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# Suffering in Silence: Spotting Signs of Feline Triaditis

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# Conflict of Interest Disclosure

• Gastrointestinal Laboratory	Director
• IDEXX Laboratories	Paid Consultant
• Nutramax Laboratories	Paid Consultant
• ISK	Paid Consultant
• CEVA Animal Health	Paid Consultant
• Glycosbio	Paid Consultant
• Bond Pet Care	Paid Consultant
• Nutramax Laboratories, IDEXX Laboratories, Paid Speaker, CEVA Animal Health, Siemens Healthineers	Paid Speaker
• Hill's Pet Care, Nutramax Laboratories	Grant Support

# Introduction

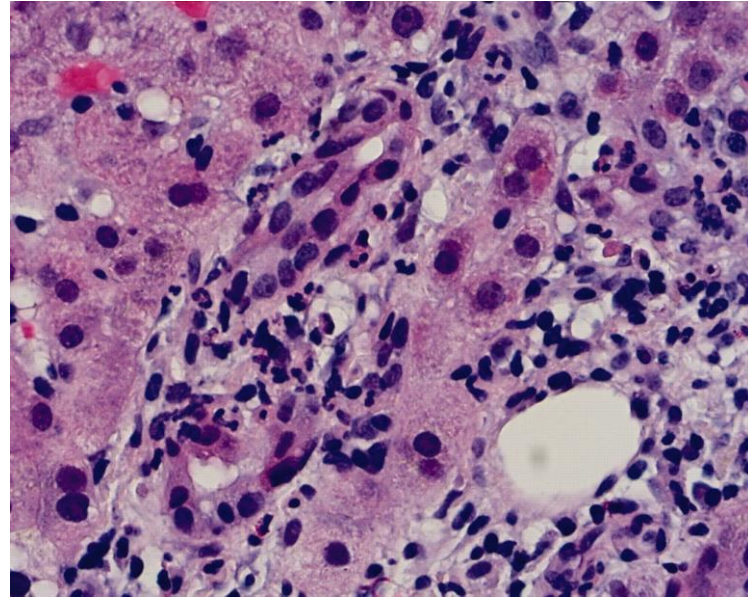
# Triaditis

- triaditis describes a syndrome in cats that is characterized by concurrent inflammation of:
  - the biliary tree (i.e., cholangitis)
  - the pancreas (i.e., pancreatitis)
  - the intestines (i.e., chronic inflammatory enteropathy)
- this also occurs in humans and dogs
- however, not termed triaditis in other species



# Triaditis in Humans

- inflammatory condition of the hepatic triad region
- reaches into the surrounding connective tissue



# Feline Triaditis

- described in several case reports
- landmark paper by Weiss et al.
  - cats with cholangiohepatitis had concurrent:
    - inflammatory bowel disease (IBD) in 83%
    - pancreatitis in 50%
    - IBD and pancreatitis (i.e., triaditis) in 39%
- however, it has not yet been demonstrated that these conditions are causally related

# Chronic Cholangitis

- characterized by infiltration of the liver and the biliary tree with a mixture of
  - neutrophils,
  - lymphocytes,
  - and plasma cells



# Chronic Pancreatitis

- chronic inflammatory condition of the pancreas
  - associated with lymphocytic-plasmocytic infiltration

# Chronic Inflammatory Enteropathy (CIE)

- previously called idiopathic inflammatory enteropathy
- group of chronic gastrointestinal disorders that are characterized by infiltration of the gastrointestinal mucosa with inflammatory cells
  - due to an identifiable cause or idiopathic
  - different predominant cell types
  - most commonly involves the small intestine
  - can also involve the stomach and/or the large intestine

# Etiology and Pathogenesis

# Etiology of Chronic Cholangitis

- idiopathic
- infectious
- an autoimmune component is likely

# Etiology / Risk Factors for Chronic Pancreatitis

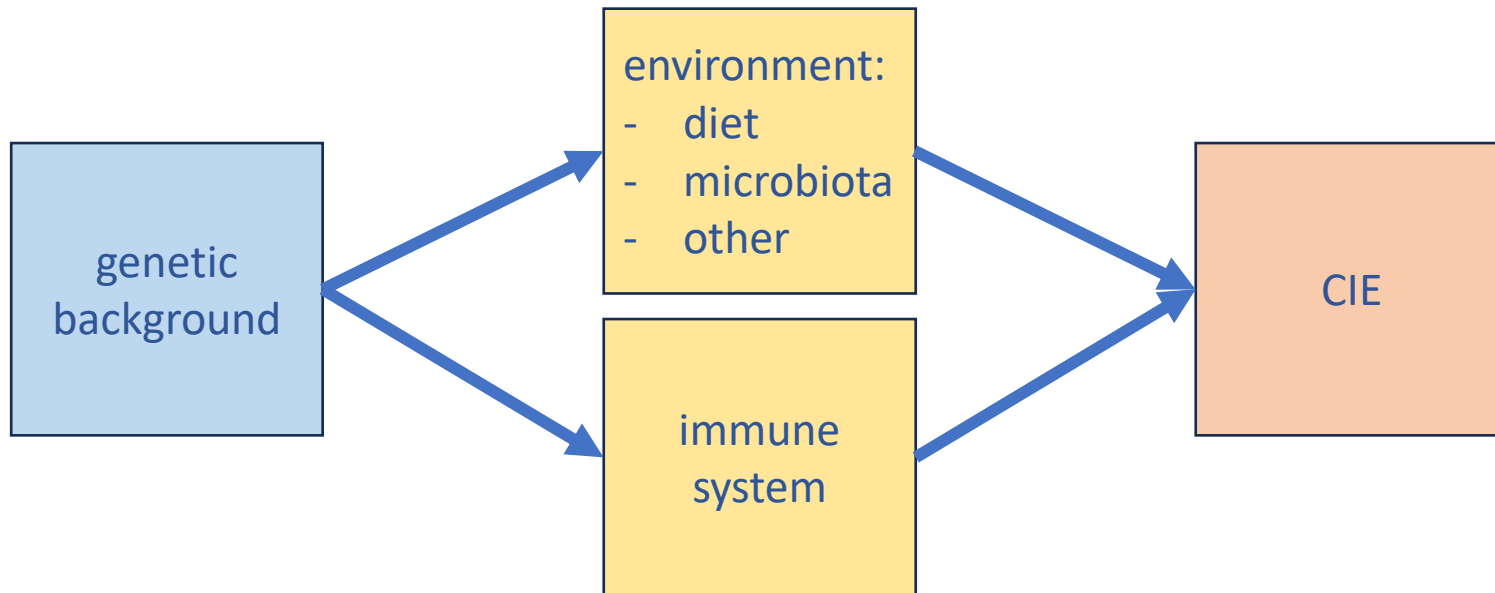
- idiopathic
- infectious
- dietary (high fat?)
- cholangitis
- pharmacological substances
- an autoimmune component is likely

# Etiology for CIE

- idiopathic
- current hypothesis
  - CIE is a heterogeneous group of diseases that have a common final manifestation
  - CIE is the common result of an abnormal interplay of antigenic stimulation and response of the immune system



# Pathogenesis of CIE



# Etiology of Triaditis

- idiopathic
- an autoimmune component is likely

# Clinical Presentation

# Clinical Signs of Chronic Cholangitis

- lethargy
- anorexia
- weight loss
- vomiting
- fever
- abdominal pain
- ⇒ non-specific
- diarrhea
- polydipsia
- polyuria
- icterus
- ascites
- encephalopathy
- bleeding diathesis
- ⇒ in case of hepatic failure

# Clinical Signs of Pancreatitis

- anorexia 87%
  - lethargy 81%
  - dehydration 54%
  - weight loss 47%
  - hypothermia 46%
  - vomiting 46%
  - icterus 37%
  - fever 25%
  - abdominal pain 19%
  - diarrhea 12%
- ⇒ non-specific even in severe cases

# Clinical Signs of CIE

- vomiting
  - most commonly in cases with gastric involvement
- diarrhea
  - most commonly small bowel diarrhea
- weight loss
- anorexia
- weakness
- other
- ⇒ non-specific



# Clinical Signs in Cats with Triaditis

- may be subclinical
- common clinical signs
  - vomiting
  - anorexia
  - diarrhea
  - weight loss
  - lethargy
- in severe cases
  - icterus and systemic clinical signs

# Abdominal Discomfort

- cholangitis and pancreatitis can be associated with abdominal discomfort
- abdominal discomfort can be difficult to diagnose
- patients with triaditis should be treated for abdominal pain/discomfort

# Clinical Pathology Findings in Chronic Cholangitis

- increase in liver enzyme activities
- hyperbilirubinemia
- hyperglobulinemia in about 50% of cases
- increased serum bile acid concentrations
- ⇒ non-specific findings for any type of hepatobiliary disease
- ⇒ depending on disease severity

# Clinical Pathology Findings in Chronic Pancreatitis

- elevation of ALT activity 68%
- hyperbilirubinemia 64%
- hypercholesterolemia 64%
- hyperglycemia 64%
- azotemia 57%
- hypokalemia 56%
- elevation of SAP activity 50%
- hypocalcemia 45%
- ⇒ non-specific findings related to systemic complications
- ⇒ maybe completely normal

# Clinical Pathology Findings in cats with CIE

- complete blood count
    - often within normal limits
    - anemia of chronic disease in some cases
    - stress leukogram or inflammatory leukogram in some cases
  - serum chemistry profile
    - often within normal limits
    - slight elevations of hepatic enzyme activities
    - serum proteins may be decreased
- ⇒ non-specific changes

# Clinical Pathology in Triaditis

- largely non-specific
  - cholangitis leads to changes suggestive of a hepatobiliary disease
- mostly dependent on severity of disease
  - liver disease vs. liver failure
  - systemic complications
- complete blood count may or may not show an inflammatory leukogram



# Abdominal Radiographs

- enlarged liver
- decreased contrast in the cranial abdomen
- thickened bowel-loops
- ⇒ these findings are very subjective
- ⇒ abdominal radiographs are not useful to arrive at a primary diagnosis of triaditis
- ⇒ however, abdominal radiographs are useful to rule out other differential diagnoses

# Abdominal Ultrasound Chronic Cholangitis

- thickened gall bladder wall
- dilated bile duct
- altered echogenicity of the liver
- ⇒ fairly suggestive of cholangitis
- ascites with hepatic failure

# Abdominal Ultrasound Chronic Pancreatitis

- fluid accumulation around the pancreas
- enlargement of the pancreas
- increased echogenicity (pancreatic fibrosis)
- pancreatic mass effect
- ⇒ sensitivity and specificity are dependent on several factors

P10-4  
K\_9 10P4  
21fps

THI/3.6 MHz  
17dB/DR65  
MapI/VEOff  
RS3/SC2

RT PANCREAS

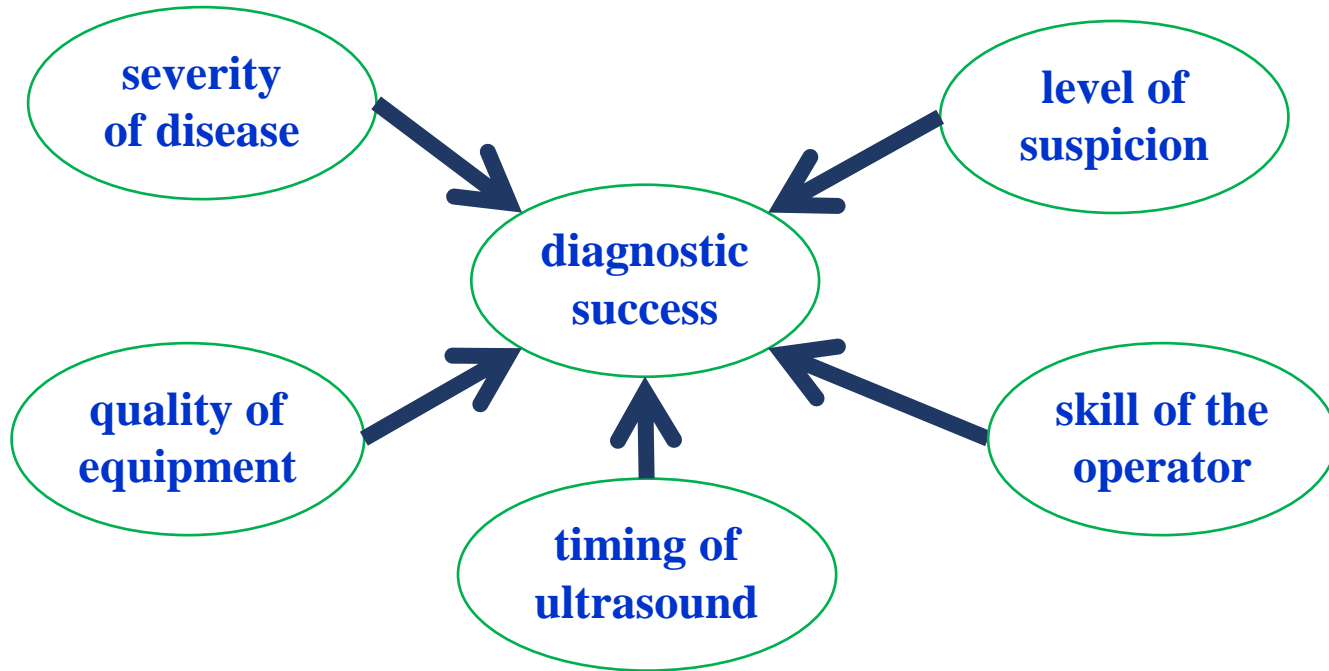
SIEMENS ANTARES

2 cm

4cm  
21fps

courtesy Dr. Jane Armstrong

# Ultrasound for the Diagnosis of Pancreatitis



# Abdominal Ultrasound CIE

- abdominal ultrasound may show thickened and fluid-filled bowel loops
- ⇒ abdominal ultrasound is more useful to exclude other causes of chronic gastrointestinal disease



# Differential Diagnoses

- isolated chronic cholangitis
- isolated CIE
- isolated chronic pancreatitis
- other hepatopathies
- hyperthyroidism
- other primary gastrointestinal diseases
  - e.g. GI lymphoma

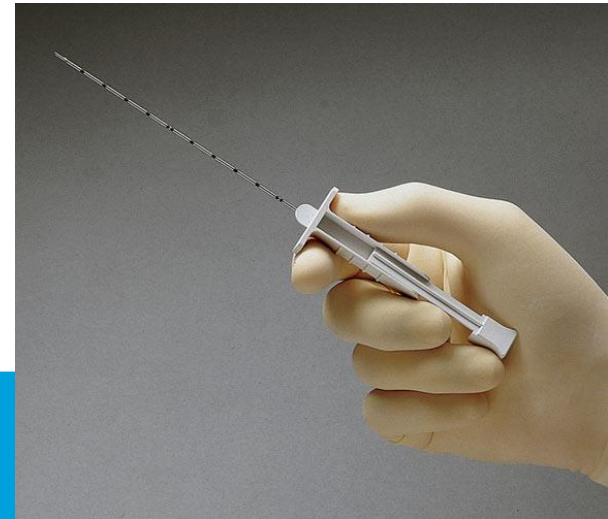
# Diagnosis

# Definitive Diagnosis

- definitive diagnosis of triaditis requires hepatic, pancreatic, and intestinal biopsies
- histopathological evaluation
  - inflammatory infiltrates in the liver, the pancreas, and the small intestines
- however, very invasive and usually not indicated
  - at least initially

# Hepatic Biopsy

- multiple pieces should be collected
- one piece should be cultured
- biopsies can be collected by
  - true-cut needle
  - laparoscopy
  - laparotomy



# Presumptive Diagnosis of Chronic Cholangitis

- ultrasonographic changes
- abnormalities on a serum chemistry profile suggesting hepatobiliary disease
- response to therapy

# Presumptive Diagnosis of Chronic Cholangitis

- ⇒ a presumptive diagnosis of chronic cholangitis is often not sufficient for long-term management
- ⇒ however, initial therapy can be initiated based on a presumptive diagnosis
- ⇒ in patients that do not respond to therapy a definitive diagnosis needs to be sought

# Presumptive Diagnosis of Chronic Pancreatitis

- ultrasonographic changes
- serum pancreatic lipase

# Serum Pancreatic Lipase

- measured by enzymatic assays
  - most assays do not specifically measure pancreatic lipase
  - most assays have not been analytically validated
  - new Catalyst PL assay has been validated and specifically measures pancreatic lipase
- measured by immunoassays
  - Spec fPL and SNAP fPL have been analytically and clinically validated

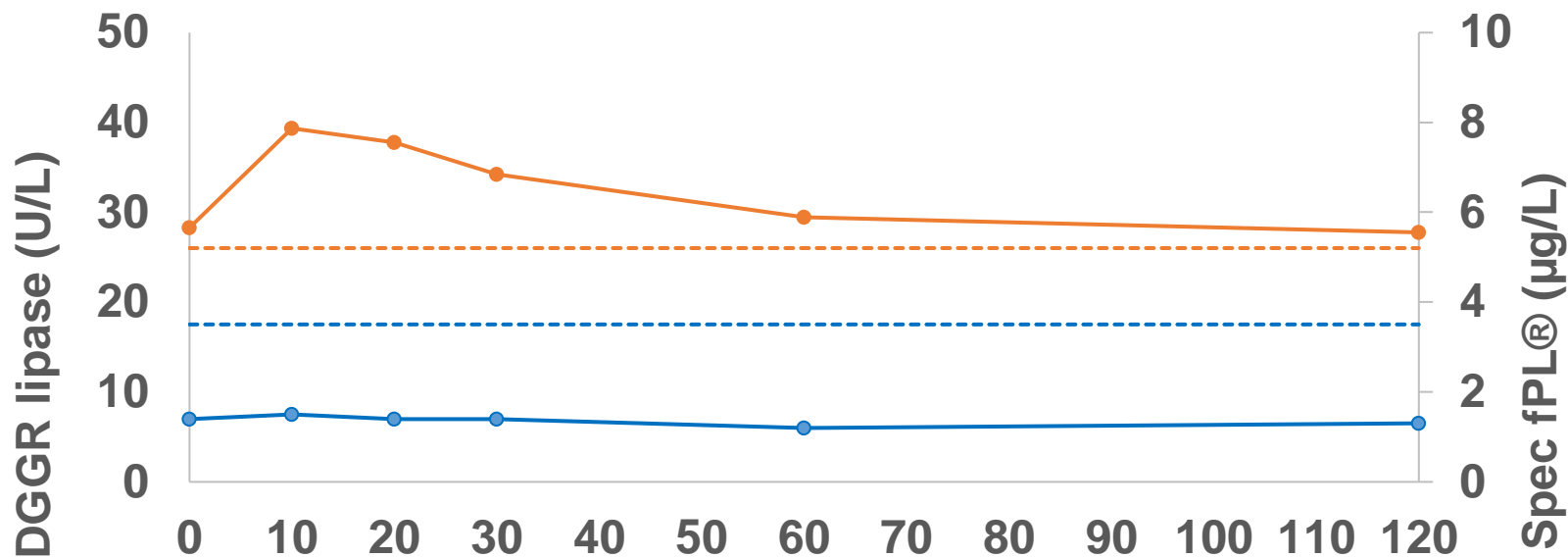


# Important Considerations

- even if assays use the same substrate they may produce completely different results
- assay conditions are crucial
  - co-factors
  - temperature
  - pH
  - other factors

# Hepatic and/or Lipoprotein Lipase

- the release of hepatic and/or lipoprotein lipase can be stimulated by administration of heparin



# DGGR Feline Study

- correlation of serum Spec fPL and DGGR lipase in 161 cats
- agreement between the two assays showed a Cohen's kappa coefficient of 0.7
- this may seem high, but it basically means that if Spec fPL has a sensitivity of approximately 80% the DGGR has a sensitivity of approximately 56%

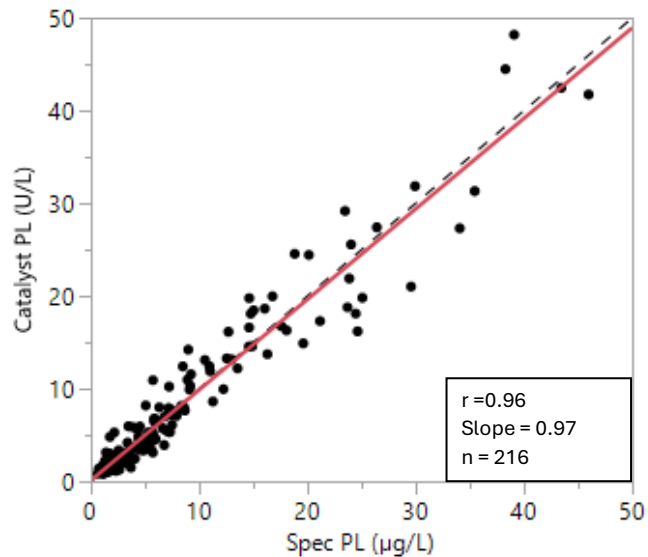
# Catalyst PL by Idexx Laboratories

- a new DGGR-based point-of-care assay for the catalyst analyzer
- first DGGR-based lipase assay on a dry-chemistry analyzer
  - ⇒ proprietary technology to keep DGGR stable
- first DGGR-based lipase assay that appears to be specific for the measurement of pancreatic lipase
  - ⇒ proprietary technology

# Catalyst PL by Idexx Laboratories

- internal analytical validation has been completed
  - external analytical validation is under way
  - provides a numerical result that has been aligned with the Spec fPL assay
  - ideal for patients with acute clinical signs that require immediate and accurate results
- ⇒ more data are under way

# Method Comparison



# Lipase Immunoassays

- use an antibody that recognizes a specific moiety of the lipase molecule
- only detect pancreatic lipase, which is only synthesized by pancreatic acinar cells
- highest sensitivity and specificity for the diagnosis of feline pancreatitis
- however, chronic mild pancreatitis maybe missed

# Presumptive Diagnosis of CIE

- chronic signs of GI disease
- rule out of other obvious causes
  - secondary GI disease
    - renal failure, hepatic failure, hyperthyroidism, or other
  - primary GI disease
    - endoparasites, *Tritrichomonas foetus*, or other
- response to therapy



# Presumptive Diagnosis of CIE

- ⇒ a presumptive diagnosis of CIE is often not sufficient for long-term management
- ⇒ however, initial therapy can be initiated based on a presumptive diagnosis
- ⇒ in cases that do not respond to therapy definitive diagnosis needs to be sought

# Presumptive Diagnosis of Triaditis

- chronic diarrhea with other nonspecific symptoms
- exclusion of other diseases
- increased activities of liver enzyme activities
- increased serum bilirubin concentration
- increased serum pancreatic lipase
- decreased serum cobalamin and/or folate
- supportive ultrasonographic changes

# Management

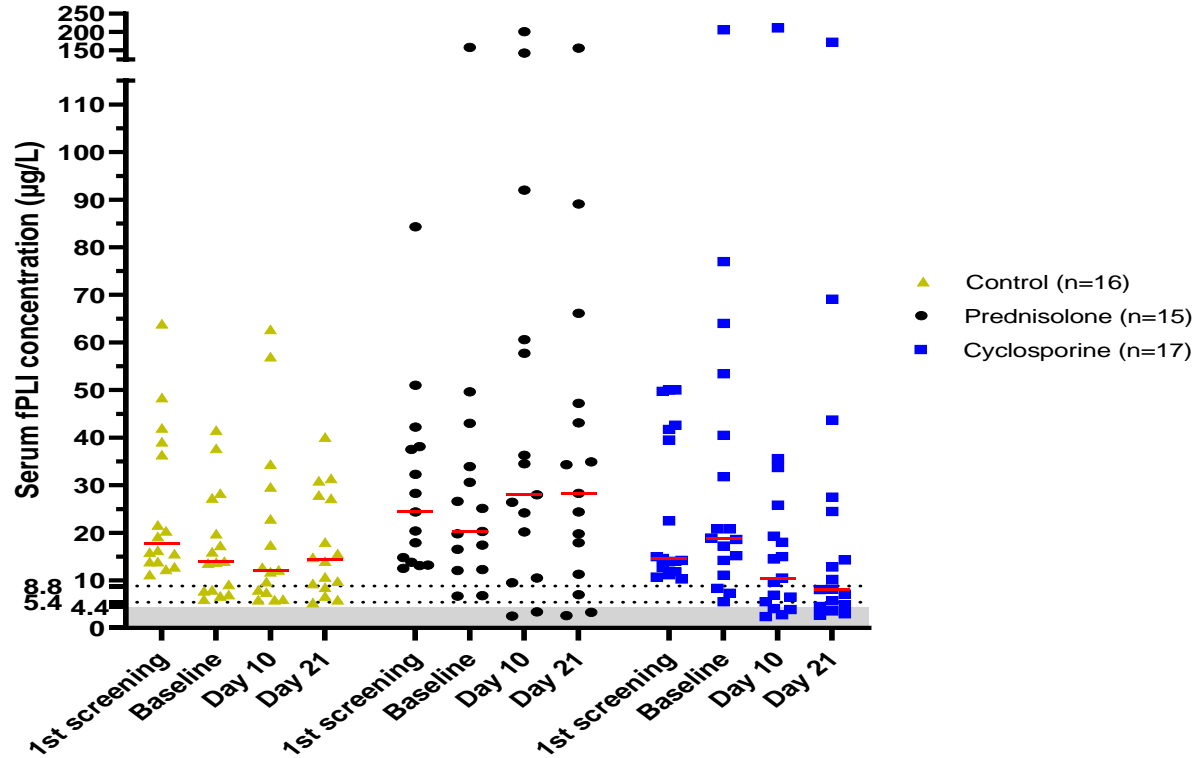
# Therapy of Chronic Cholangitis

- treatment of the cause
  - antibiotic therapy
  - ideally based on culture and sensitivity
- anti-inflammatory therapy
- supportive therapy
- therapy of complications
  - hepatic failure
  - hepatic lipidosis

# Therapy of Chronic Pancreatitis

- treatment of cause
- treatment of concurrent conditions
- dietary management
- anti-nausea agents
- analgesics
- anti-inflammatory agents
- antioxidants
- monitoring

# Immunosuppressive Therapy



# Monitoring

- serum fPLI concentration or Catalyst PL
- initially every 2-3 weeks
- after amelioration of pancreatitis with decreasing frequency

# Principles of Therapy of CIE

- treat underlying cause
  - e.g., anthelmintic agents for GI parasites
- treat complications
  - e.g., cobalamin supplementation
- dietary trial
- anti-inflammatory and immunosuppressive therapy



# Therapy of Triaditis

- moderately fat-restricted diet
  - easily digestible diet or home-made diet
- antibiotic agent for cholangitis (initially)
- supportive therapy for cholangitis
- cobalamin supplementation if indicated
- immunosuppressive therapy
- monitoring
  - clinical signs
  - chemistry profile and serum pancreatic lipase

# Prognosis

# Prognosis

- depends on severity and systemic complications
- short term: good
- long term: guarded
  - relapses are common

# Take Home Points

- ① triaditis should be viewed as a combination of inflammatory conditions of the liver, the pancreas, and the small intestines
- ② definitive diagnosis requires biopsies of all 3 organs, which, at least initially, is rarely in the best interest of the patient

# Take Home Points

- ③ a presumptive diagnosis of triaditis can be made based on the clinical presentation, abdominal ultrasound, and clinical pathology results
- ④ successful management requires careful monitoring and adjustment of management







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with all our **heARTS***

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