Exocrine Pancreatic Insufficiency

Historical perspective, serum TLI, and cats

David A. Williams MA VetMB PhD

MÉMOIRE

SUR

LE PANCRÉAS

ET SUR

LE ROLE DU SUC PANCRÉATIQUE

DANS LES PHÉNOMÈNES DIGESTIFS,

PARTICULIÈREMENT

DANS LA DIGESTION DES MATIÈRES GRASSES NEUTRES;

PAR M. CLAUDE BERNARD,

Membre de l'Institut (Académie des Sciences), Professeur de Médecine au Collège de France et de Physiologie générale à la Faculté des Sciences, etc.

Avec neuf planches gravées, en partie coloriées.

A PARIS,

CHEZ J.-B. BAILLIÈRE,

LIBRAIRE DE L'ACADÉMIE IMPÉRIALE DE MÉDECINE,

Rue Hautefeuille, 19.

LONDRES, H. BAILLIÈRE, 219, REGENT-STREET. | NEW-YORK, H. BAILLIÈRE, 290, BROADWAY.

MADRID, C. BAILLY-BAILLIÈRE, CALLE DEL PRINCIPE, 11.

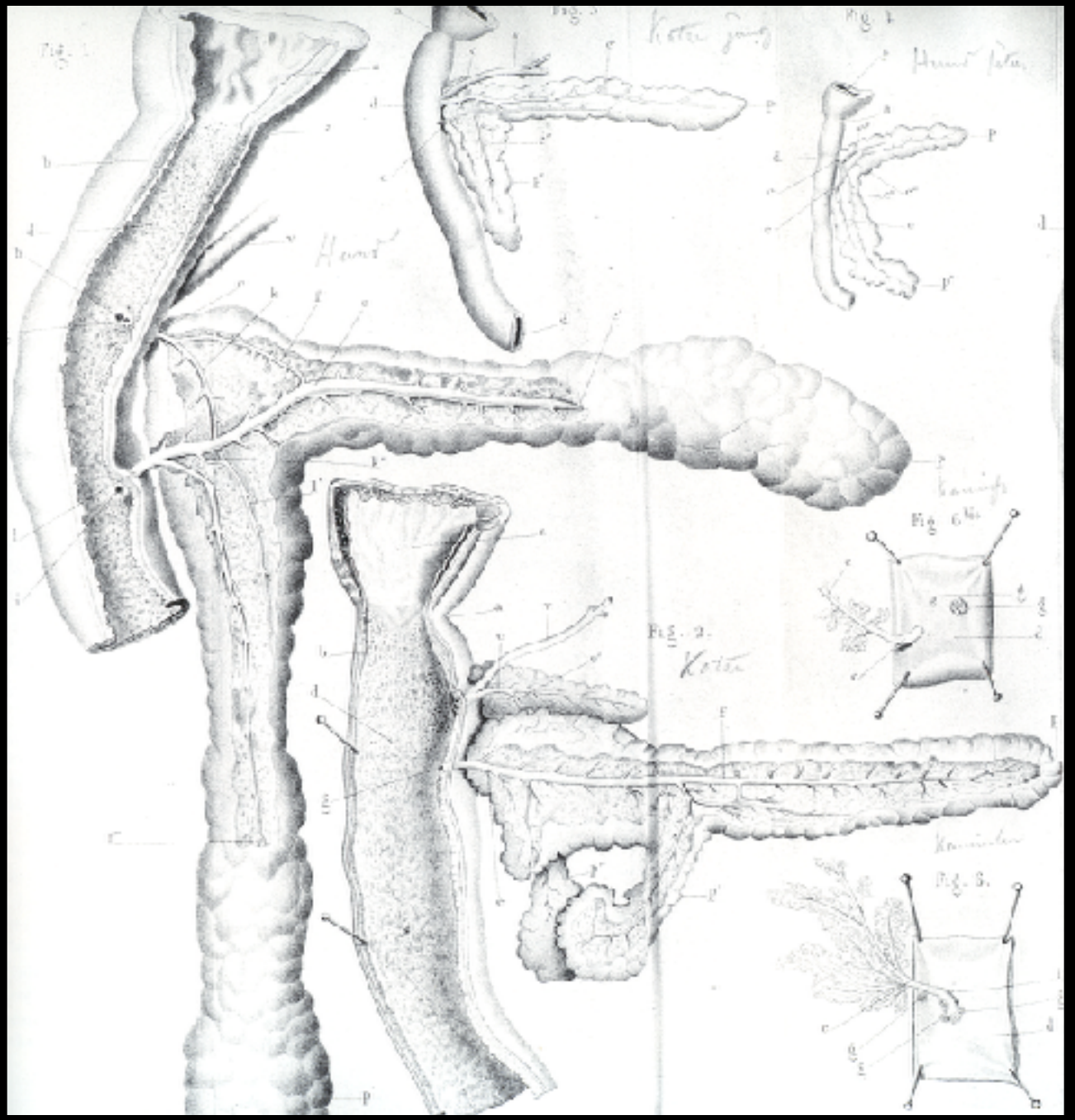
1856

MONOGRAPHS OF THE PHYSIOLOGICAL SOCIETY NO. 42

MEMOIR ON THE PANCREAS

BY CLAUDE BERNARD

TRANSLATED BY JOHN HENDERSON



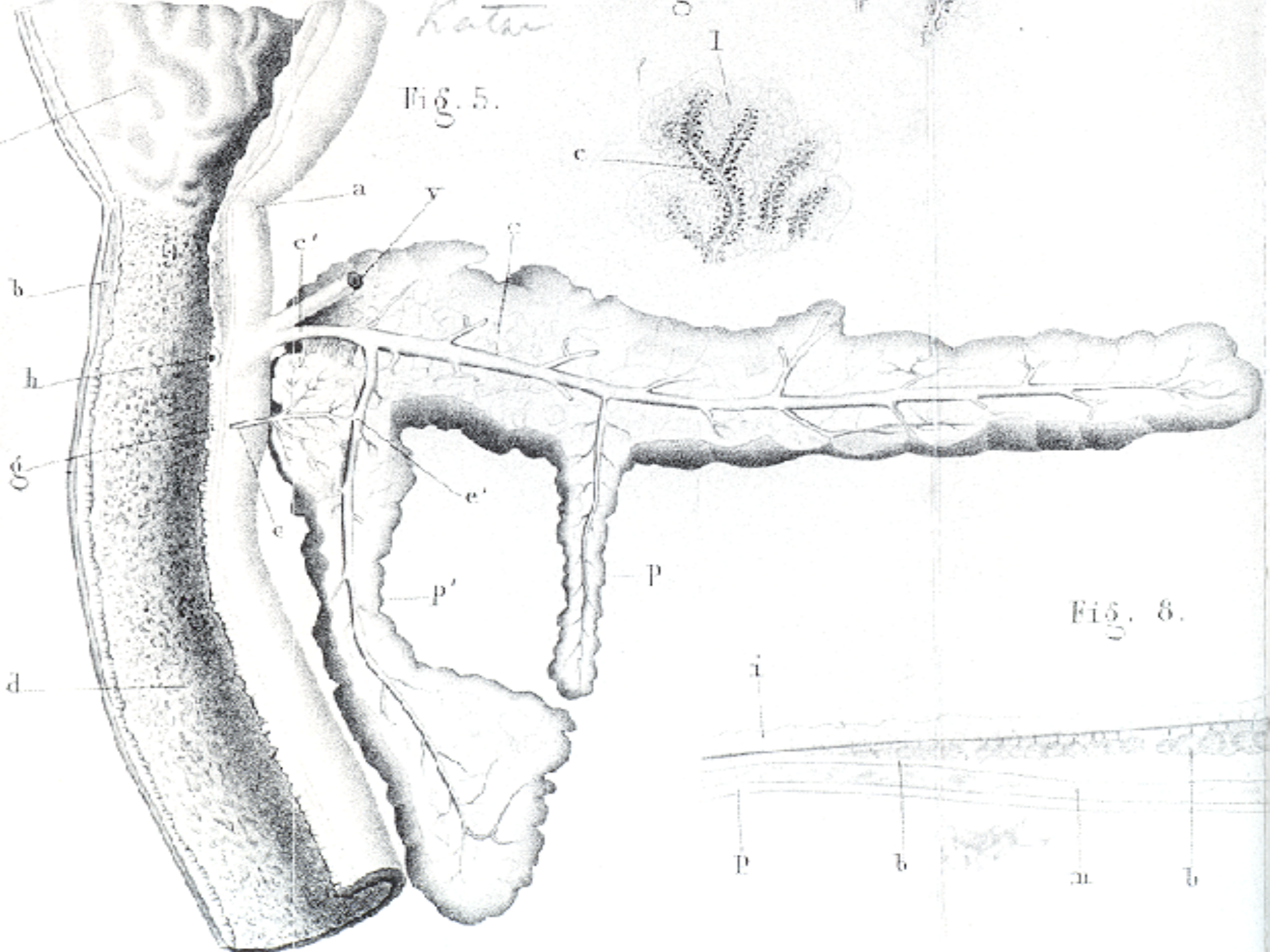


Fig. 5.
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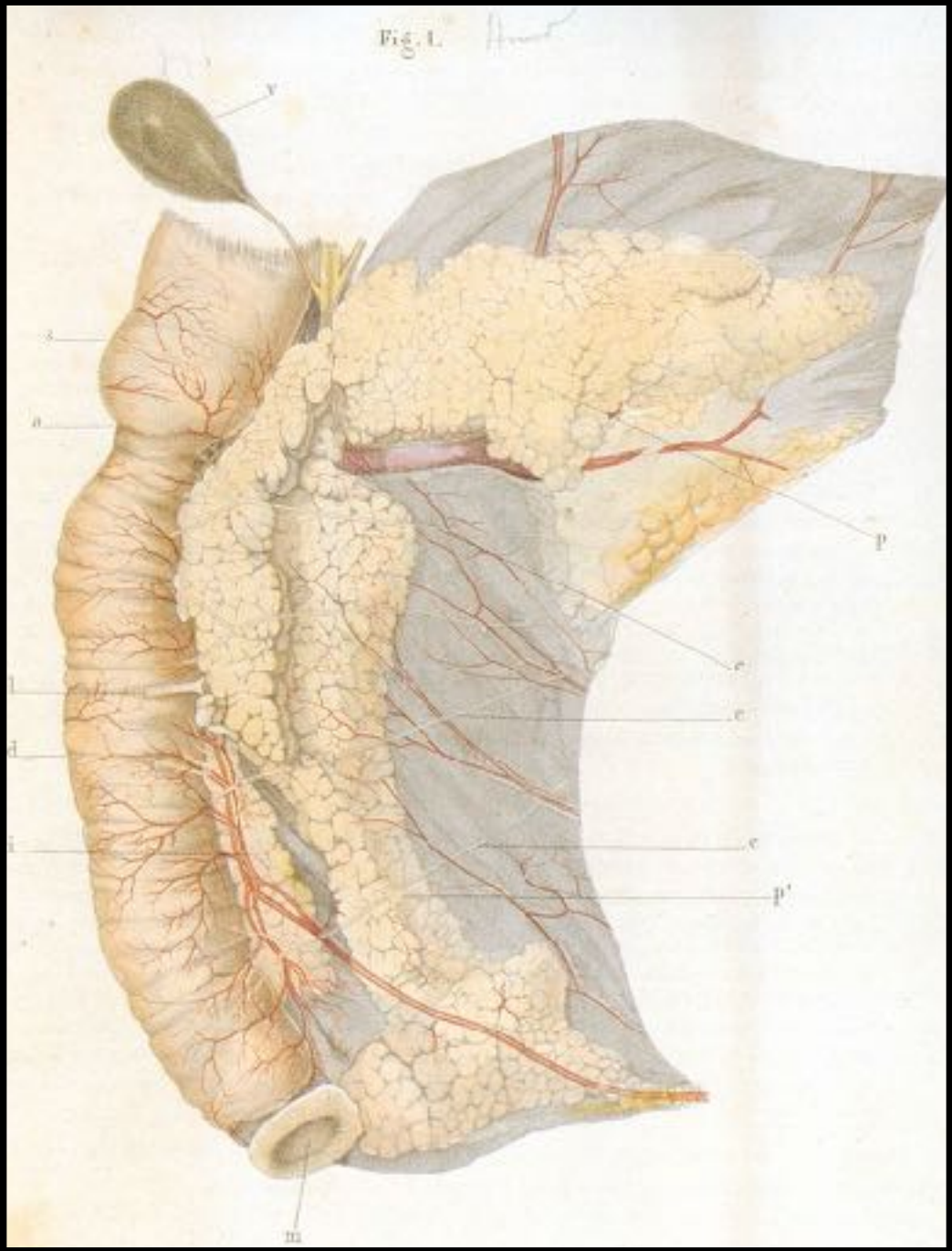
Fig. 1.
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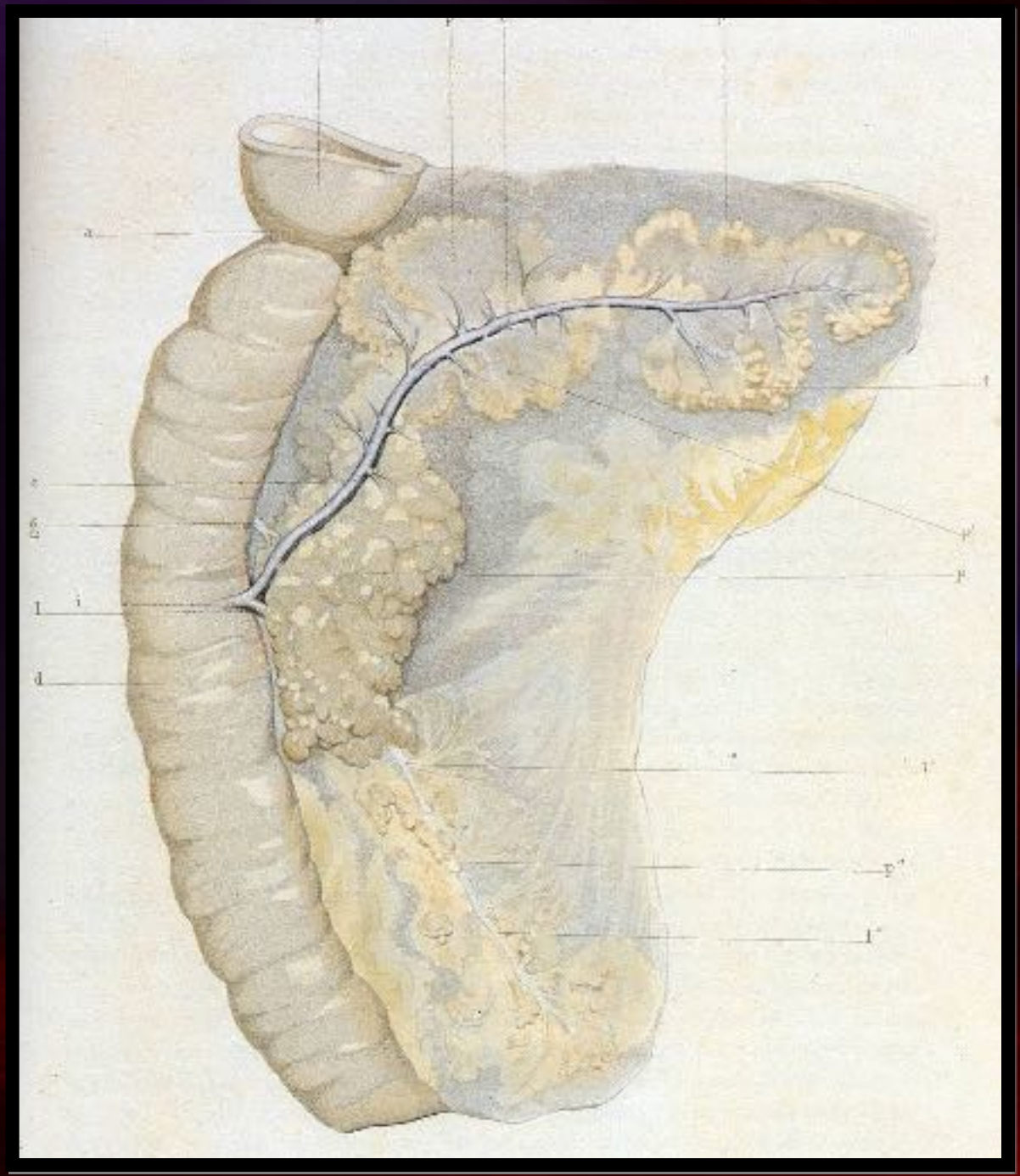

Exocrine pancreatic insufficiency

- 1850s - Bernard
- 1950s - Anderson
- 1970s - Sateri
- 1980s - Batt
- 1980s, 1990s, 2000s – Westermarck
- 1980s, 1990s, 2000s, 2010s
  Williams and progeny from GI Lab
  Steiner, Suchodolski, others

FUNDING EPI RESEARCH

- PhD Student(s) – Salary plus 44%
- Approx $70,000 per year for 3-5 year
- Sample collection - $300 per sample
- Microbiomics - $200 per sample
- Metabolomics - starts at $20,000
- Metagenomics -

ON-GOING EPI RESEARCH

- "State" funded salaries - $1,000,000
- Tuition waivers for MSc - $30,000
- Out of pocket salary - $50,000
- Grants - $30,000 – Nestle-Purina
- Gifts – EPI4Dogs $15k, Peskins $10k, Nestle-Purina $20k
- Other small other sources such as University professional development

- Approx $70,000 per year for 3-5 year

- Sample collection - $300 per sample
- Microbiomics - $200 per sample
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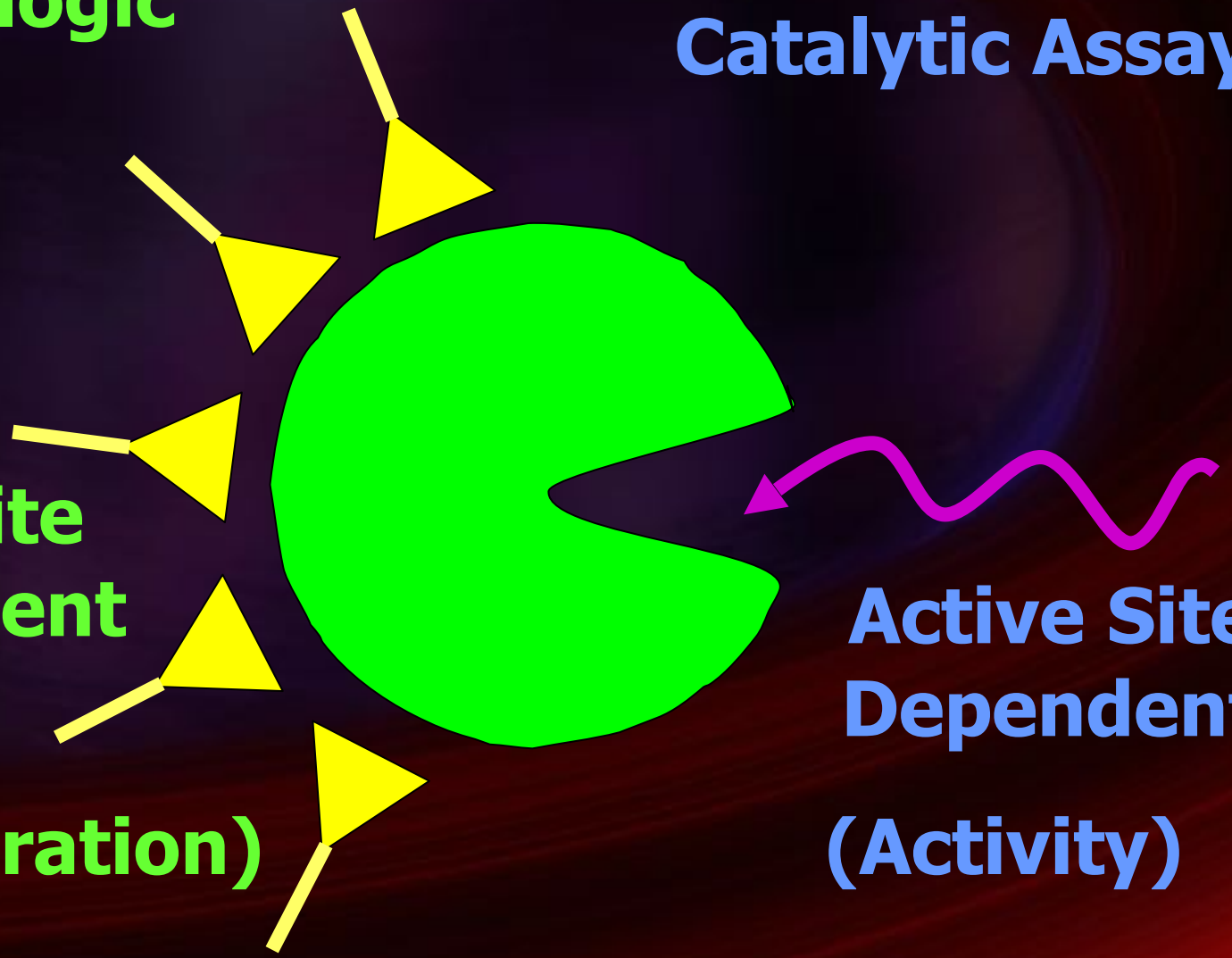
Canine and Feline EPI Clinical Signs

- Weight loss (mild to severe)
- Appetite ↑, ↓ (40% of cats), or ←→
- Diarrhea (variable)
  - "voluminous" <50% cats,>90% dogs)
- Borborygmus, flatulence
  - (88% dogs, 8% cat)
- Vomiting (cat > dog)
- Poor hair coat (unkempt cats)

Enzyme Assay

Immunologic Assay

Catalytic Assay



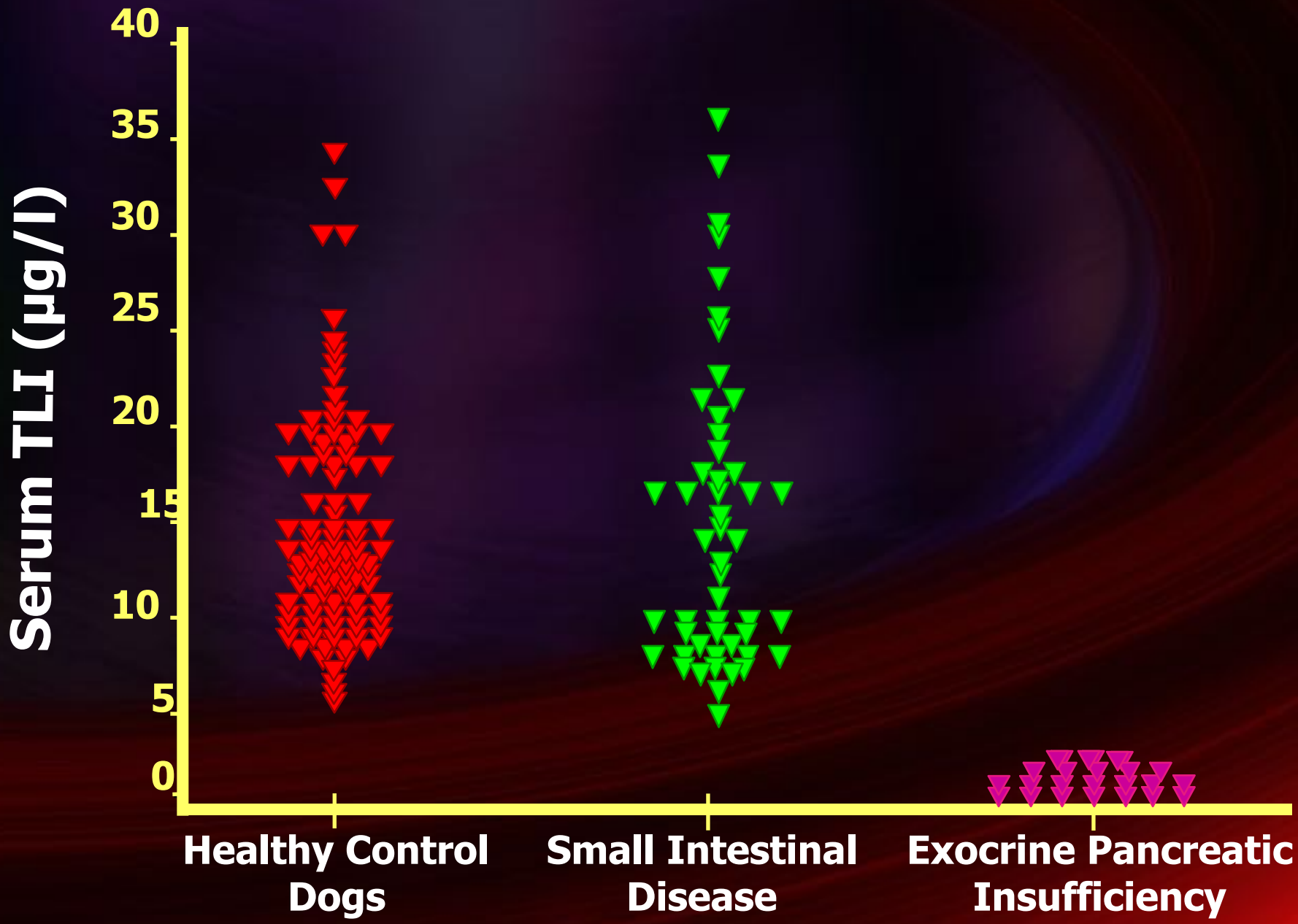
Active Site Independent

(Concentration)

Active Site Dependent

(Activity)

Serum Trypsin-Like Immunoreactivity



- **Serum TLI (cTLI, fTLI) - trypsinogen**
- **Serum PL (cPL, fPL) –pancreatic lipase**

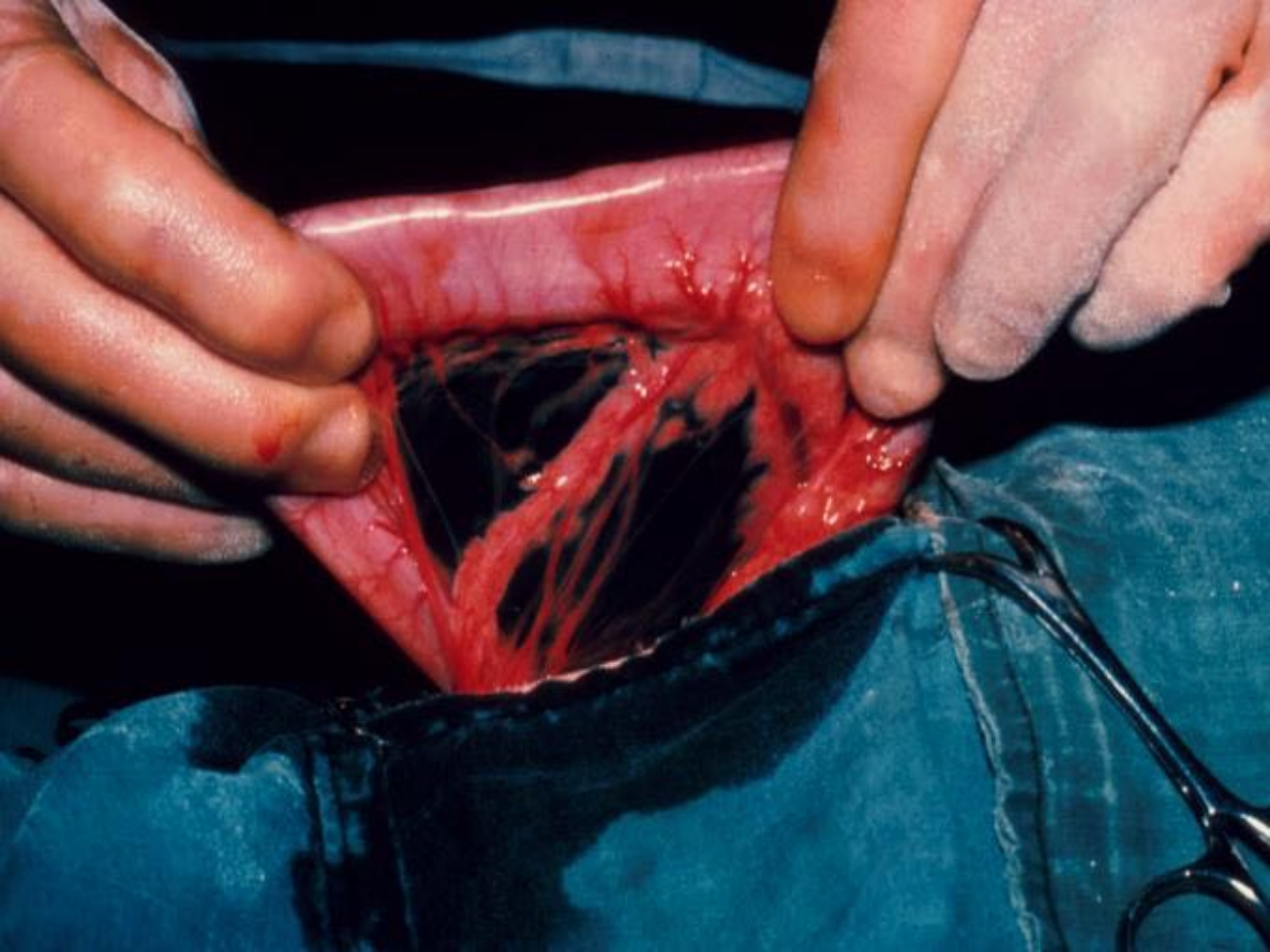
–Why are they good at what they are used to diagnose?

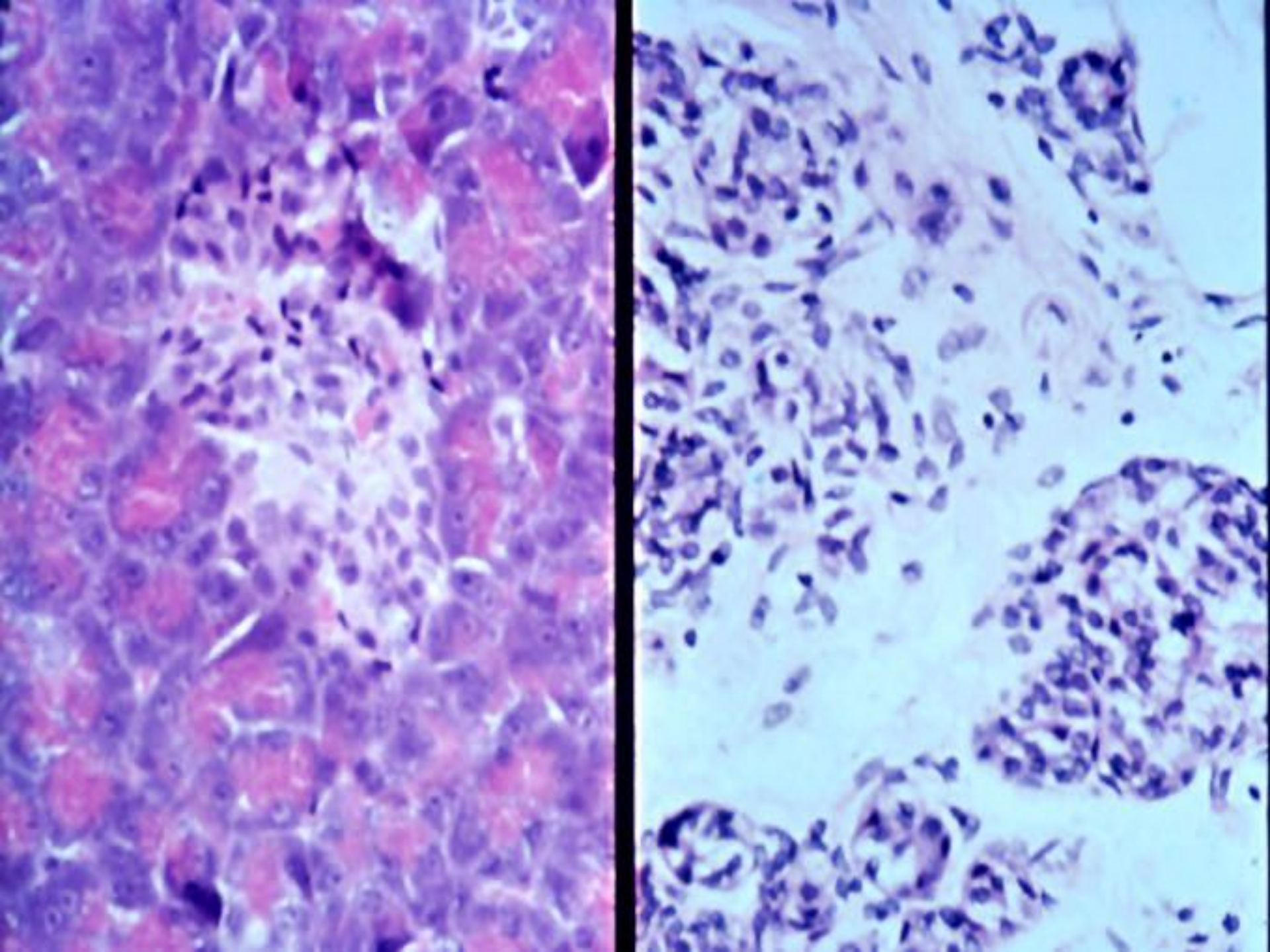
- **Organ specific**
- **Size, charge, half-life in plasma**
- **TLI – pancreatic mass - EPI**
- **PL – pancreatic leakage – pancreatitis**

- **Recommended initial testing in all patients is serum TLI, PL, cobalamin, & folate**

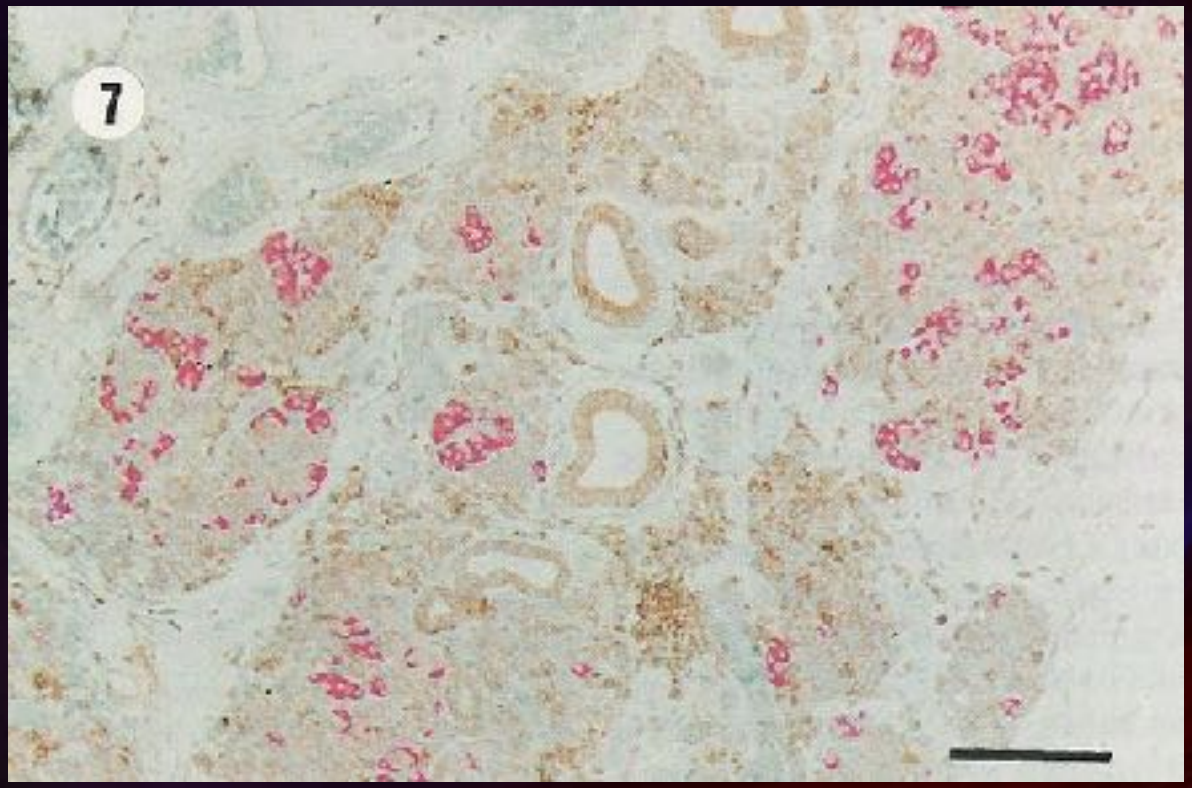
Canine EPI May Be Associated With:

- Decreased cholesterol
- Increased liver enzymes (ALT)
- Lymphopenia
- Eosinophilia
- Increased serum bile acids
- **BUT USUALLY UNREMARKABLE!**





Subclinical EPI (SEPI)



Late Lymphocytic Pancreatitis

Wiberg, Saari and Westermarck Vet Pathol 36:530-541 (1999)

Canine Pancreatic Acinar Atrophy

- The most common cause of EPI in the dog
- Not associated with diabetes mellitus
- End stage of immune-mediated lymphocytic pancreatitis in the GSD and Rough Collie

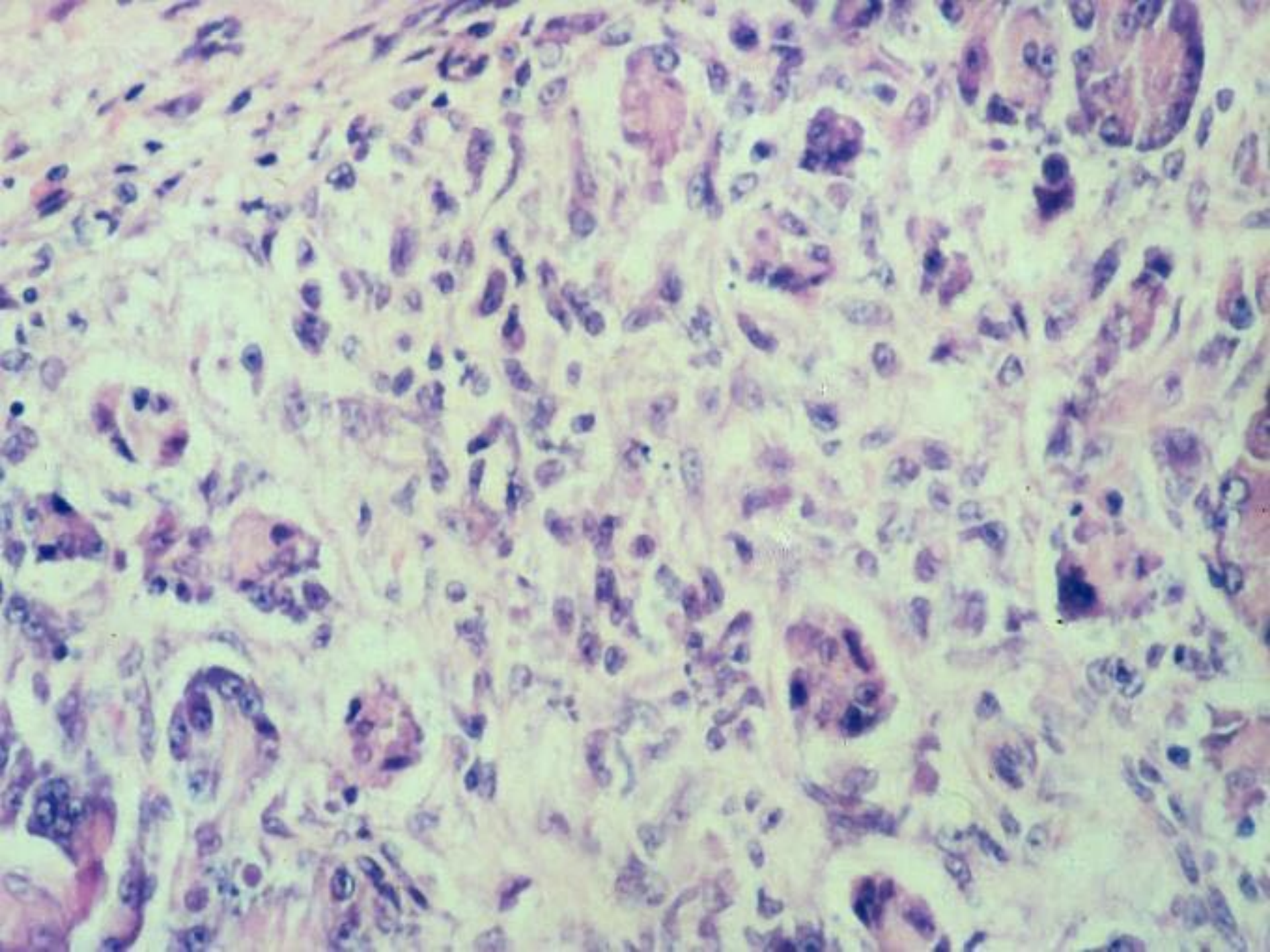
Canine Pancreatic Acinar Atrophy

- **Progression of immune-mediated lymphocytic pancreatitis is very unpredictable**

- **Immunosuppression did not have a demonstrable beneficial effect**
  (Wiberg et al. JVIM 2002)

Canine Pancreatic Acinar Atrophy

- Not a simple autosomal recessive mode of inheritance ($$$)
- None of the progeny from two affected parents developed disease after 10 years!!!



Chronic Pancreatitis

- An uncommon cause of EPI in the dog
- Probably the leading cause of EPI in the cat
- Often associated with diabetes mellitus

IMMULITE®

Assay Requirements

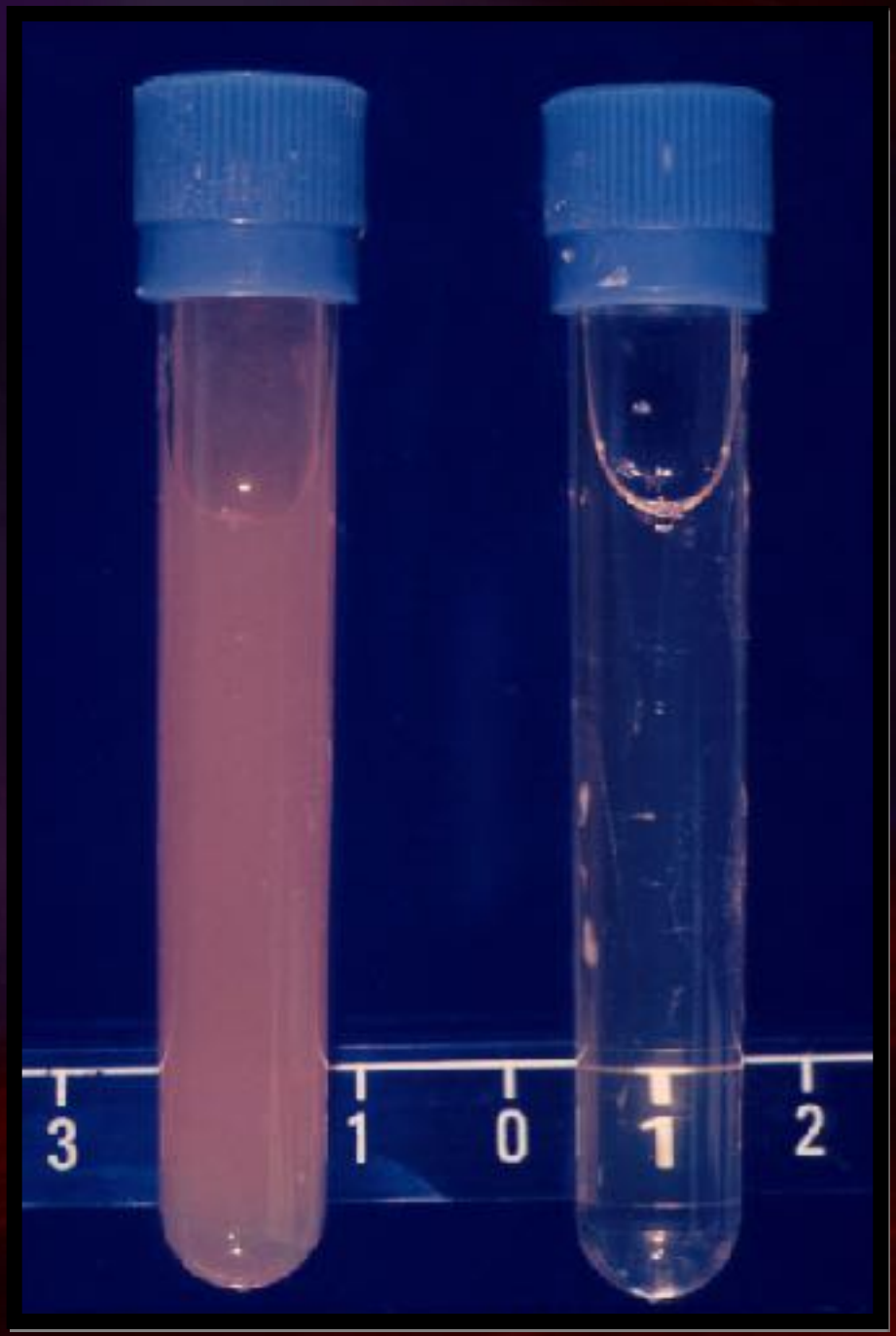
Reagent Wedge | **Test Unit** | **Sample Cup** | **Substrate**

Subnormal Serum TLI

- **2.5-5.0 µg/l – "gray zone" (control> 5.0 ug/L)**
  - **Assay variation is greater at lower values (and higher values) – do not over-interpret the number reported!!!**
  - **There is lab to lab variation, especially for cobalamin and folate**
  - **Immulite (everyone uses this now) not as precise or sensitive as radioimmunoassay**
  - **Dogs vary from day to day – usually clinically insignificant unless value is around 2.5ug/L**

Subnormal Serum TLI

- 2.5-5.0 µg/l – "gray zone" (control> 5.0 ug/l)
  - Subclinical chronic pancreatitis
  - EPI – immediately after a meal
  - Subclinical (immune-mediated) lymphocytic pancreatitis (SEPI)
  - No magical "cut-off" value for developing signs of EPI – extrapancreatic digestive capacity varies widely from dog to dog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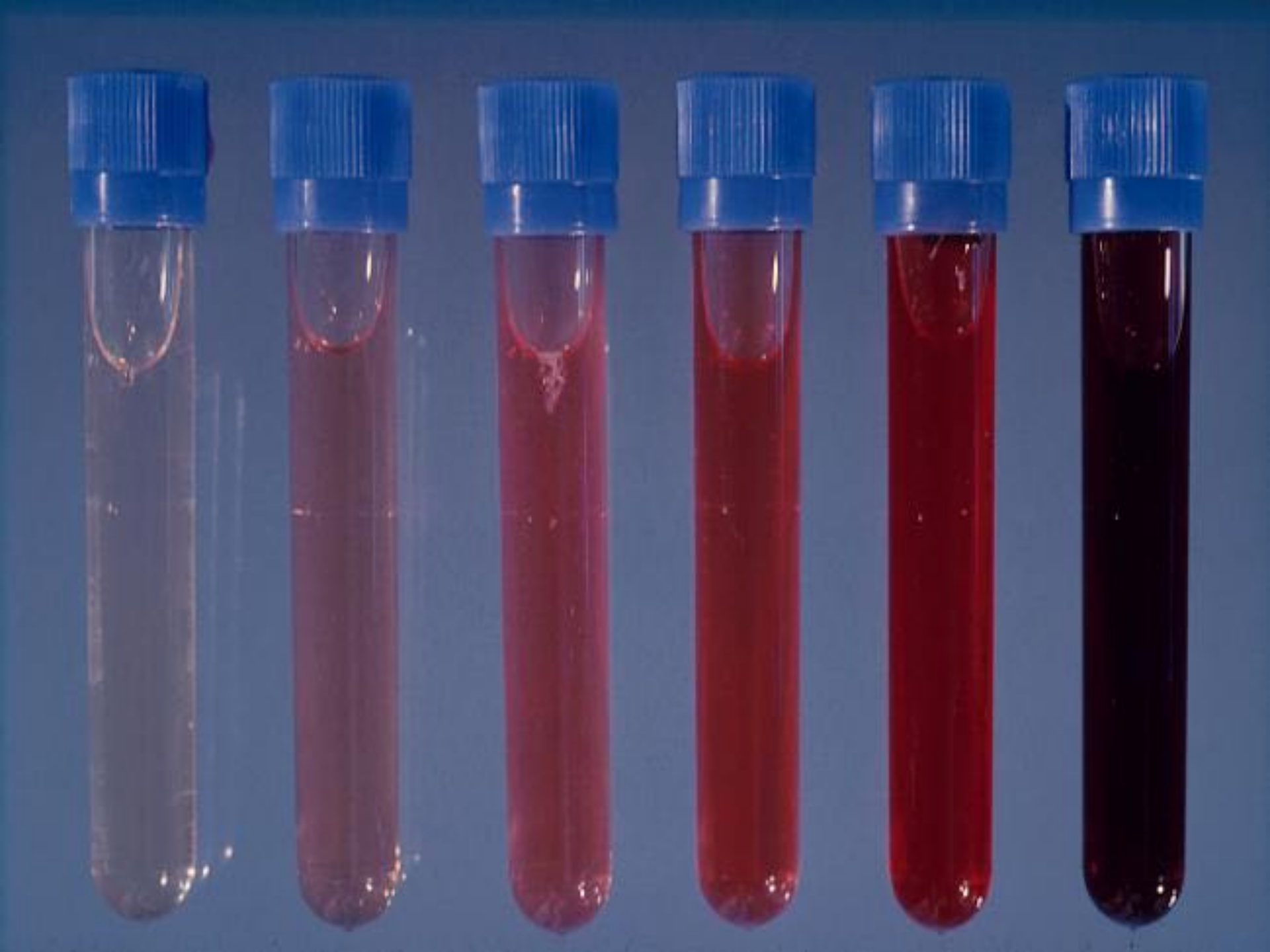
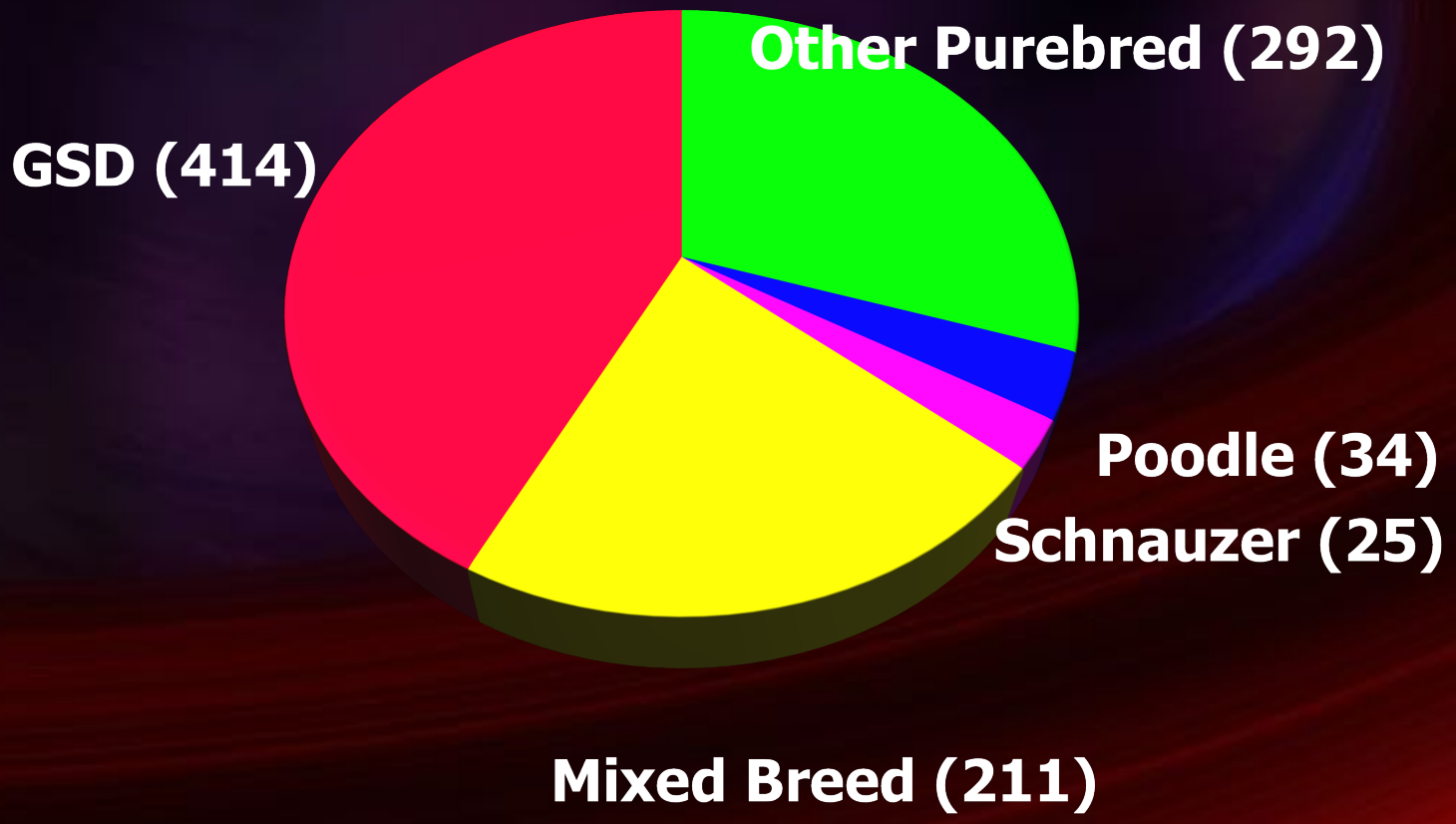
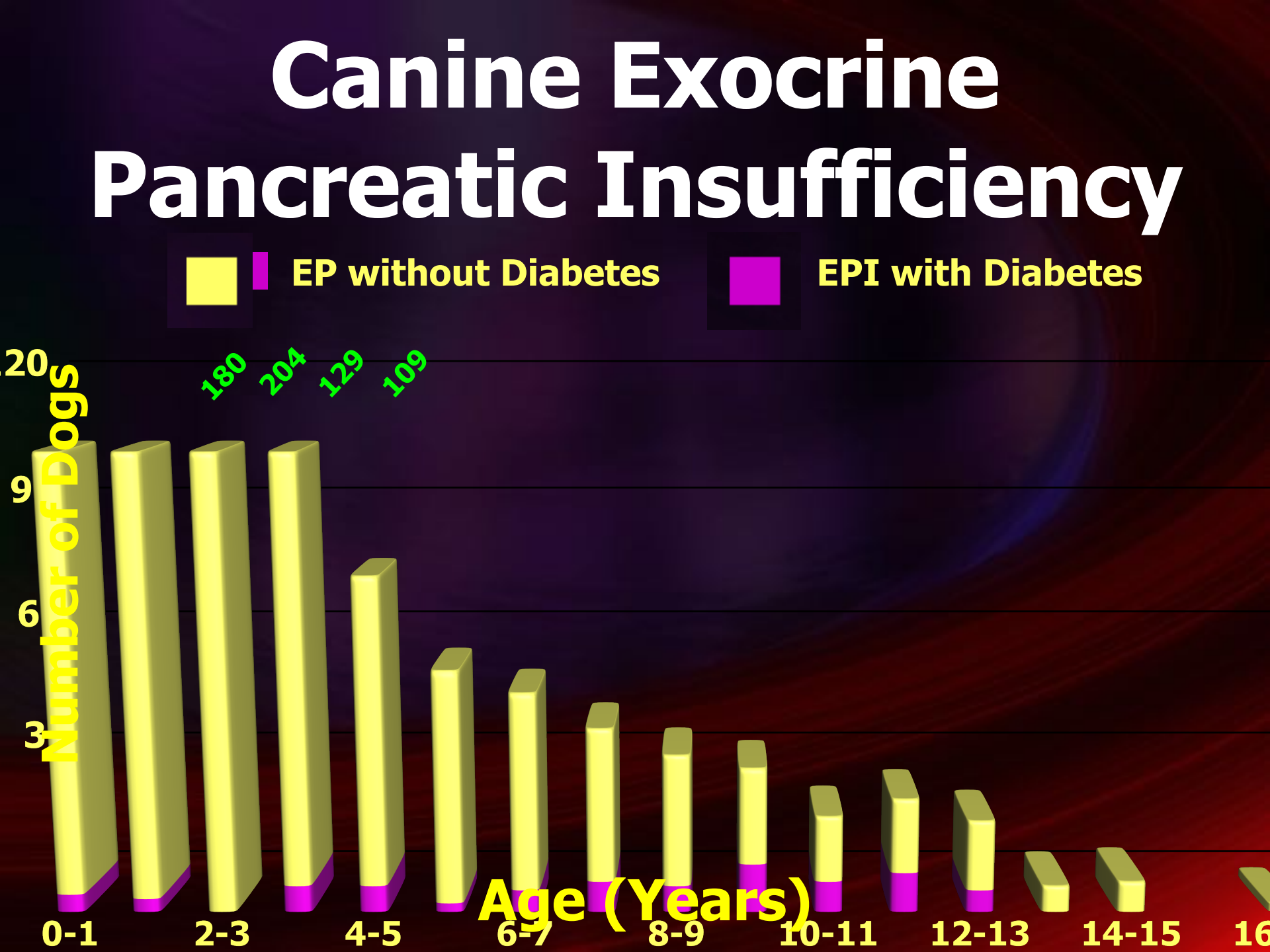


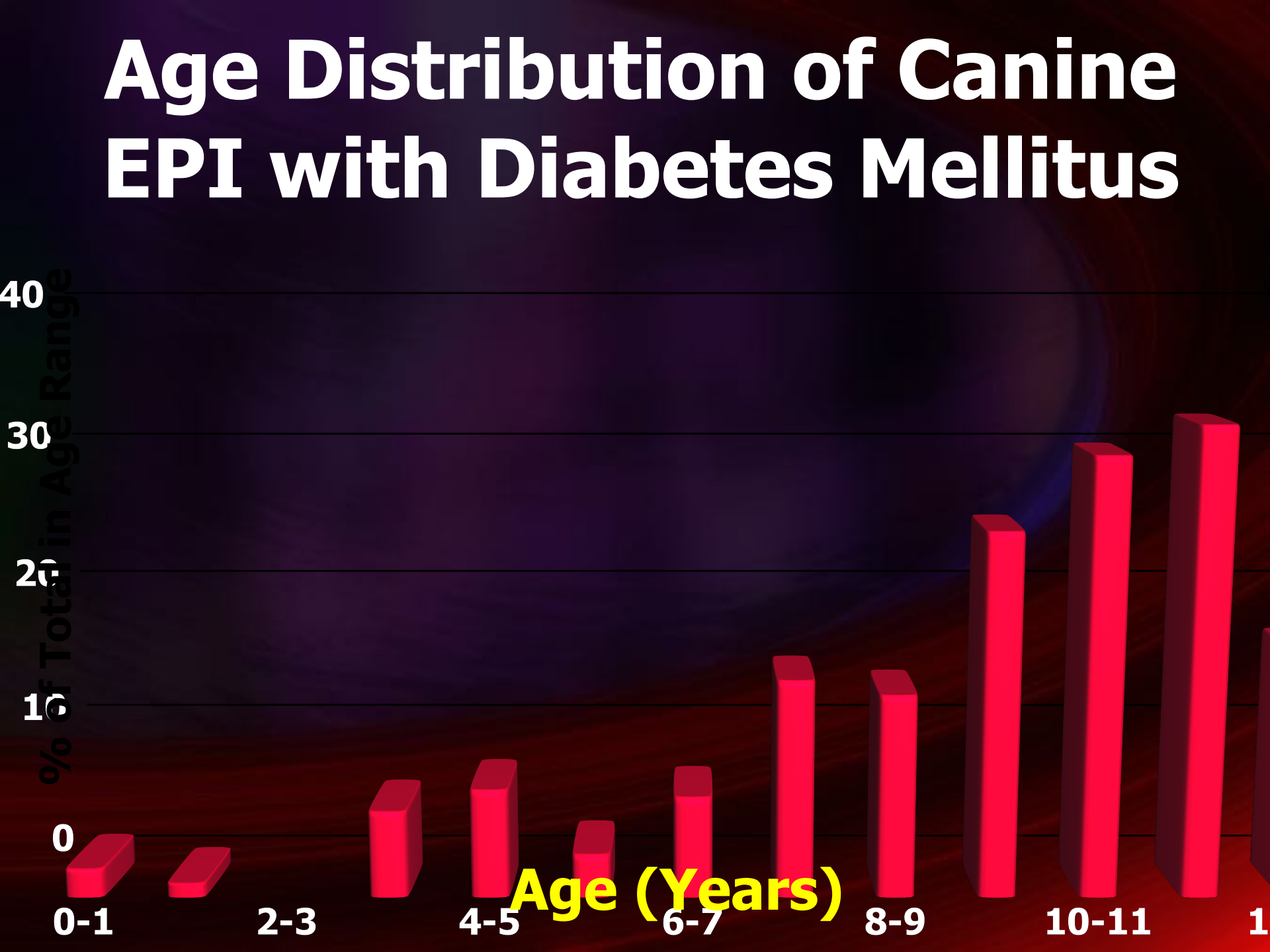
EPI Without Diabetes (976 Total)



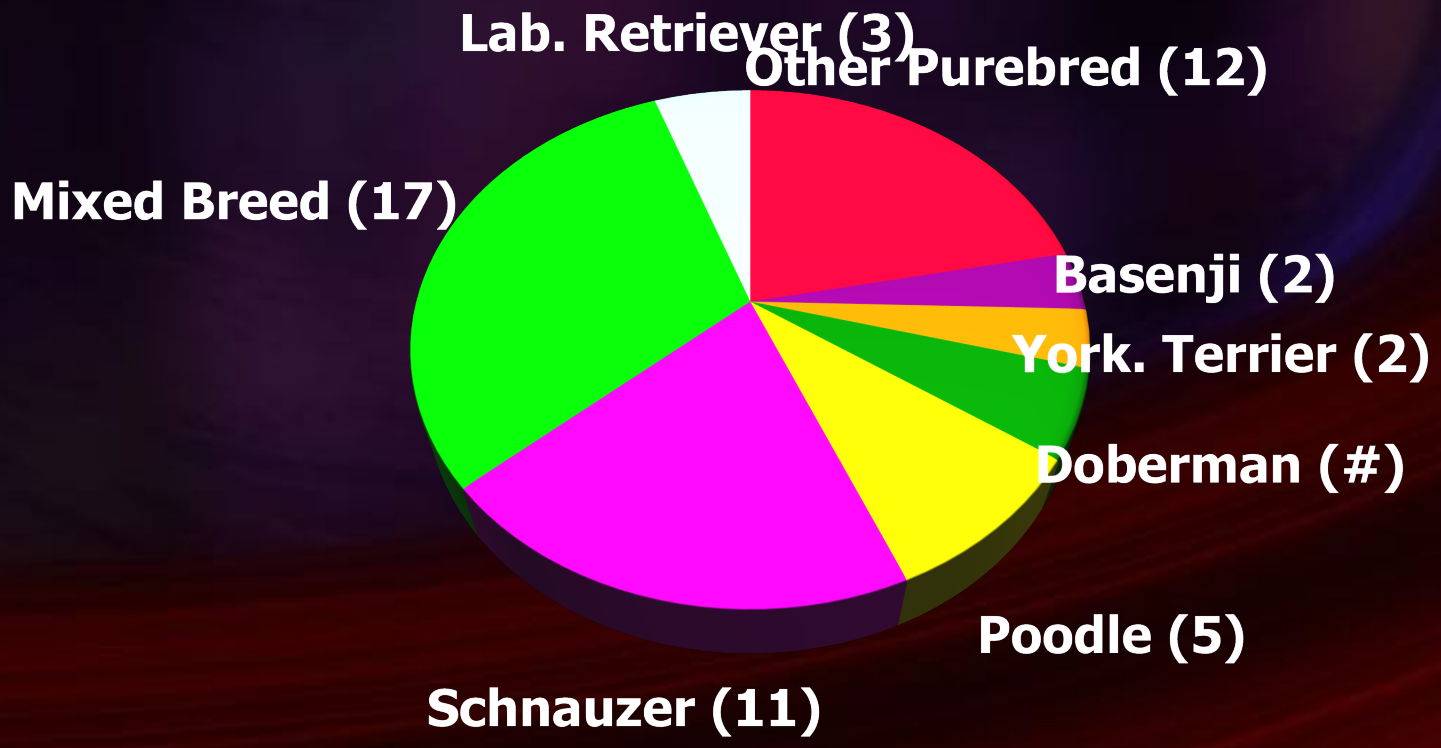
Canine Exocrine Pancreatic Insufficiency



Age Distribution of Canine EPI with Diabetes Mellitus

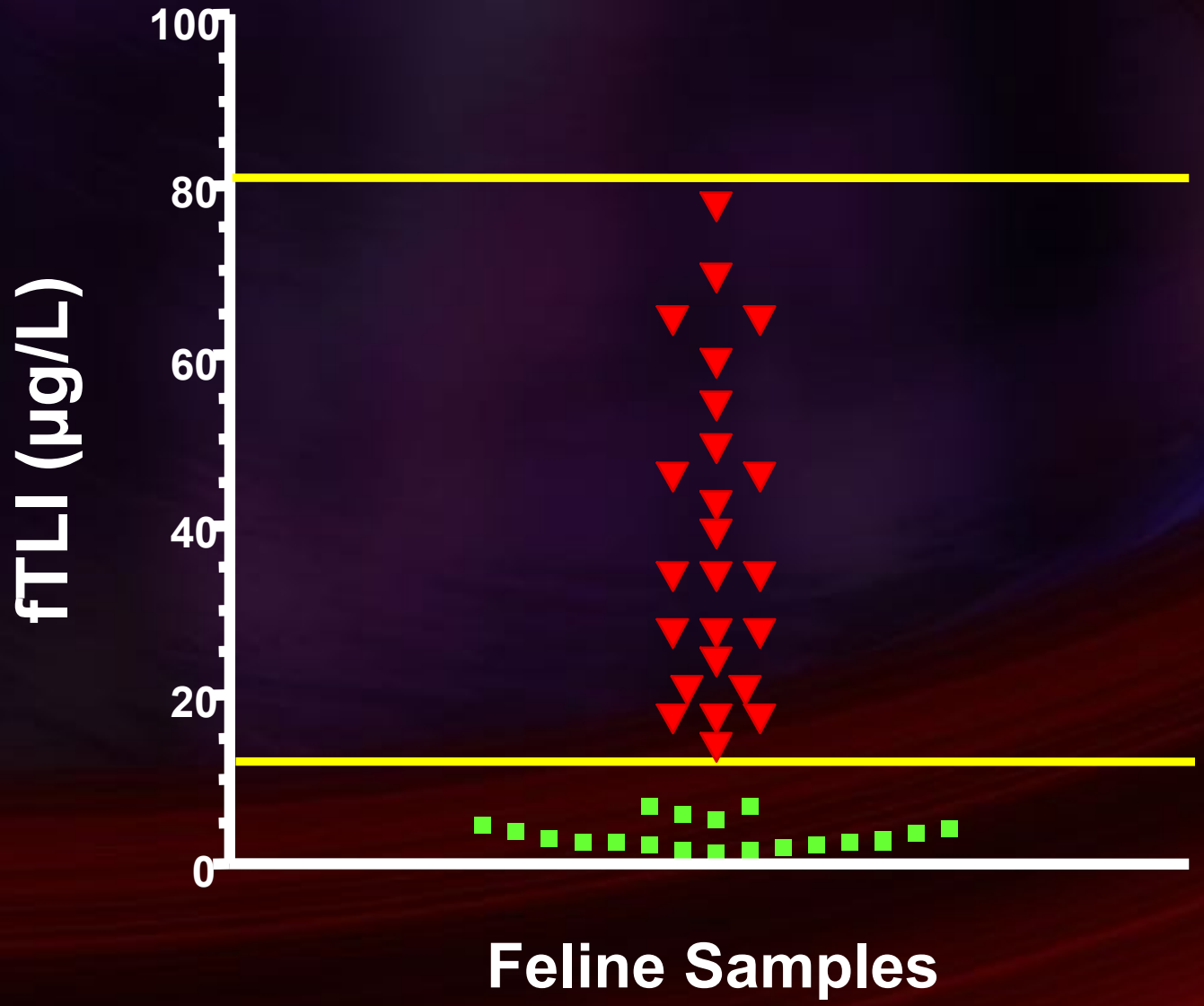


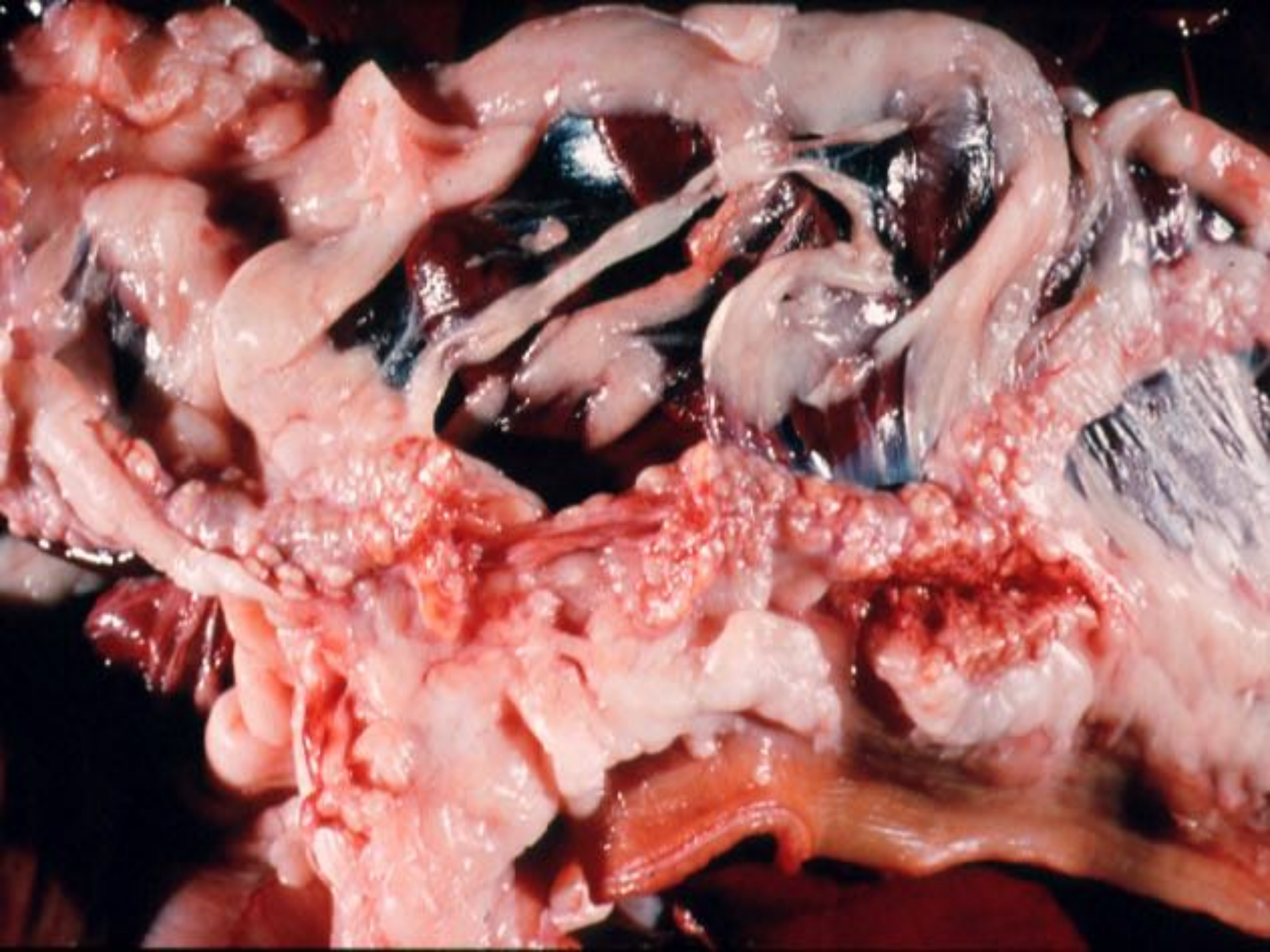
EPI With Diabetes (55 Total)

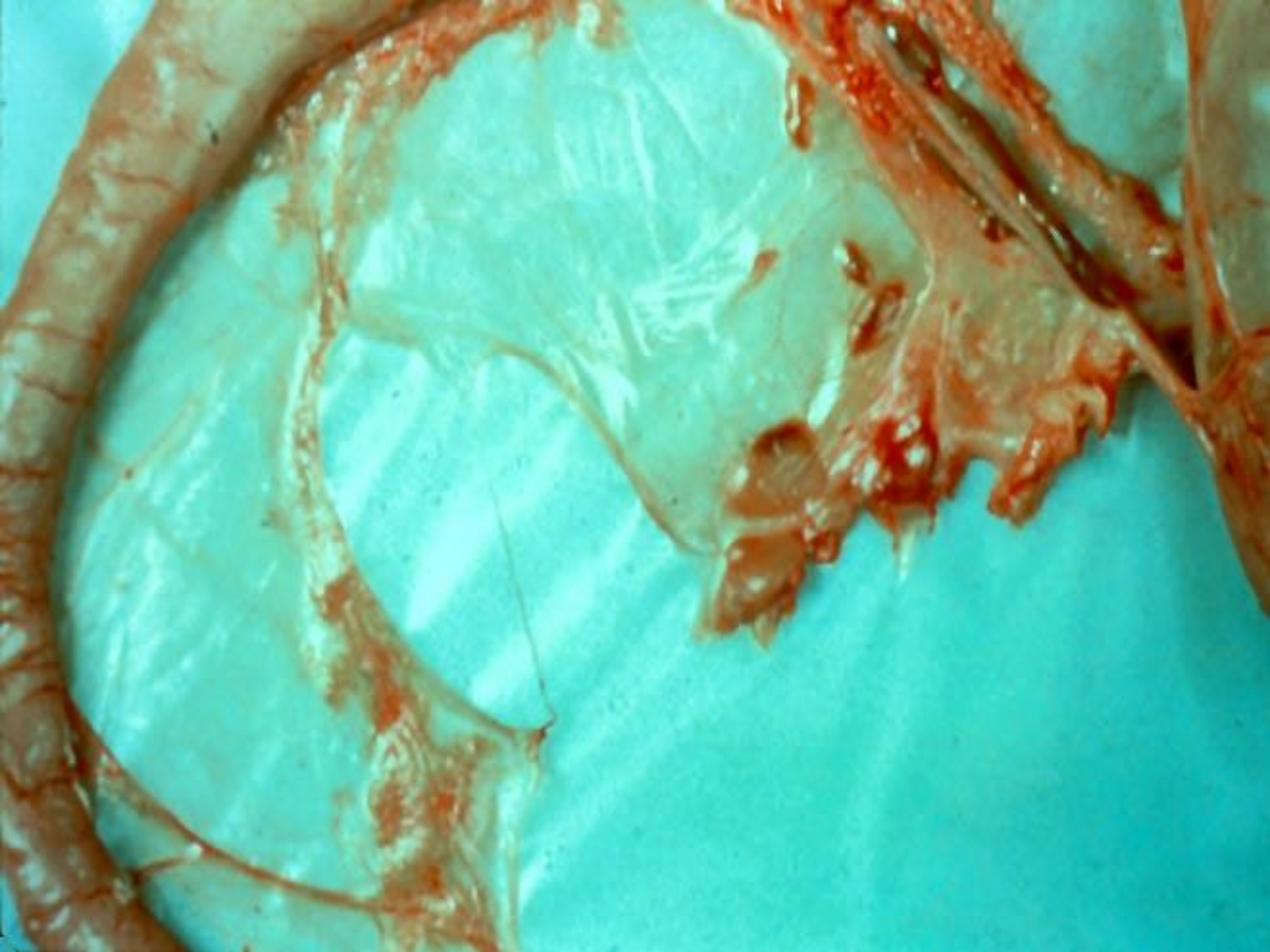


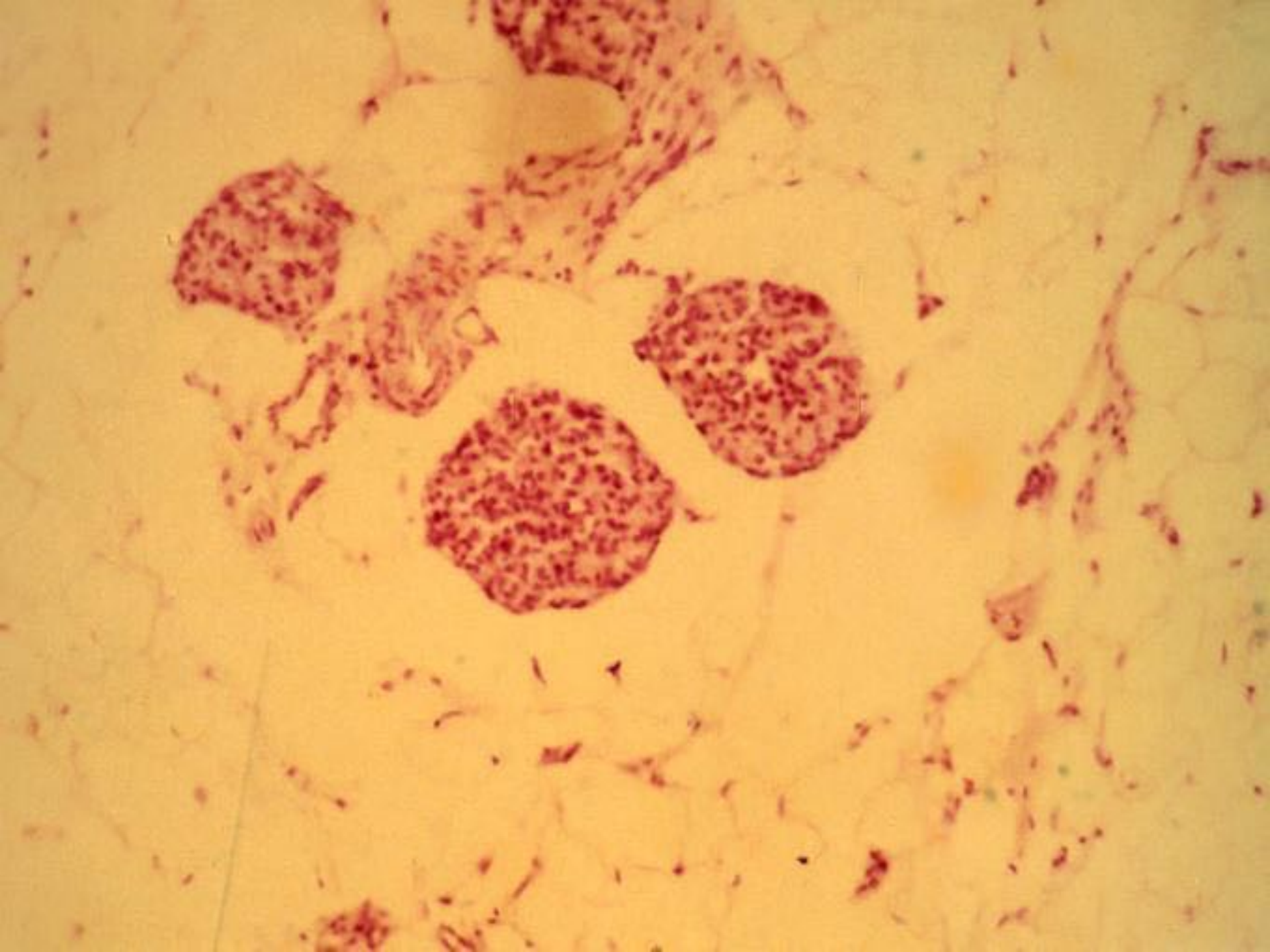

FTU TRACER

Feline TLI

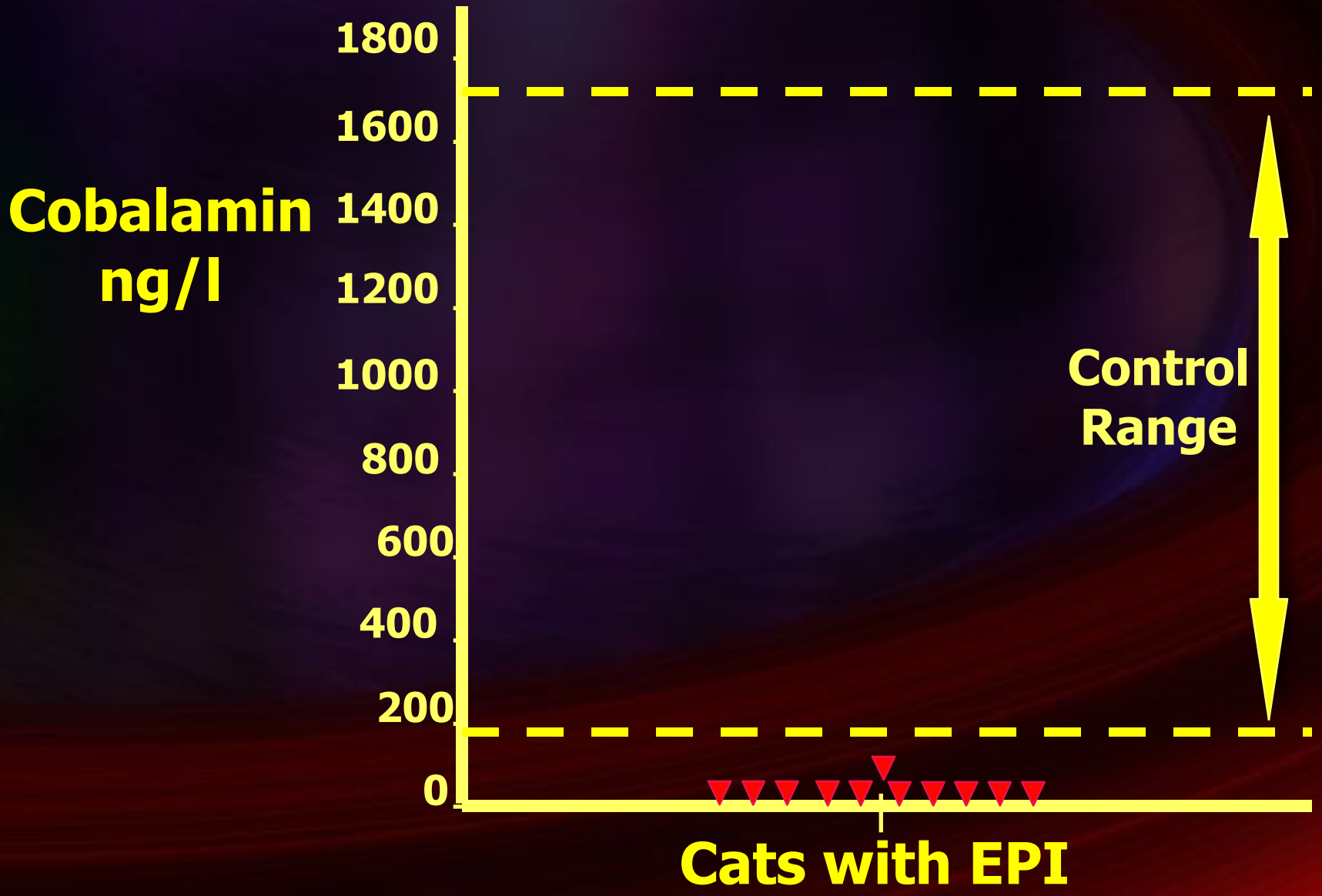








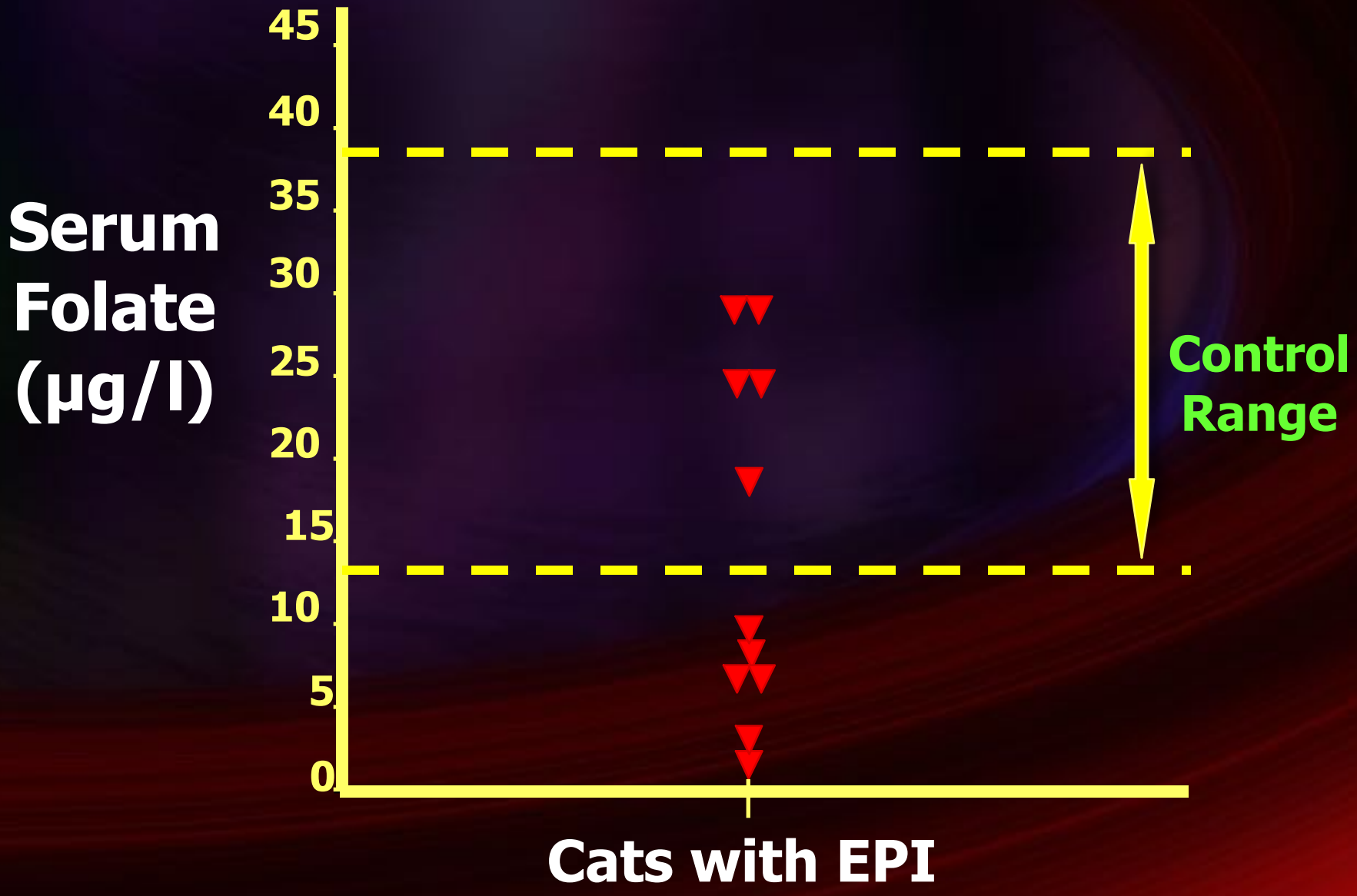
Serum Cobalamin in Cats With EPI

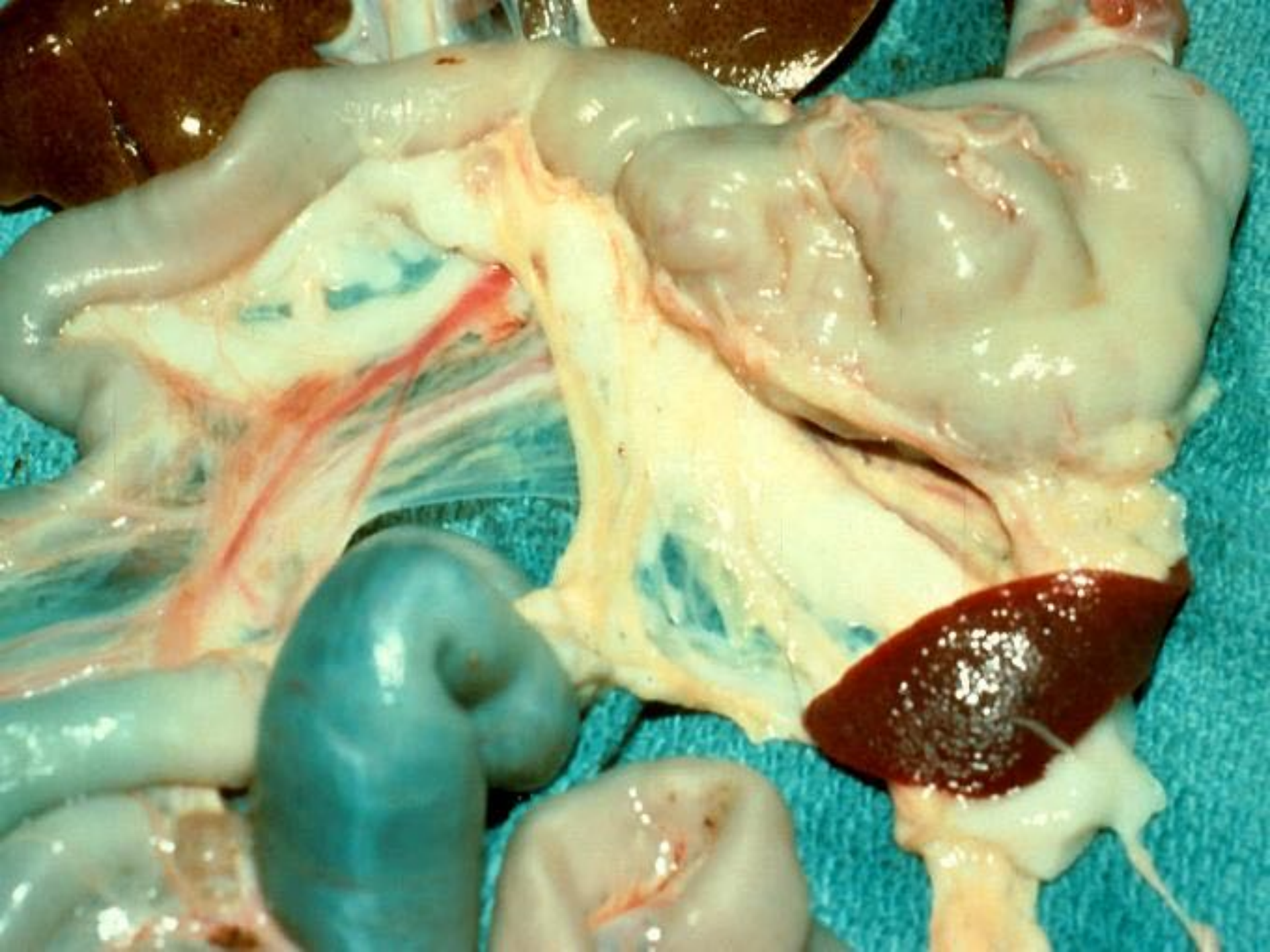


INTRINSIC FACTOR - COBALAMIN

Cobalamin deficient cats

Serum Folate in Cats With EPI





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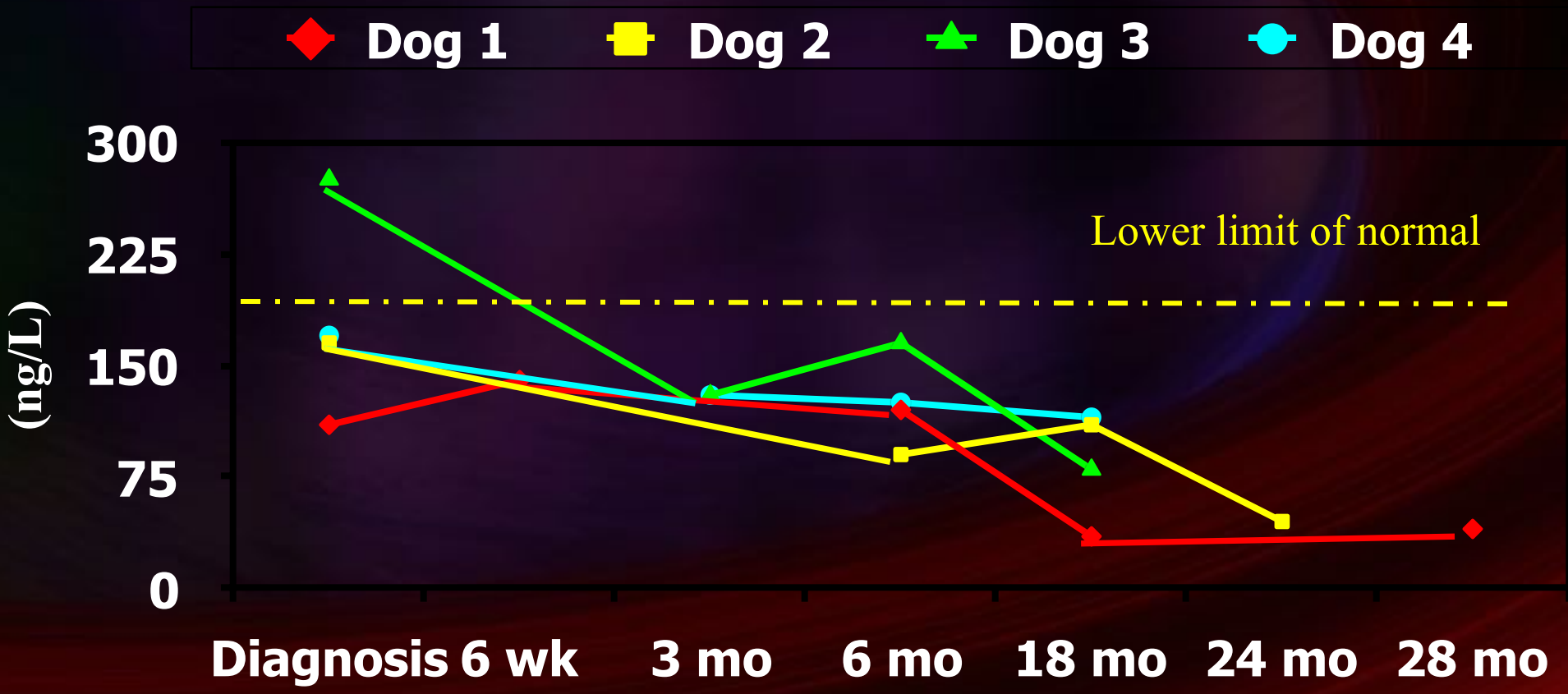

Exocrine Pancreatic Insufficiency