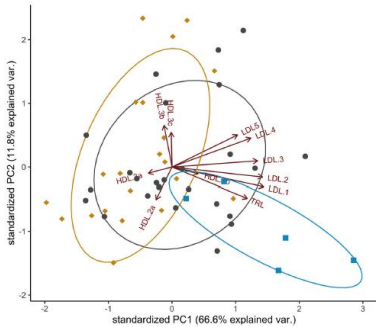


TABLE 1 Eleven density lipoprotein fractions identified in dogs using a continuous lipoprotein density profiling method that uses bismuth sodium ethylenediaminetetraacetic acid as a self-generating density gradient solution.

Fraction	Density (g/mL)	Classification ^a
R1	<1.017	TRL
R2	1.019–1.023	LDL ₄
R3	1.023–1.029	LDL ₂
R4	1.029–1.039	LDL ₃
R5	1.039–1.050	LDL ₁
R6	1.050–1.063	LDL ₅
R7	1.063–1.091	HDL _{2b}
R8	1.091–1.110	HDL _{2a}
R9	1.110–1.133	HDL _{3a}
R10	1.133–1.156	HDL _{3b}
R11	1.156–1.179	HDL _{3c}



- Espectro de fenótipos de lipoproteínas em cães NTG, HT1 e HT2 não é justificado por, idade, sexo, ECC ou teor gordura na dieta...
- Avaliação TG sozinho não mostra estas diferenças...
- Origens, respostas a terapia e consequências diferentes?

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Genética?

- Não foi possível identificar uma causa monogênica para HTG em Schnauzers
- Resultado de múltiplas variantes complexas acumuladas + ambiente
- Estudo não permite descartar papel destas variantes genéticas



Genes 2024, 15, 193. <https://doi.org/10.3390/genes15020193>



Article

Sequence Analysis of Six Candidate Genes in Miniature Schnauzers with Primary Hypertriglyceridemia

Nicole M. Tate ^{1,*}, Michaela Underwood ², Alison Thomas-Hollands ³, Katie M. Minor ¹, Jonah N. Cullen ⁴, Steven G. Friedenberg ¹, James R. Mickelson ⁵, Panagiotis G. Xenoulis ^{6,7}, Joerg M. Steiner ⁷ and Eva Furrow ¹

Table 1. Six candidate genes previously associated with primary hypertriglyceridemia in people.

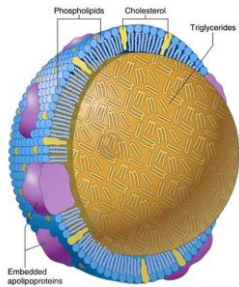
Gene Symbol	Gene Name	Function
<i>LPL</i>	Lipoprotein lipase	Hydrolyzes circulating triglycerides [19]
<i>APOC2</i>	Apolipoprotein C-II	Essential cofactor for LPL activity [19,20]
<i>APOA5</i>	Apolipoprotein A-V	Stimulates LPL-mediated triglyceride hydrolysis [19,21]
<i>LMF1</i>	Lipase maturation factor 1	Essential for proper LPL function [19,22]
<i>GPIHBP1</i>	Glycosylphosphatidylinositol-anchored HDL binding protein 1	Facilitates LPL toward cell surface and promotes processing of triglyceride-rich lipoproteins [19,23]
<i>APOE</i>	Apolipoprotein E	Regulates clearance of chylomicron remnants and VLDL [10]

LPL, lipoprotein lipase; VLDL, very-low-density lipoprotein.

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Hiperlipidemia em Gatos

- Hiperquilomicrinemia Felina (Jones et al, 1986; Ginzinger et al, 1996)
 - Idiopática
 - Genética
 - Autossômica recessiva (éxon 8 do gene LPL)
 - Birmaneses mais predispostos (Kluger et al, 2009)



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Repercussões Clínicas da Hiperlipidemia

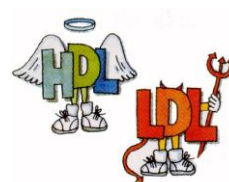
Hipertrigliceridemia

- Pancreatite
- Lipemia retinal,
- Ceratopatia lipídica
- Humor aquoso lipêmico
- Convulsões
- Neuropatias periféricas
- Alterações comportamentais
- Hepatopatia vacuolar/mucocele
- Proteinúria
- Resistência insulínica



Hipercolesterolemia

- Mucocele
- Arcos lipídicos corneais
- Aterosclerose

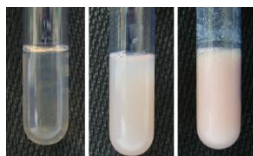


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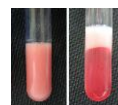
Repercussões da Hiperlipidemia na Patologia Clínica

• ELEVAÇÃO

- ALT, AST, FAS
- Ácidos biliares
- Bilirrubinas
- Cálcio
- Creatinina
- Glicose
- Hemoglobina
- Fósforo
- PPT (refratometria)
- Hormônios (exceto RIE)



HEMÓLISE



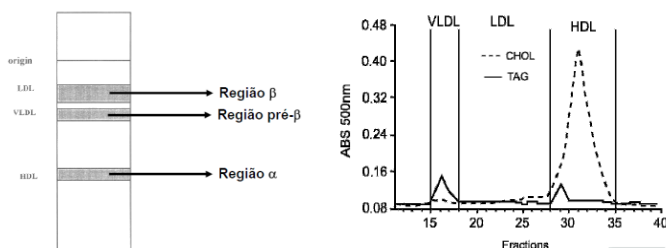
• REDUÇÃO

- Albumina
- Amilase
- Lipase
- Frutosamina
- Eletrólitos

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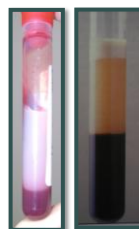
Determinação das Frações de VLDL, LDL e HDL

- Cromatografia ou Eletroforese (métodos de eleição)



- Métodos matemáticos (Fórmula de Friedwald) não é acurada em cães e gatos

- Prova do Quilomícron

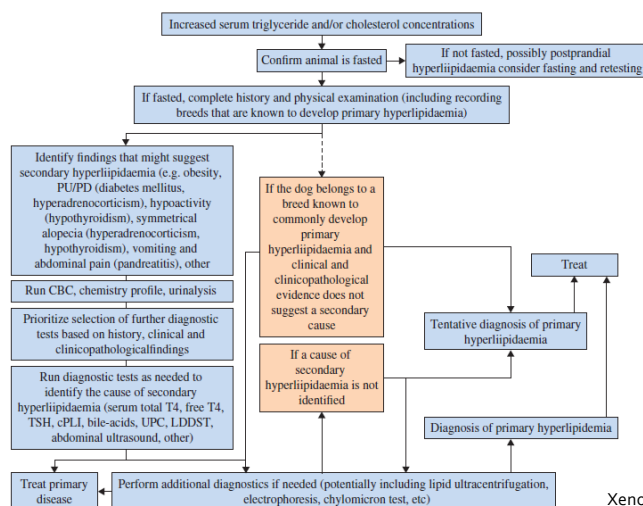


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Abordagem do Paciente Hiperlipidêmico

2º) Descartado erro, identificar fatores que justifiquem hiperlipidemia secundária e realizar exames complementares e de diagnóstico...

TRATAR A DOENÇA PRIMÁRIA



1º) Confirmar se estava realmente em jejum e eventual erro de digitação...

3º) Na ausência de causas secundárias, especialmente em raças predispostas, assumir diagnóstico de hiperlipidemia primária e tratar.

Xenolius & Steiner, 2015

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Abordagem Nutricional no Tratamento da Hiperlipidemia

✓ Banir guloseimas deve ser o primeiro passo!

✓ Petiscos somente ultra baixo em gorduras



✓ Frutas e legumes podem ser opções de petisco em pequenas quantidades (< 10% REM para o paciente) – TABELA TACO



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Abordagem Nutricional no Tratamento da Hiperlipidemia

• Tratamento Dietético Sempre que Possível como primeira opção!

➢ Cães com hiperlipidemia secundária:

✓ Tratamento doença de base

✓ Dietas c/ baixo teor gorduras (<10%)

✓ Observar EM e teor de fibras (Colesterol)

➢ Cães com hiperlipidemia primária

✓ Ultra Low-Fat (5%)



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❖ Avaliações entre 30 dias e 1 dia antes da mudança de dieta → Seguimento 30 e 60 dias após mudança

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STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM
American College of Veterinary Internal Medicine

Effect of a low-fat diet on serum triglyceride and cholesterol concentrations and lipoprotein profiles in Miniature Schnauzers with hypertriglyceridemia

Panagiotis G. Xenoulis¹ | Paul J. Cammarata² | Rosemary L. Walzem³ |
Jan S. Suchodolski¹ | Jörg M. Steiner¹

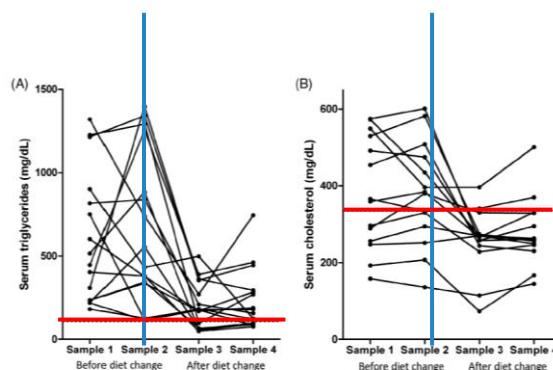


FIGURE 1 A, Serum triglyceride and B, cholesterol concentrations in dogs with hypertriglyceridemia before and after diet change. Samples 1 and 2 were collected while dogs were on their original diets. Samples 3 and 4 were collected approximately 8 and 12 weeks, respectively, after the dogs were placed on the study diet. There was a significant decrease in serum triglyceride ($P < .001$) and cholesterol ($P < .001$) concentrations after the diet change. The dotted lines represent the upper limit of the reference interval. See also Tables 4 and 5

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Jan S. Suchodolski¹ | Jörg M. Steiner¹



- Dieta sozinha foi suficiente para:
- ✓ Normalizar Tg e Colesterol em alguns casos
- ✓ Baixar Tg < 500 mg/dL em quase todos os casos
- ✓ Normalizar perfil de Lipoproteínas
- Falta de resposta em alguns casos pode estar associada a diferenças na patologia

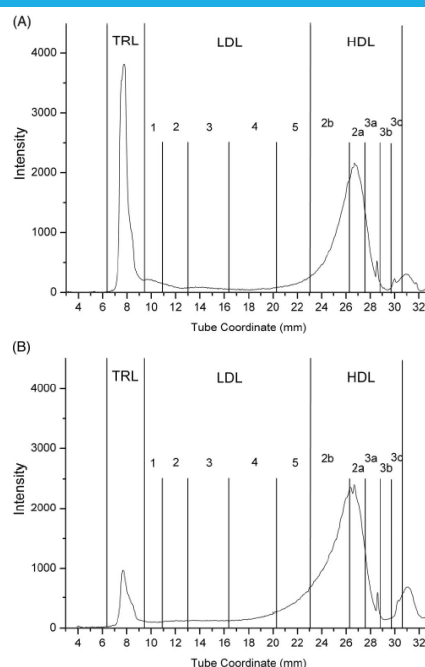


FIGURE 4 Lipoprotein density profiles from a representative dog in group 1. A, Lipoprotein profile of the dog before the diet change. B, Lipoprotein profile of the same dog 8 weeks after the diet change. This dog had normal serum triglyceride and cholesterol concentrations at that point. Note the dramatic decrease in TRL. A decrease in LDL₁ and increases in HDL_{2b} and HDL_{2a} are also evident. HDL, high-density lipoproteins; LDL, low-density lipoproteins; TRL, triglyceride-rich lipoproteins

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E quando a dieta sozinha não controla a HIPERTRIGLICERIDEMIA?

- Ω -3 (EPA e DHA) → 200-300 mg/kg/dia
- Bezafibrato 2,5 a 5 mg/kg/dia (sid a bid)
- Fenofibrato 10 mg/kg/dia sid
- Ciprofibrato 5-10 mg/kg/dia
- Gemfibrozil 10 mg/kg bid
- Fibra de maracujá 15 g/kg/dia
- Niacina 50-200 mg/dia (eritema facial/prurido)

- ❖ Regulação de fatores de transcrição levando a redução da lipogênese
- ❖ Incremento na beta-oxidação
- ❖ Ativação da LPL

Fibratos e ativação do PPAR- α (*peroxisome proliferator-activated receptor*)

The PPARs: From Orphan Receptors to Drug Discovery[†]

Timothy M. Willson,* Peter J. Brown, Daniel D. Sternbach, and Brad R. Henke

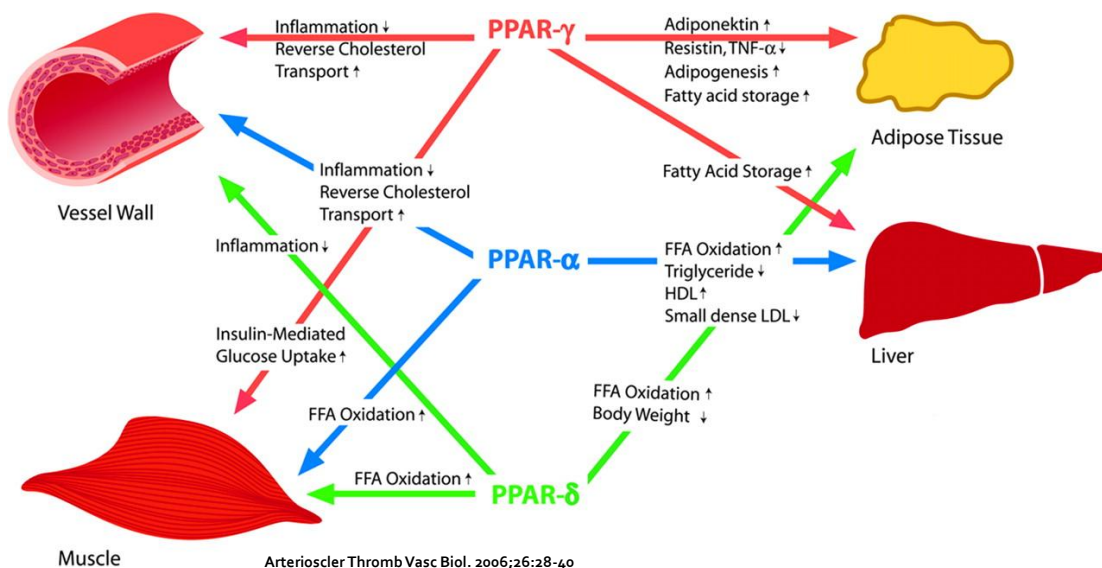
Table 1. Activity of PPAR Agonists in Cell-Based Transactivation Assays^a

compound	murine receptor EC ₅₀ (μ M)			human receptor EC ₅₀ (μ M)		
	PPAR α	PPAR γ	PPAR δ	PPAR α	PPAR γ	PPAR δ
Wy-14643	0.63	32	ia at 100	5.0	60	35
clofibrate ^b	50	~500	ia at 100	55	~500	ia at 100
fenofibrate ^b	18	250	ia at 100	30	300	ia at 100
bezafibrate	90	55	110	50	60	20

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Obesity, Peroxisome Proliferator-Activated Receptor, and Atherosclerosis in Type 2 Diabetes

Florian Blaschke, Yasunori Takata, Evren Caglayan, Ronald E. Law, Willa A. Hsueh



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Cristal, Yorkshire, 5 anos

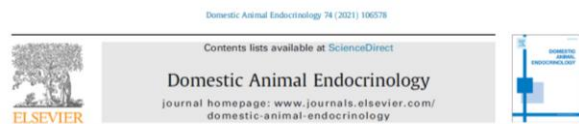
- Apresentação inicial para limpeza de cálculo dental, achado incidental de lipemia e FA 468 u/L...
- Colesterol 557 mg/dL
- Tg 4452 mg/dL

Low Fat + Bezafibrato 15 mg bid



Fecha	Tg (mg/dL)	Colesterol (mg/dL)
29/11/09	4452	557
09/01/10	352	197
20/03/10	63	147
15/06/10	53	154
09/11/10	1494	191
20/01/11	84	129

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Fenofibrate treatment for severe hypertriglyceridemia in dogs

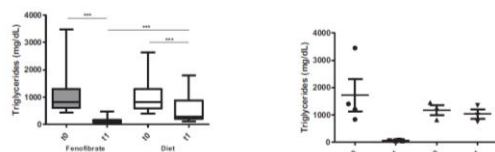


Fig. 1. A box and whisker graph of triglyceride concentrations in dogs with secondary hypertriglyceridemia treated with fenofibrate or low-fat diet, before (0) and after 1 month of treatment (1). Boxes represent 25th and 75th percentiles with median in between. The whiskers represent values at 1.5 × IQR (interquartile range). *** $P < 0.001$.

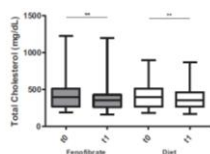
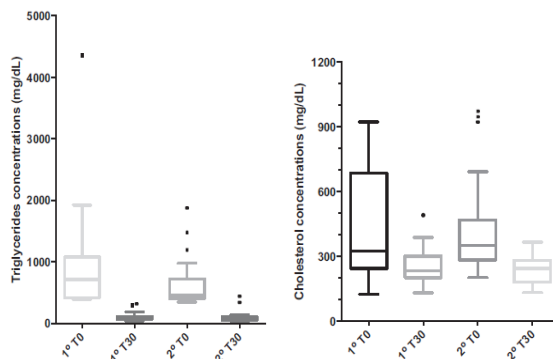


Fig. 3. Box and whisker graph of total cholesterol concentrations in dogs with hypertriglyceridemia treated with fenofibrate or low-fat diet, before (0) and after 1 month of treatment (1). Boxes represent 25th and 75th percentiles with median in between. The whiskers represent values at 1.5 × IQR (interquartile range). ** $P < 0.01$.



Therapy of Canine Hyperlipidemia with Bezafibrate

V. De Marco, K.S.M. Noronha, T.C. Casado, E.R. Nakandakare, J.C. Florio, E.Z. Santos, and C. Gilor



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Therapy for feline secondary hypertriglyceridemia with fenofibrate

Diego D Miceli^{1,3}, Juan M Guevara⁴, Sergio Ferraris³, Omar P Pignataro² and María F Gallelli⁵

Journal of Feline Medicine and Surgery
1-7
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SAGE

Abstract

Objectives The aim of this study was to assess the short-term safety and efficacy of fenofibrate in controlling secondary hypertriglyceridemia in cats.

Methods This was a prospective cohort study. Seventeen adult cats with hypertriglyceridemia (serum triglycerides [TG] >160 mg/dl) were enrolled. Cats received a median dose of 5 mg/kg (range 3.2–6) fenofibrate (q24h PO) for 1 month. Serum TG, total cholesterol (TC), creatine kinase and liver enzymes (alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase) were evaluated before (t0) and after 1 month (t1) of fenofibrate treatment.

Results The causes of secondary hypertriglyceridemia were diabetes mellitus (DM; 29.4%), obesity (29.4%), hyperadrenocorticism (HAC) and DM (11.7%), HAC without DM (5.9%), hypersomatotropism (HST) and DM (5.9%), hypothyroidism (5.9%), long-term treatment with glucocorticoids (5.9%) and chylothorax (5.9%). Serum TG (t0 median 920 mg/dl [range 237–1780]; t1 median 51 mg/dl [range 21–1001]; $P=0.0002$) and TC (t0 median 278 mg/dl [range 103–502]; t1 median 156 mg/dl [range 66–244]; $P=0.0001$) concentrations showed a significant decrease after 1 month of fenofibrate treatment. Fifteen cats normalized their TG concentration at t1 (88.2%). Of the eight cats that were hypercholesterolemic at t0, six (75%) normalized their TC concentrations at t1. One of 17 cats (5.9%) presented with diarrhea; the remaining 16 did not show any adverse effects.

Conclusions and relevance DM and obesity are the most common endocrine causes of secondary hyperlipidemia, although it can also be found in cats with HAC, HST or hypothyroidism. This study suggests that fenofibrate treatment was associated with reduction and normalization of TG and TC concentrations in cats with moderate and severe hypertriglyceridemia, regardless of the cause of secondary hypertriglyceridemia. Further work should focus on controlled studies with a greater number of cases.

	t0	t1	P value
TG (mg/dl)*	920 (237–1780)	51 (21–1001)	0.0002
TC (mg/dl)†	278 (103–502)	156 (66–244)	0.0001
ALT (U/l)‡	68 (25–198)	48 (21–105)	0.12
AST (U/l)§	32 (5–73)	25 (2–51)	0.18
ALP (U/l)¶	91 (40–123)	91 (36–195)	0.13
CK (U/l)∞	110 (65–716)	110 (71–710)	0.75
Creatinine (mg/dl)§	1.1 (0.7–1.2)	1.08 (0.6–1.2)	0.9
BUN (mg/dl)**	34 (17–44)	34 (19–42)	0.64
UPC††	0.15 (0.05–0.39)	0.14 (0.06–0.37)	0.73

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PLOS ONE

RESEARCH ARTICLE

Supplementation of omega-3 and dietary factors can influence the cholesterolemia and triglyceridemia in hyperlipidemic Schnauzer dogs: A preliminary report

Paula de Albuquerque¹, Viviani De Marco^{1,2,*}, Thiago Henrique Annibale Vendramini³, Andressa Rodrigues Amaral⁴, Sergio Catanozi¹, Kelly Gomes Santana⁴, Valéria Sutti Nunes⁵, Edna Regina Nakandakare⁶, Marcio Antonio Brunetto³

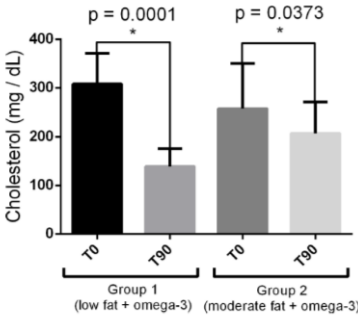


Fig 1. Serum cholesterol concentrations in the experimental groups before (T0) and 90 days after treatment (T90).

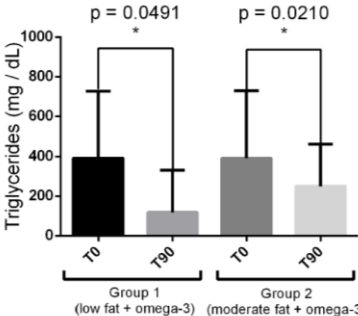


Fig 2. Serum triglyceride concentrations in the experimental groups before (T0) and 90 days after treatment (T90).

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ORIGINAL RESEARCH

Association Between Omega-3 Fatty Acid Intake and Dyslipidemia: A Continuous Dose–Response Meta-Analysis of Randomized Controlled Trials

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BACKGROUND: Previous results provide supportive but not conclusive evidence for the use of omega-3 fatty acids to reduce blood lipids and prevent events of atherosclerotic cardiovascular disease, but the strength and shape of dose–response relationships remain elusive.

METHODS AND RESULTS: This study included 90 randomized controlled trials, reported an overall sample size of 72 598 participants, and examined the association between omega-3 fatty acid (docosahexaenoic acid, eicosapentaenoic acid, or both) intake and blood lipid changes. Random-effects 1-stage cubic spline regression models were used to study the mean dose–response association between daily omega-3 fatty acid intake and changes in blood lipids. Nonlinear associations were found in general and in most subgroups, depicted as J-shaped dose–response curves for low-/high-density lipoprotein cholesterol. However, we found evidence of an approximately linear dose–response relationship for triglyceride and non-high-density lipoprotein cholesterol among the general population and more evidently in populations with hyperlipidemia and overweight/obesity who were given medium to high doses (>2 g/d).

CONCLUSIONS: This dose–response meta-analysis demonstrates that combined intake of omega-3 fatty acids near linearly lowers triglyceride and non-high-density lipoprotein cholesterol. Triglyceride-lowering effects might provide supportive evidence for omega-3 fatty acid intake to prevent cardiovascular events.

Key Words: 1-stage regression ■ hyperlipidemia ■ long-chain fatty acids ■ non-HDL cholesterol ■ triglyceride

CLINICAL PERSPECTIVE

What Is New?

- Intake of omega-3 fatty acids of more than 2 g/d appears to have a near-linear association with reductions in triglyceride and non-high-density lipoprotein cholesterol.
- Omega-3 polyunsaturated fatty acid supplementation at lower doses is associated with an increased level of low-density lipoprotein cholesterol.

What Are the Clinical Implications?

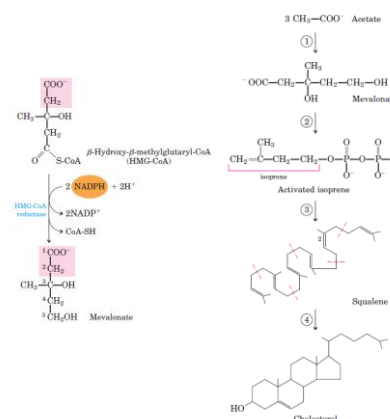
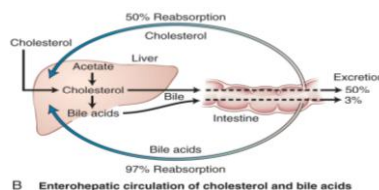
- A medium dose of omega-3 fatty acids is potentially needed for the management of dyslipidemia, and a higher dose may afford more benefits for people who are at high risk of developing cardiovascular diseases.
- The recommendation for omega-3 fatty acid supplementation to reduce cardiovascular disease risks could be supported in patients with a high level of triglyceride in the context of guideline-directed statin therapies.

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E quando a dieta sozinha não controla a HIPERCOLESTEROLEMIA?

➤ Normalmente 2ª e não demanda tto específico, além do menor grau de complicações relacionadas

- Sinvastatina 1-2 mg/kg/dia?? (outras estatinas??)
- Fibras de maracuyá 15 g/kg/dia
- Omegas
- Fibratos
- Ligadores de ácidos biliares (Colestiramina)
- Ezetimiba 0,1-0,8 mg/kg/dia
- Dieta rica em fibras

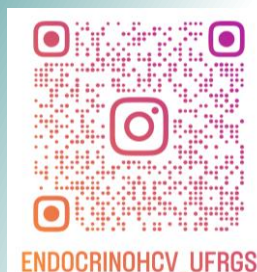


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- ✓ Hiperlipidemia é um achado frequente em exames de rotina e pode ser resultado de um distúrbio primário.
- ✓ Excesso de triglicerídeos e colesterol no sangue pode ser fisiológico ou secundário à doenças; mas cronicamente elevados podem causar repercussões clínicas nos pacientes
- ✓ O manejo da alimentação é fundamental, e potencialmente eficaz; porém muitos casos precisarão de manejo medicamentoso em paralelo.

PONTOS CHAVES!!

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Obrigado pela
Atenção!



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