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Integrative Approach to Gastrointestinal Health

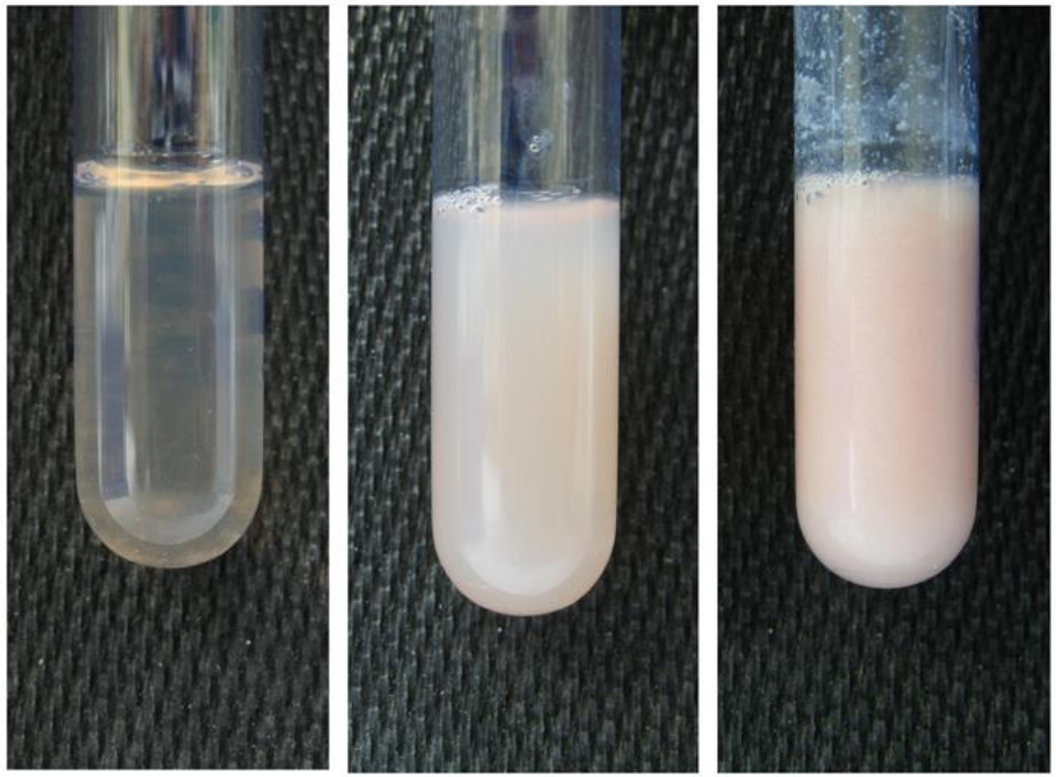
Tackling Complex Hyperlipidemia Cases: Your Next Steps for Effective Management

Dr. Panos Xenoulis,

DVM, Dr.med.vet., PhD - Professor of Medicine, University of Thessaly, Adjunct Professor, Texas A&M University

What is hyperlipidemia?

Increased triglycerides and/or cholesterol in the blood



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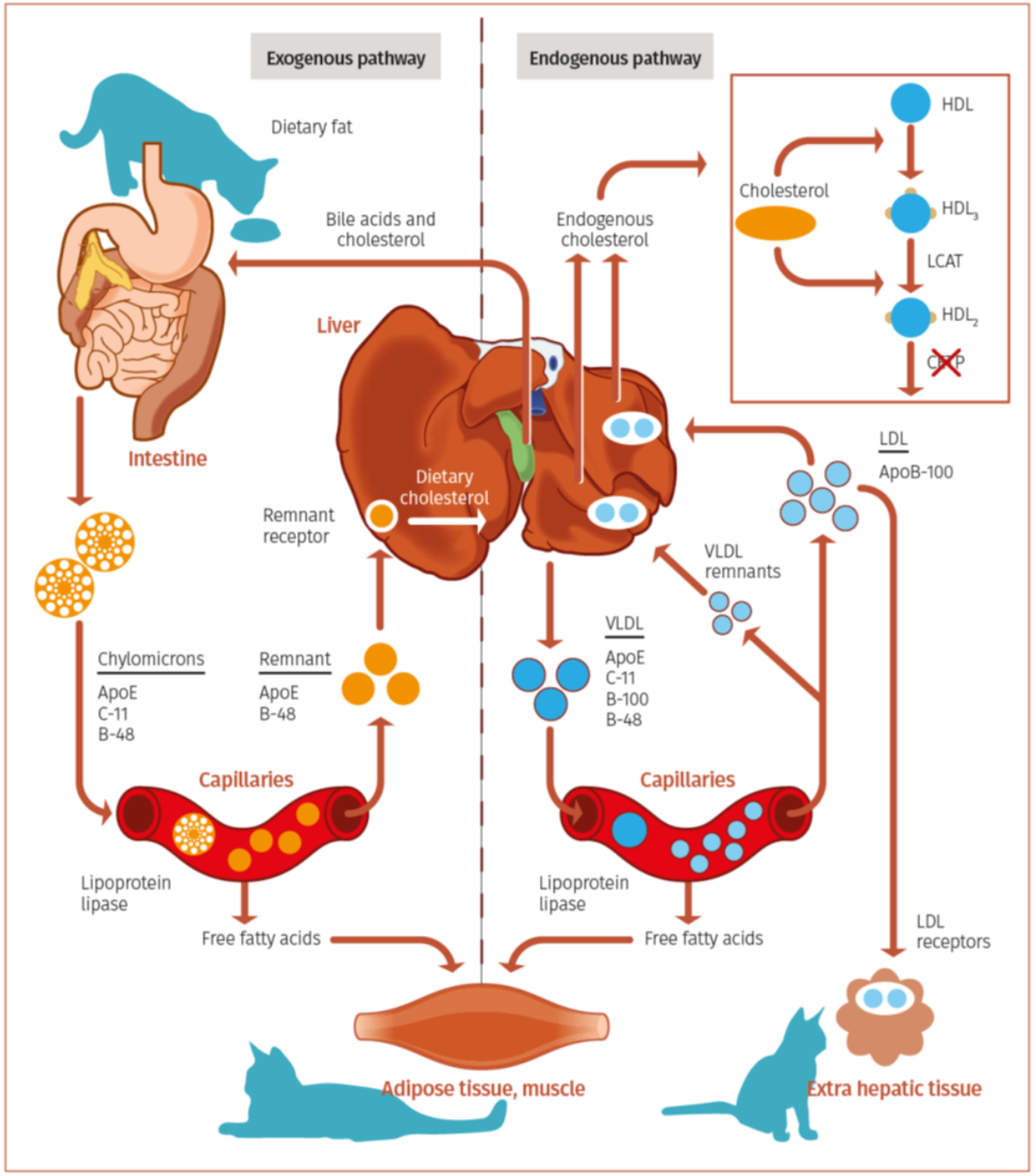

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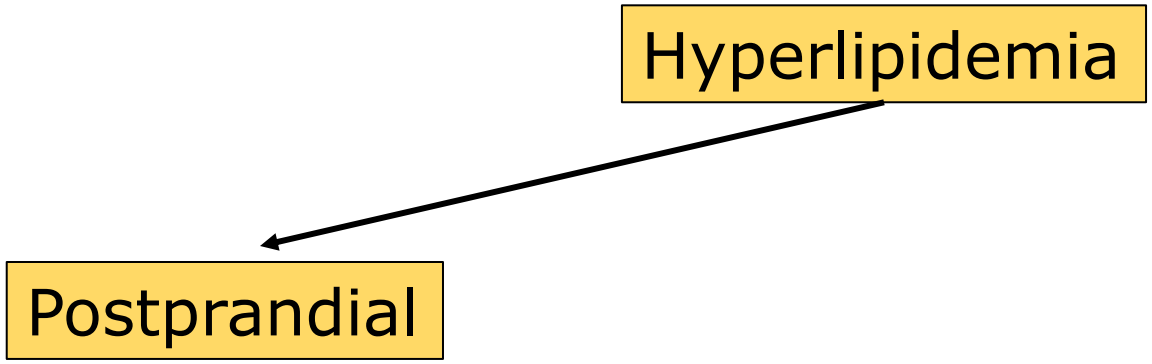
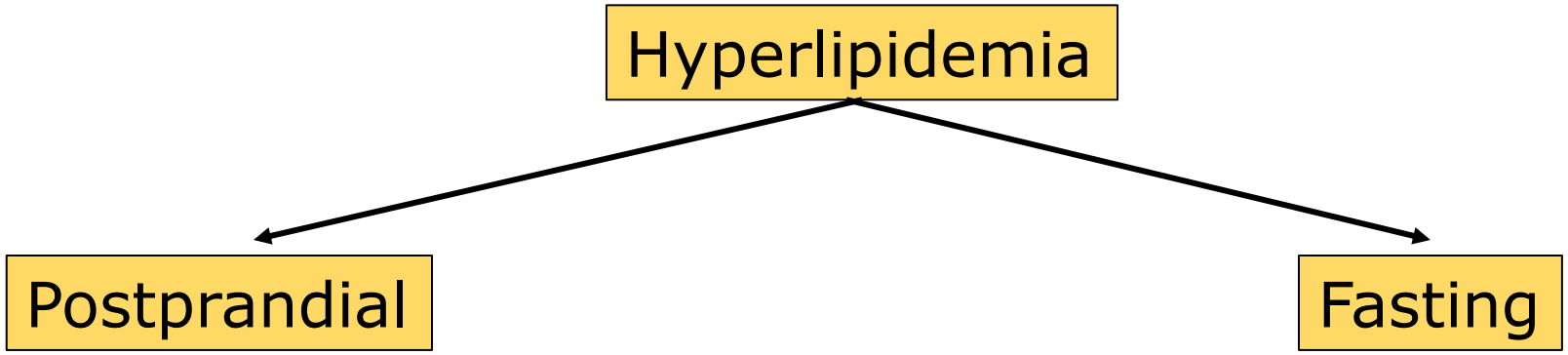
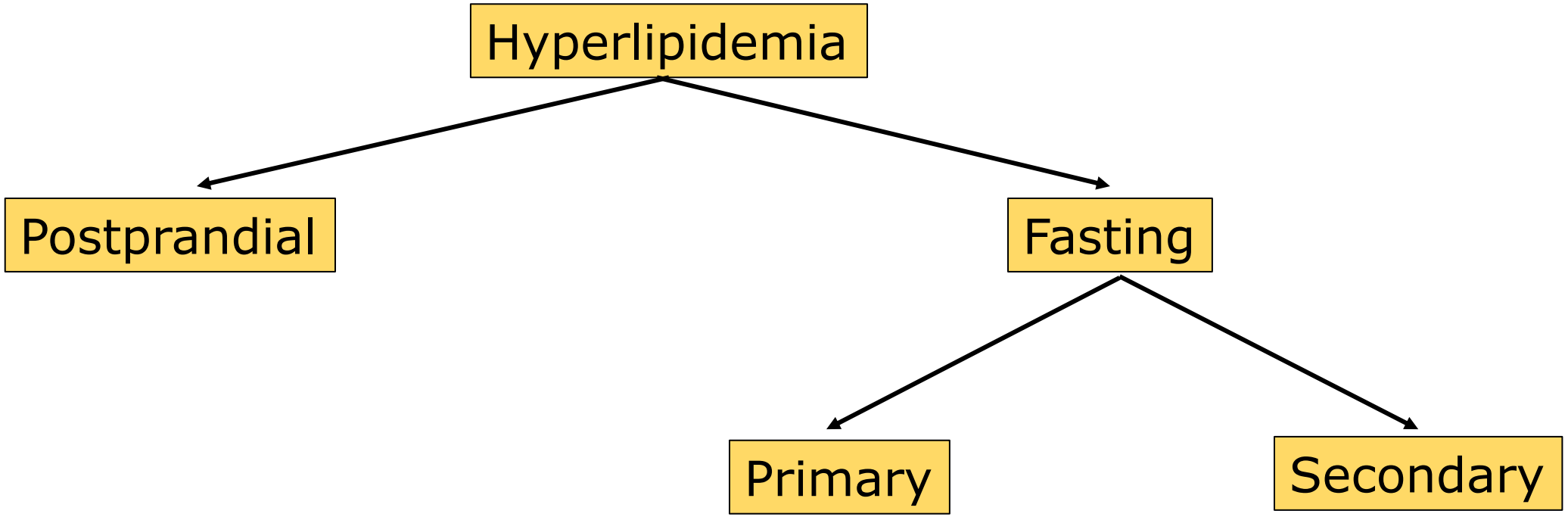
Causes of hyperlipidemia



Causes of hyperlipidemia



Causes of hyperlipidemia

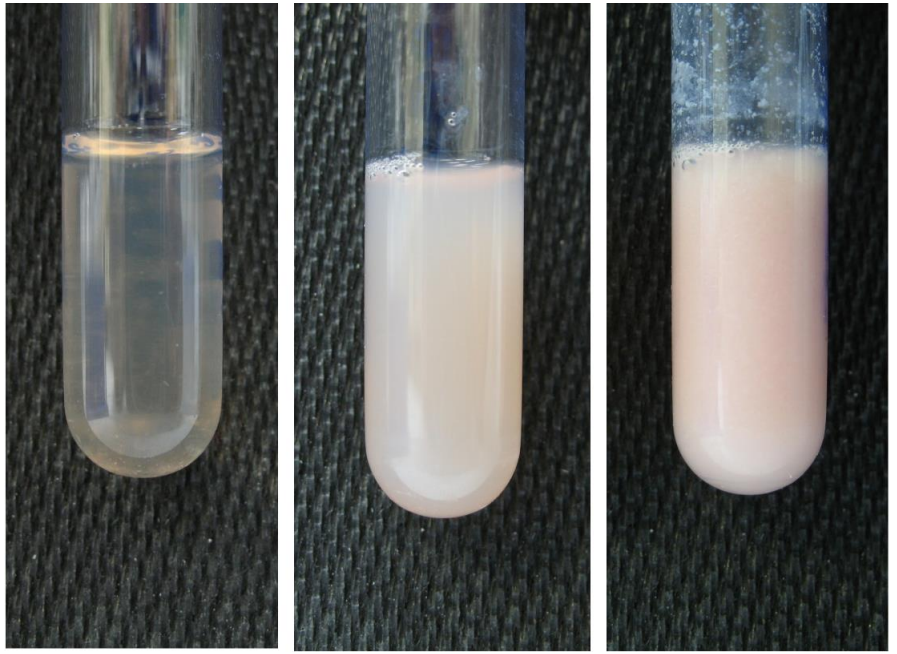


Secondary hyperlipidemia

- Most common pathologic form of hyperlipidemia in dogs
- Several diseases have been reported to cause hyperlipidemia
  - Endocrine diseases
  - Pancreatitis
  - Obesity
  - Protein-losing nephropathy
  - Cholestasis
  - Other
  - Drugs

Primary hyperlipidemia

- More commonly associated with specific breeds
  - Miniature Schnauzer
  - Beagle
  - Shetland Sheepdog
  - Doberman pincher
  - Rottweiler



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Primary hyperlipidemia in MS

- Primary hyperlipidemia in Miniature Schnauzers was the first breed-related primary lipid disorder described in dogs
- It was first reported in Miniature Schnauzers in the United States (Roger et al, 1975)
  - Japan
  - South America
  - Europe

Primary hyperlipidemia in MS

- Characterized by
  - Hypertriglyceridemia +/- Hypercholesterolemia
  - Increased VLDL and/or chylomicrons

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Primary hyperlipidemia in MS

J Vet Intern Med 2007;21:1224–1230

Investigation of Hypertriglyceridemia in Healthy Miniature Schnauzers

Panagiotis G. Xenoulis, Jan S. Suchodolski, Melinda D. Levinski, and Jörg M. Steiner

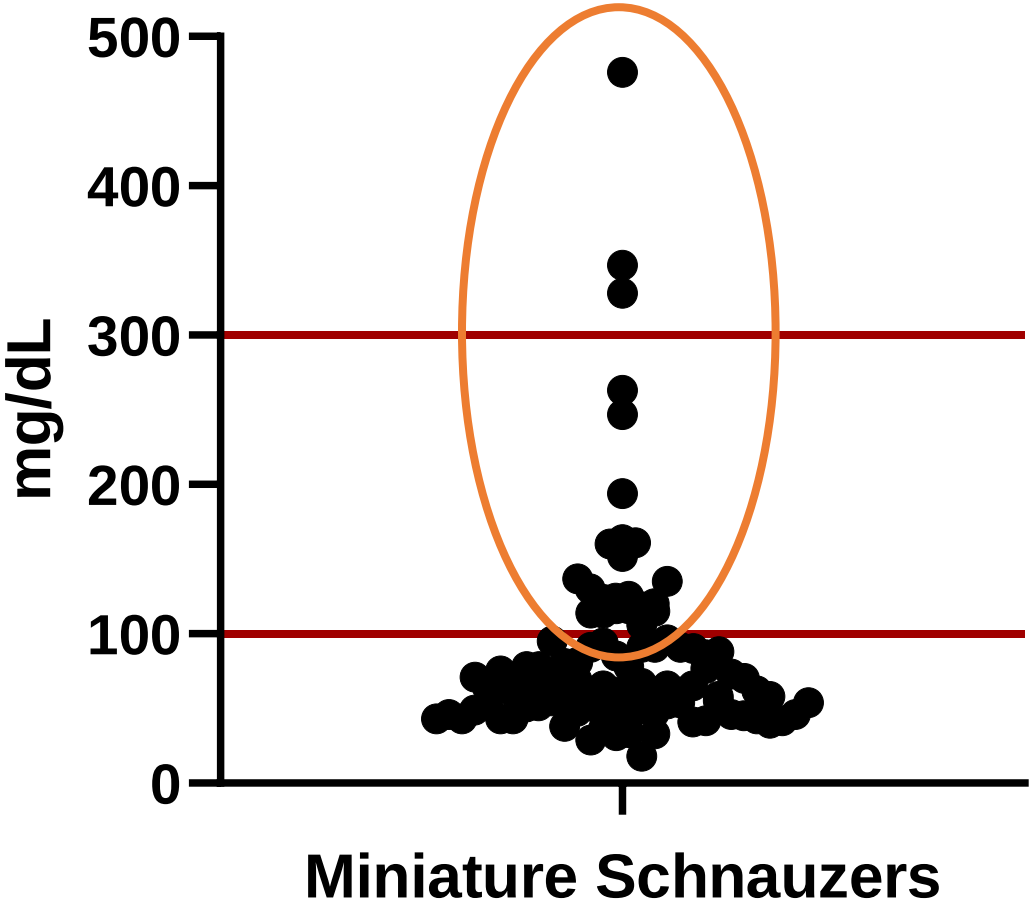
- 192 healthy MS
- Hypertriglyceridemia was present in 32.8%
  - Mild hypertriglyceridemia: 21.3%
  - Moderate to severe hypertriglyceridemia: 11.5%
- Hypercholesterolemia was present in 9%
  - Only in association with hypertriglyceridemia

Primary hyperlipidemia in MS

ACVIM FORUM 2024

Prevalence of primary hyperlipidemia in Miniature Schnauzers in Europe

Pitropaki M.N., Vecchio M., Ruhnke I., Steiner J.M., Xenoulis P.G.



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Diagnostic approach

- Hyperlipidemia is diagnosed by measurement of fasting serum triglyceride and cholesterol concentrations
- Serum triglyceride and cholesterol concentrations should be part of every chemistry panel
  - Hyperlipidemia is an important diagnostic clue for dogs with secondary hyperlipidemia
  - Often the only abnormality in dogs with primary hyperlipidemia

Diagnostic approach

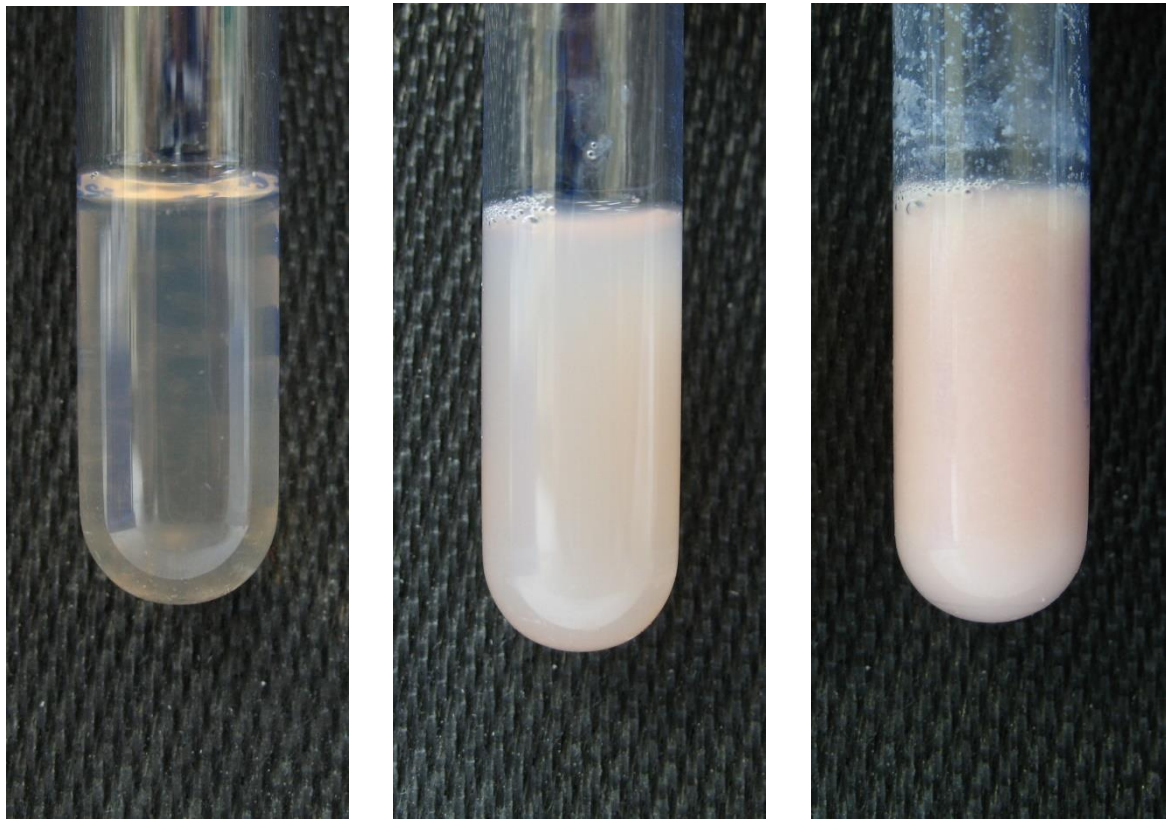
- After hyperlipidemia has been diagnosed:
  - Determination of whether the patient has a primary or a secondary lipid disorder
- If hyperlipidemia is secondary, the primary disease causing hyperlipidemia should be diagnosed and treated

Diagnostic approach

- Diagnostic tests
  - CBC
  - Chemistry panel
  - Urinalysis
  - Thyroid panel (serum tT4, fT4, TSH)
  - Serum and urine glucose concentration glucose
  - Pancreatic-lipase immunoreactivity (Spec cPL)
  - Serum bile-acid concentrations
  - Urine protein:creatinine ratio
  - Low-dose dexamethasone suppression test

Further characterization of HTG

› Serum turbidity



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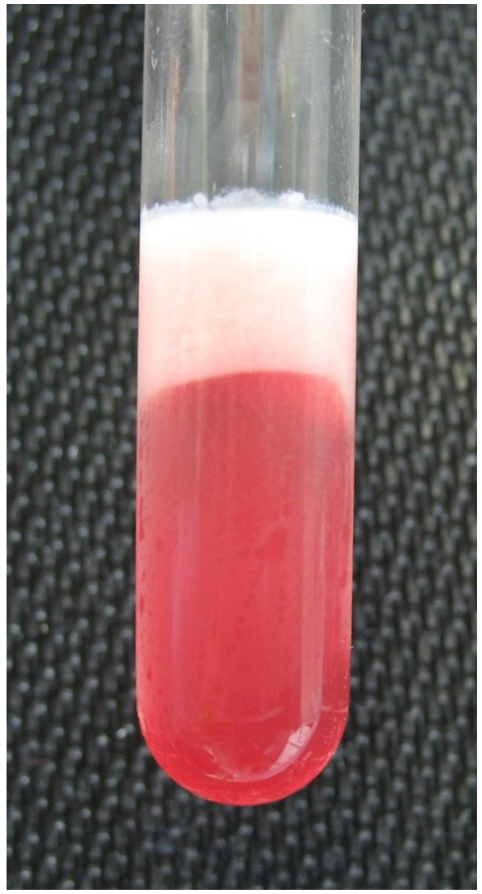
Laboratory evaluation

- Chylomicron test (refrigeration test)



Does it matter?

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Does it matter?

- Pancreatitis
- Liver disease
  - Lipidosis
  - Biliary mucocele
- Insulin resistance
- Chronic inflammation
- Proteinuria
- Neurologic disease
- Ocular disease

J Vet Intern Med 2011;25:20–25

Serum Triglyceride Concentrations in Miniature Schnauzers with and without a History of Probable Pancreatitis

P.G. Xenoulis, M.D. Levinski, J.S. Suchodolski, and J.M. Steiner

Serum liver enzyme activities in healthy Miniature Schnauzers with and without hypertriglyceridemia

SMALL ANIMALS/ EXOTIC

Panagiotis G. Xenoulis, DVM; Jan S. Suchodolski, Dr med vet, PhD; Melinda D. Levinski, BS, BA; Jörg M. Steiner, Dr med vet, PhD, DACVIM

Increased lipogenesis and lipidosis of gallbladder epithelium in dogs with gallbladder mucocele formation

Jody L. Gookin[1]*, Dennis E. Jewell[2], Kathleen M. Aicher[3], Gabriela S. Seiler[4], John M. Cullen[5], Kyle G. Mathews[1]

Association of hypertriglyceridemia with insulin resistance in healthy Miniature Schnauzers

Panagiotis G. Xenoulis, DVM, Dr med vet; Melinda D. Levinski, DVM; Jan S. Suchodolski, Dr med vet, PhD; Jörg M. Steiner, Dr med vet, PhD, DACVIM

DOI: 10.1111/jvim.18418

STANDARD ARTICLE

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

Associations among serum insulin, calprotectin, and C-reactive protein concentrations in Miniature Schnauzers with idiopathic hyperlipidemia before and after feeding an ultra-low-fat diet

Panagiotis G. Xenoulis[1,2] | Romy M. Heilmann[3] | Eva M. Stavroulaki[1] | Denise S. Riggers[3] | Laura J. Gneipel[3] | Jan S. Suchodolski[2] | Jörg M. Steiner[2]

Glomerular Lesions in Proteinuric Miniature Schnauzer Dogs

E. Furrow[1], G. E. Lees[2], C. A. Brown[3], and R. E. Cianciolo[4]

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Goals of treatment

- Traditionally, hypertriglyceridemia was treated only when exceeding 500 mg/dL or even 1000 mg/dL
- Insulin resistance, hepatobiliary disease, and possibly other complications of hyperlipidemia can exist with serum triglycerides <500 mg/dL
  - Even mild hypertriglyceridemia should be treated

Case 1: Rudy, 5yo, MN Mixed breed, 18kg

- History
  - Asymptomatic
  - Increased liver enzymes for the last 3 years
- Physical examination
  - BCS: 6/9

Case 1: Rudy, 5yo, MN Mixed breed, 18kg

- CBC: normal
- Biochemical analysis:

	28/06/23
Triglycerides (20-112 mg/dL)	**2701**
Cholesterol (135-270 mg/dL)	**349**
ALP (<90 IU/L)	**689**

What would you do next?

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Case 1: Rudy, 5yo, MN Mixed breed, 18kg

- tT4: 2.6 µg/dl (1.7-3.6 µg/dl)
- U/S: hepatomegaly, vacuolation of the liver
- Diagnosis – primary hyperlipidemia

First step in the management of hyperlipidemia

- Low-fat diet
- Calculate fat based on metabolizable energy
  - % fat is not accurate enough
- Fat content
  - <20 gr/1000Kcal

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First step in the management of hyperlipidemia

- Take into account the dog's previous diet's fat content
  - If the dog is consuming a diet that has a fat content of 26 gr/1000 Kcal then going to a low-fat diet with a fat content of 20 gr/1000 Kcal will likely make no much difference
- Canned and dry form of the same diet can have vastly different fat content

Case 1: Rudy, 5yo, MN Mixed breed, 18kg

- Low-fat diet
  - 18 g/1000 Kcal

	28/06/23	18/07/23	
Triglycerides (20-112 mg/dL)	**2701**	110	
Cholesterol (135-270 mg/dL)	**349**	**285**	
ALP (<90 IU/L)	**689**	**460**	

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Case 1: Rudy, 5yo, MN Mixed breed, 18kg

- Low-fat diet
  - 18 g/1000 Kcal

	28/06/23	18/07/23	07/09/23
Triglycerides (20-112 mg/dL)	**2701**	110	109
Cholesterol (135-270 mg/dL)	**349**	**285**	**290**
ALP (<90 IU/L)	**689**	**460**	**463**

Case 2: Willy, 12 yo, MS Jack Russel

- History
  - Asymptomatic
  - Increased liver enzymes for 1 year
- Physical examination
  - Hypotrichosis in the abdomen
  - BCS 5/9

Case 2: Willy, 12 yo, MN Jack Russel

- CBC: normal
- Biochemical analysis:

	13/06/23
Triglycerides (20-112 mg/dL)	**1091**
Cholesterol (135-270 mg/dL)	**412**
ALP (<90 IU/L)	**1241**
ALT (10-94 IU/L)	**395**

What would you do next?

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Case 2: Willy, 12 yo, MN Jack Russel

- tT4: 2.4 µg/dl (1.7-3.6 µg/dl)
- LDDST: normal
- U/S: mild hepatomegaly, liver nodules, gallbladder mucocele

Case 2: Willy, 12 yo, MN Jack Russel

- Low-fat diet
  - 14 g/1000 Kcal
- Reexamination in 8 weeks

	13/06/23	04/08/23
Triglycerides (20-112 mg/dL)	**1091**	**757**
Cholesterol (135-270 mg/dL)	**412**	**433**
ALP (<90 IU/L)	**1241**	**1036**
ALT (10-94 IU/L)	**395**	**349**

Case 2: Willy, 12 yo, MN Jack Russel

- What would be the next step?

- Things to consider
  - Secondary hyperlipidemia but we have not correctly identified the primary cause?
  - Primary hyperlipidemia that is not responding to a low-fat diet?

DOI: 10.1111/jvim.15880

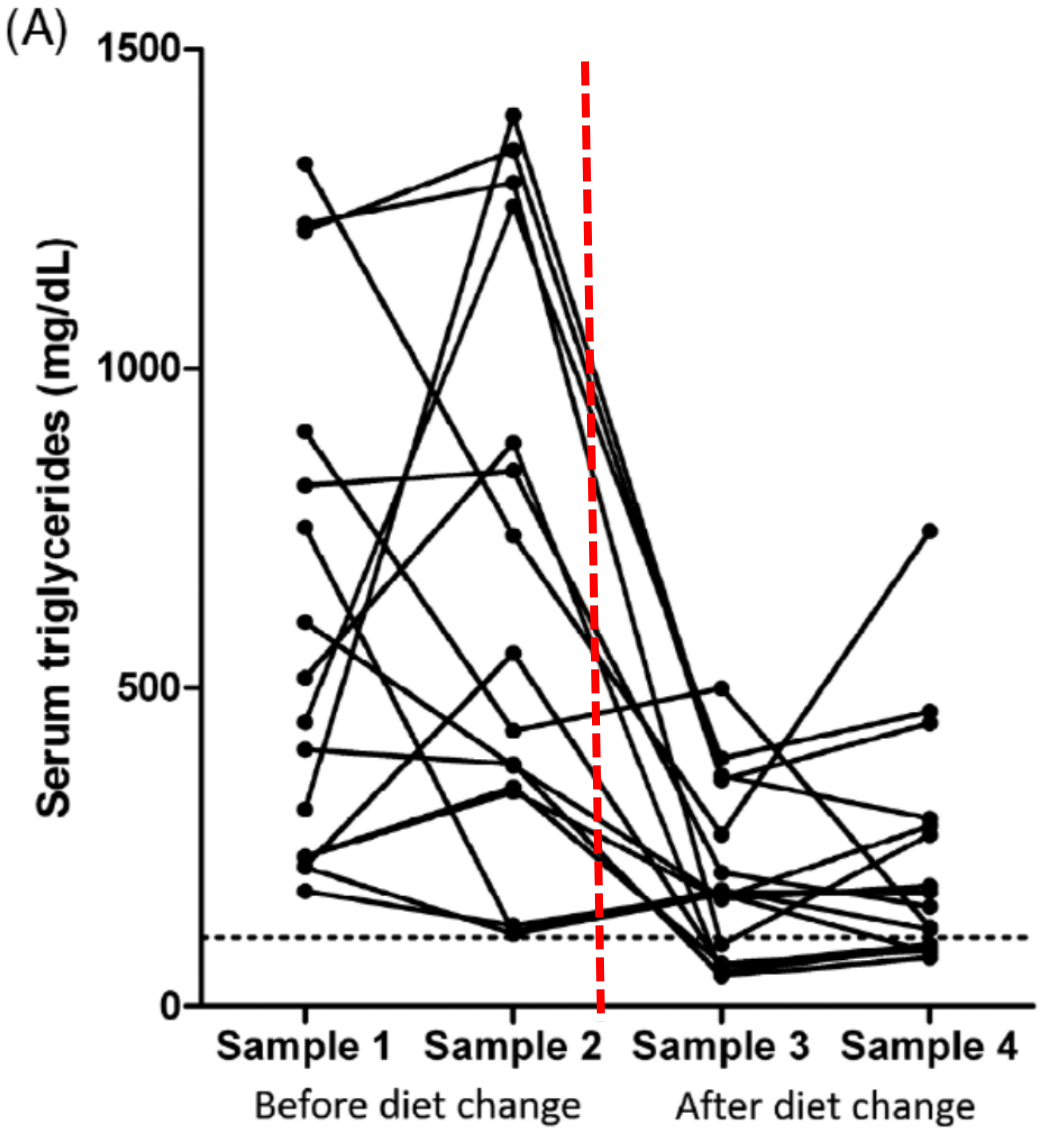
STANDARD ARTICLE

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

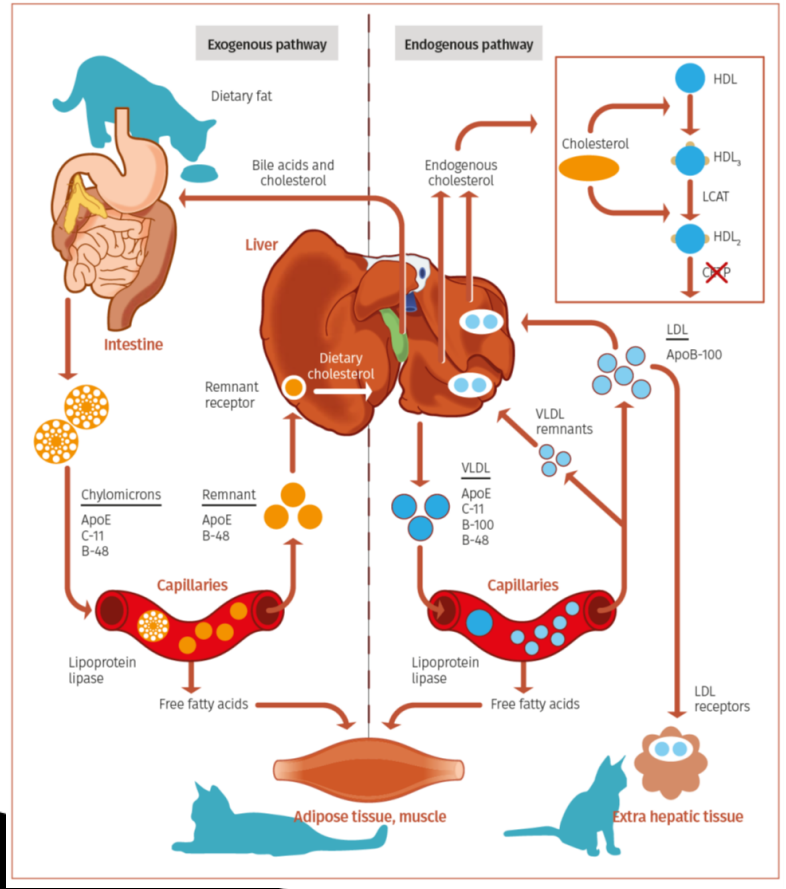
Effect of a low-fat diet on serum triglyceride and cholesterol concentrations and lipoprotein profiles in Miniature Schnauzers with hypertriglyceridemia

Panagiotis G. Xenoulis[1] | Paul J. Cammarata[2] | Rosemary L. Walzem[3] | Jan S. Suchodolski[1] | Jörg M. Steiner[1]



Hyperlipidemia not responding to low-fat diet

› Why does this happen?



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Case 2: Willy, 12 yo, MN Jack Russel

› Phenofibrate 10 mg/kg (plus low-fat diet)

	13/06/23	04/08/23	16/09/23
Triglycerides (20-112 mg/dL)	**1091**	**757**	90
Cholesterol (135-270 mg/dL)	**412**	**433**	269
ALP (<90 IU/L)	**1241**	**1036**	**662**
ALT (10-94 IU/L)	**395**	**349**	**349**

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Case 3: Ornela, 8 yo, FS, Miniature Schnauzer

- History
  - History of pancreatitis
  - Asymptomatic at presentation
- Physical examination
  - Normal
  - BCS 7/9

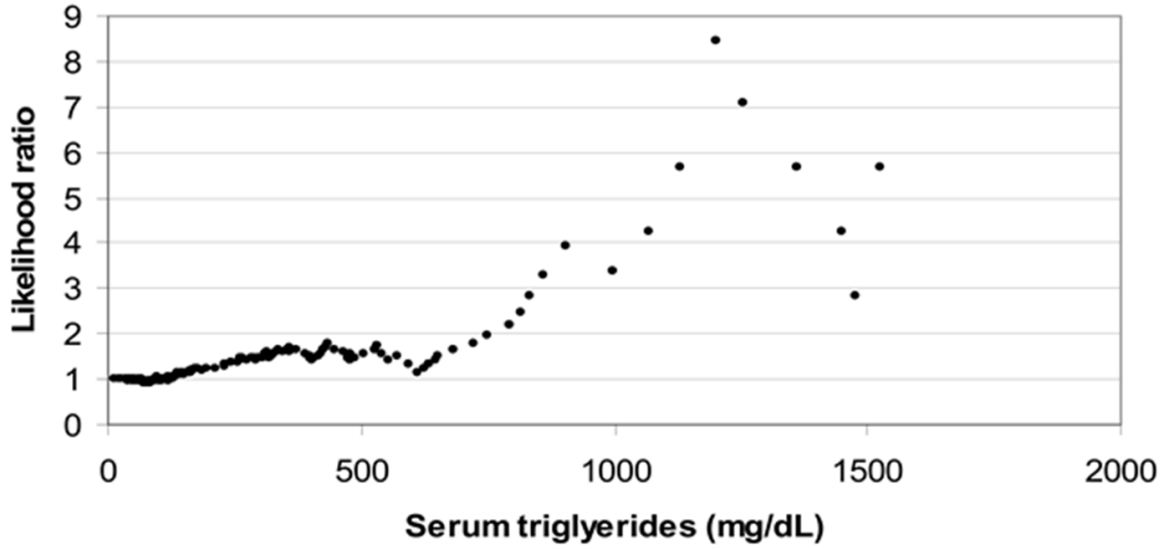
Case 3: Ornela, 8 yo, FS, Miniature Schnauzer

- CBC: normal
- Biochemical analysis:

	20/02/20
Triglycerides (20-112 mg/dL)	**1832**
Cholesterol (135-270 mg/dL)	**444**
Spec cPL (<200 µg/L)	**701**

Case 3: Ornela, 8 yo, FS, Miniature Schnauzer

- What is the relationship between hyperlipidemia and pancreatitis?
- Severe hypertriglyceridemia is a well recognized risk factor for pancreatitis in humans and dogs



Association Between Serum Triglyceride and Canine Pancreatic Lipase Immunoreactivity Concentrations in Miniature Schnauzers

J Am Anim Hosp Assoc 2010;46:229-234.

Panagiotis G. Xenoulis, DVM, Dr.med.vet.

Jan S. Suchodolski, med.vet., Dr.med.vet., PhD

Craig G. Ruaux, BVSc (Hons), PhD, MACVSc, Diplomate ACVIM

Jörg M. Steiner, med.vet., Dr.med.vet., PhD, Diplomate ACVIM, Diplomate ECVIM

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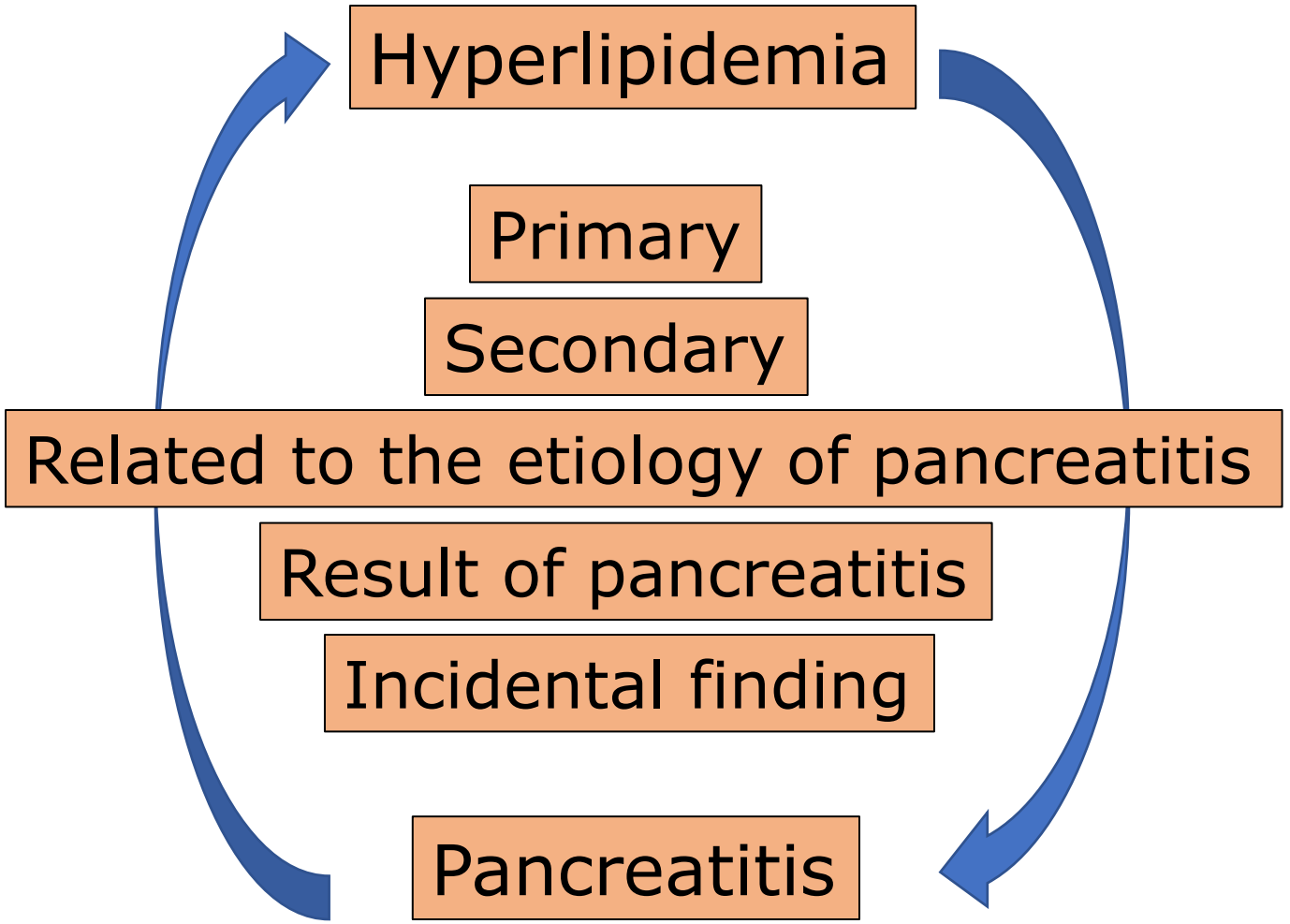
Case 3: Ornela, 8 yo, FS, Miniature Schnauzer

- What is the relationship between hyperlipidemia and pancreatitis?
- Hyperlipidemia can be the result of pancreatitis

Case 3: Ornela, 8 yo, FS, Miniature Schnauzer



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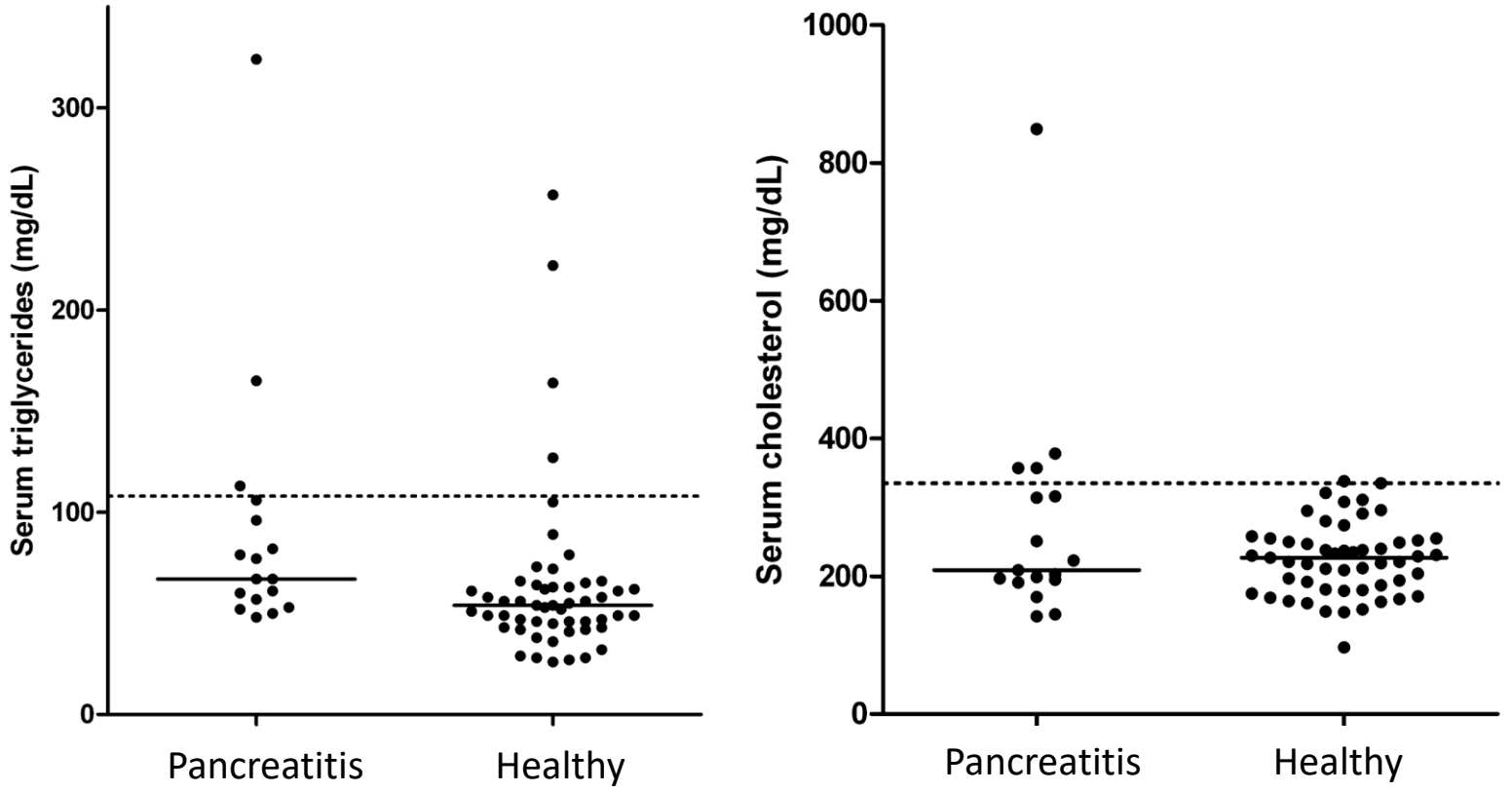
Journal of Veterinary Internal Medicine Open Access
ACVIM American College of Veterinary Internal Medicine

STANDARD ARTICLE

Serum triglyceride and cholesterol concentrations and lipoprotein profiles in dogs with naturally occurring pancreatitis and healthy control dogs

Panagiotis G. Xenoulis[1,2] | Paul J. Cammarata[3] | Rosemary L. Walzem[4] | Jan S. Suchodolski[1] | Jörg M. Steiner[1]



Case 3: Ornela, 8 yo, FS, Miniature Schnauzer

- Problem list
  - Severe hyperlipidemia
  - Pancreatitis/increased Spec cPL
  - Obesity
- Goals of treatment
  - Correction of hyperlipidemia
  - Weight loss
  - Decrease in Spec cPL?

Case 3: Ornela, 8 yo, FS, Miniature Schnauzer

- Which diet?
- Common misconception
  - Weight loss or fiber-enhanced diets are not necessarily low-fat diets

	Purina EN Low-fat Canine Dry	Purina OM Canine Dry
Fat content (gr/1000 Kcal)	**14**	**17**

	Gastrointestinal Low-fat Canine Dry	Satiety Canine Dry
Fat content (gr/1000 Kcal)	**15,6**	**26**

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Case 3: Ornela, 8 yo, FS, Miniature Schnauzer

- Low-fat diet
  - 14 g/1000 Kcal
- Reexamination in 4 weeks

	20/02/20	17/03/20
Triglycerides (20-112 mg/dL)	**1832**	**903**
Cholesterol (135-270 mg/dL)	**444**	**343**
Spec cPL (<200 µg/L)	**701**	**493**

Case 3: Ornela, 8 yo, FS, Miniature Schnauzer

- Chitosan
  - Sugar that comes from the outer skeleton of shellfish (including crab, lobster, shrimp)
  - Reduces the absorption of triglycerides and cholesterol from the GI tract

Comparative evaluation between chitosan and atorvastatin on serum lipid profile changes in hyperlipidemic cats

Mosallanejad, B.[1*]; Avizeh, R.[1]; Razi Jalali, M.[1] and Pourmahdi, M.[2]

[1]Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran; [2]Department of Food Hygiene, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran

[*]***Correspondence:*** *B. Mosallanejad, Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran. E-mail: bmosallanejad@scu.ac.ir*

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Case 3: Ornela, 8 yo, FS, Miniature Schnauzer

- Low-fat diet
  - 14 g/1000 Kcal
- Reexamination in 4 weeks

	20/02/20	17/03/20	15/05/20
Triglycerides (20-112 mg/dL)	**1832**	**903**	**193**
Cholesterol (135-270 mg/dL)	**444**	**343**	241
Spec cPL (<200 µg/L)	**701**	**493**	**381**

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Case 4: Misti, 9 yo, FS, Labrador

- History
  - Healthy
  - Came for regular check up
- Physical examination
  - Normal
  - BCS 5/9

Case 4: Misti, 9 yo, FS, Labrador

- CBC: normal
- Biochemical analysis:

Triglycerides (20-112 mg/dL)	**498**
Cholesterol (135-270 mg/dL)	**281**

Case 4: Misti, 9 yo, FS, Labrador

- No primary condition identified
- Low-fat diet
  - 14 gr/1000 Kcal

Triglycerides (20-112 mg/dL)	**498**	**435**
Cholesterol (135-270 mg/dL)	**281**	**270**

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Case 4: Misti, 9 yo, FS, Labrador

- No primary condition identified
- Low-fat diet
  - 14 gr/1000 Kcal
- Addition of omega-3 fatty acids

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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

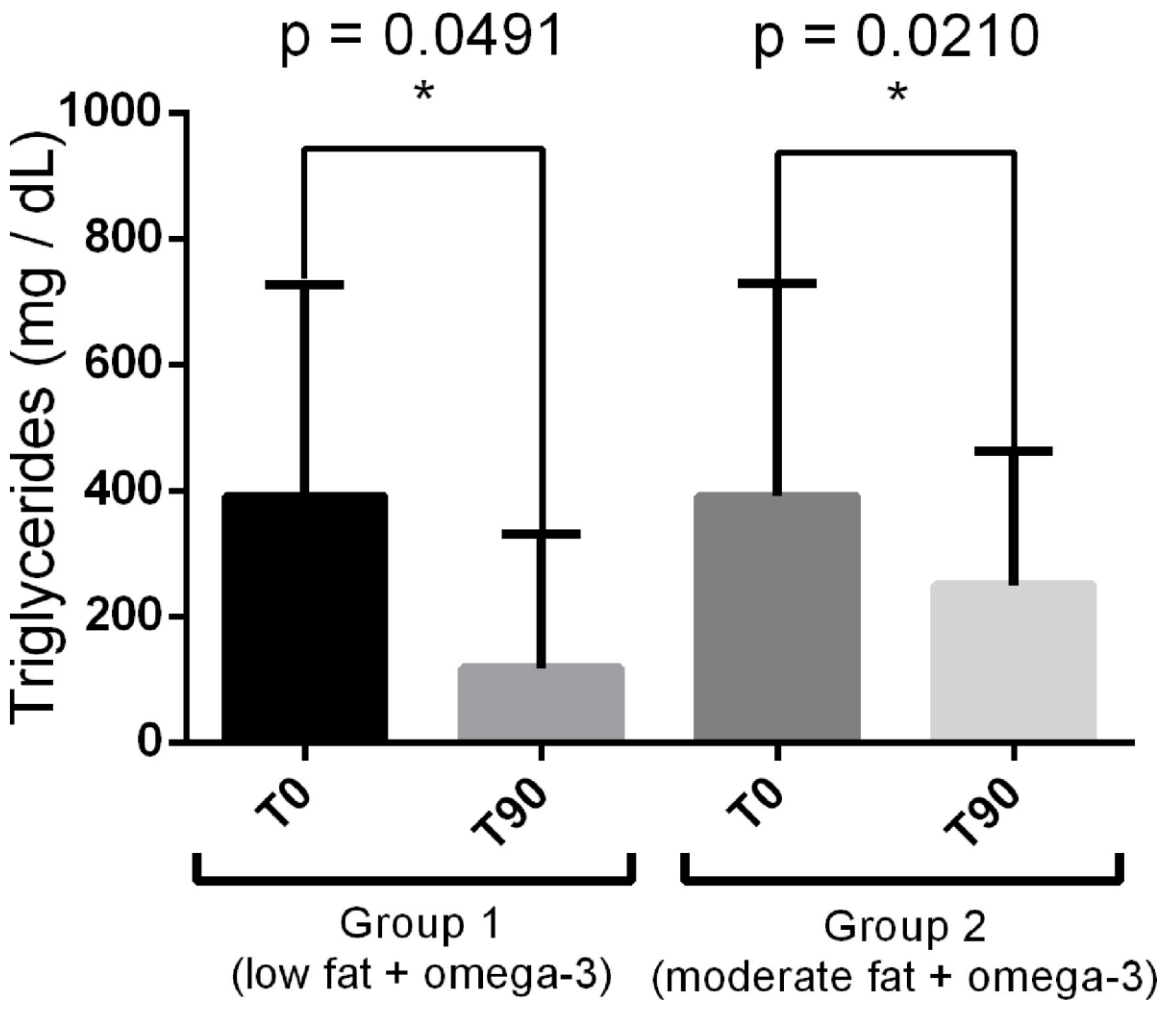
Paula de Albuquerque[1], Viviani De Marco[1,2]*, Thiago Henrique Annibale Vendramini[3], Andressa Rodrigues Amaral[3], Sergio Catanozi[4], Kelly Gomes Santana[4], Valéria Sutti Nunes[4], Edna Regina Nakandakare[4], Marcio Antonio Brunetto[3]*

1 Universidade de Santo Amaro, São Paulo, Brazil, **2** Faculdade de Medicina Veterinária e Zootecnia, Centro de Pesquisa em Nutrologia de Cães e Gatos, Universidade de São Paulo, Sao Paulo, SP, Brazil, **3** Faculdade de Medicina, Laboratorio de Lipides (LIM—10), Hospital das Clinicas HCFMUSP, Universidade de São Paulo, Sao Paulo, SP, Brazil, **4** Naya Especialidades, São Paulo, SP, Brazil

* vivianidemarco@gmail.com (VM); mabrunetto@usp.br (MAB)

Check for updates

- Dose: ~100 mg EPA+DHA/kg BW



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Case 4: Misti, 9 yo, FS, Labrador

- No primary condition identified
- Low-fat diet
  - 14 gr/1000 Kcal
- Addition of omega-3 fatty acids

Triglycerides (20-112 mg/dL)	**498**	**435**	**189**
Cholesterol (135-270 mg/dL)	**281**	**270**	254

Case 5: Max, 5 yo, MN, Cocker Spaniel

- History
  - Healthy
  - Came for regular check up
- Physical examination
  - Normal
  - BCS 5/9

Case 5: Max, 5 yo, MN, Cocker Spaniel

- CBC: normal
- Biochemical analysis:

Triglycerides (20-112 mg/dL)	**540**
Cholesterol (135-270 mg/dL)	210

Case 5: Max, 5 yo, MN, Cocker Spaniel

- No primary condition identified
- Low-fat diet
  - 14 gr/1000 Kcal

Triglycerides (20-112 mg/dL)	**540**	**398**
Cholesterol (135-270 mg/dL)	210	221

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Case 5: Max, 5 yo, MN, Cocker Spaniel

- No primary condition identified
- Low-fat diet
  - 14 gr/1000 Kcal
- Addition of omega-3 fatty acids

Triglycerides (20-112 mg/dL)	**540**	**398**	**620**
Cholesterol (135-270 mg/dL)	210	221	**321**

Why did that happen?

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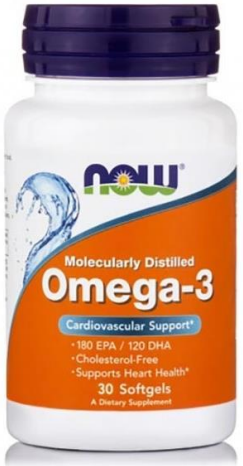

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Integrative Approach to Gastrointestinal Health

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Thank you!