

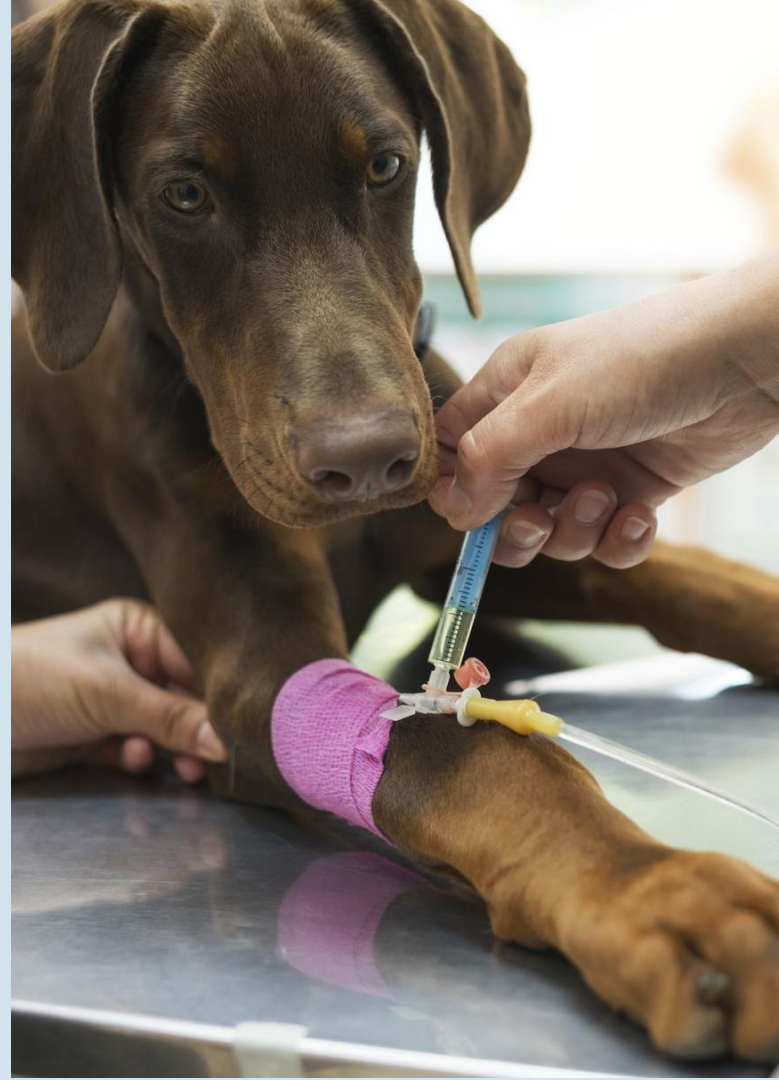
Oral Iron Consumption for Prevention of Post-Operative Epilepsy in Canines

Carrie Elaine Smith

Microbiology, Pre-Veterinary Track

2nd Year

(Ruben, 2015)





Introduction

- Surgical concerns (Huenerfauth, E., Nessler, J., Erath, J., & Tipold, A.)
 - 11.3% of post-operative seizures in canines
 - Probable Sudden Unexpected Death in Dogs (pSUDED)
 - 51% with post operative seizures die
 - 25% with post operative seizures are euthanized

(Smith, 2022)

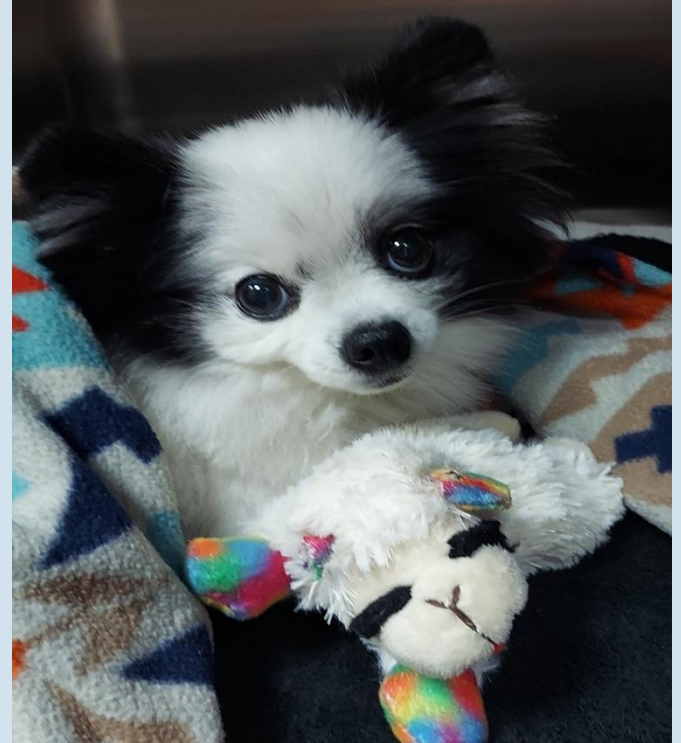
Background Literature

01 Iron-Induced Epilepsy

02 Treatment in Humans

03 Iron Usage in Veterinary Medicine

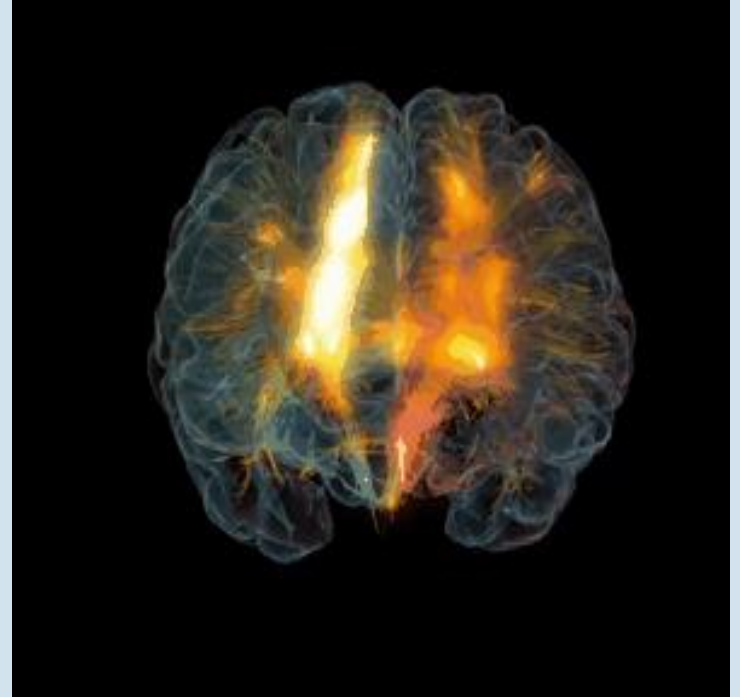
04 Inducing Seizures



(Smith, 2022)

01 Iron Induced Epilepsy

- Epilepsy: the occurrence of one episode of unprovoked seizure with a high risk for another episode (Padda J, Khalid K, Syam M, et al)
- Seizure: hyper arousal of the neurons
- After first seizure, likelihood increases to 40-52% of reoccurrence
- Occurrence of epilepsy decreases with time (Shinya MANAKA, Buichi ISHIJIMA, Yoshiaki MAYANAGI)



(University of California 2020)



AMGEN Foundation

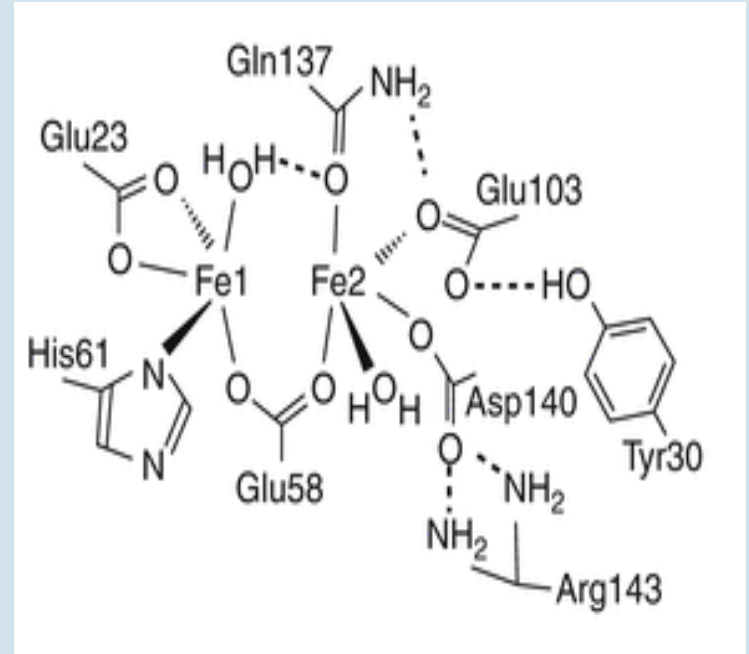


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01 Iron Induced Epilepsy

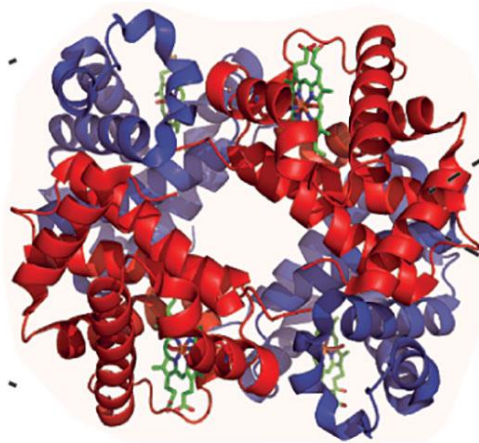
- Iron is stored in ferritin in the body (U.S. National Library of Medicine)
 - Mineral $[\text{FeO}(\text{OH})]_8[\text{FeO}(\text{H}_2\text{PO}_4)]$
 - Better storage than hemoglobin
 - Used to measure amount of iron in the body
 - Used for:
 - Oxygen transportation
- Digested in mucosal cells of the small intestine (Agraham)



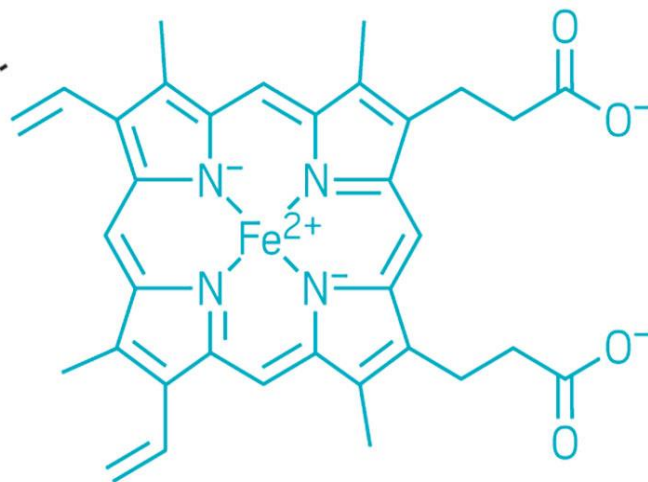
(Thiel 1970)



Red blood cell



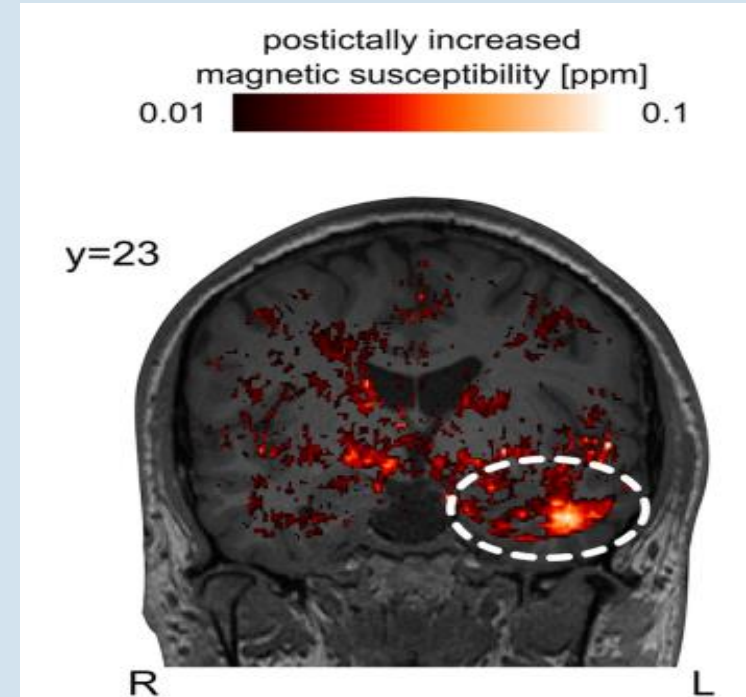
Hemoglobin



Heme group

01 Iron Induced Epilepsy

- Iron deficiency causes: (Padda J, Khalid K, Syam M, et al)
 - Drop in gamma aminobutyric acid inhibitory neurotransmitters (GABA)
 - Lessens ability of neuron transmission
 - Reduction in brain oxygenation
 - Haemorrhage, haemolysis, Peroxidation, cell death



(Zimmer et al., 2021)

Background Literature

01

Iron-Induced Epilepsy

02

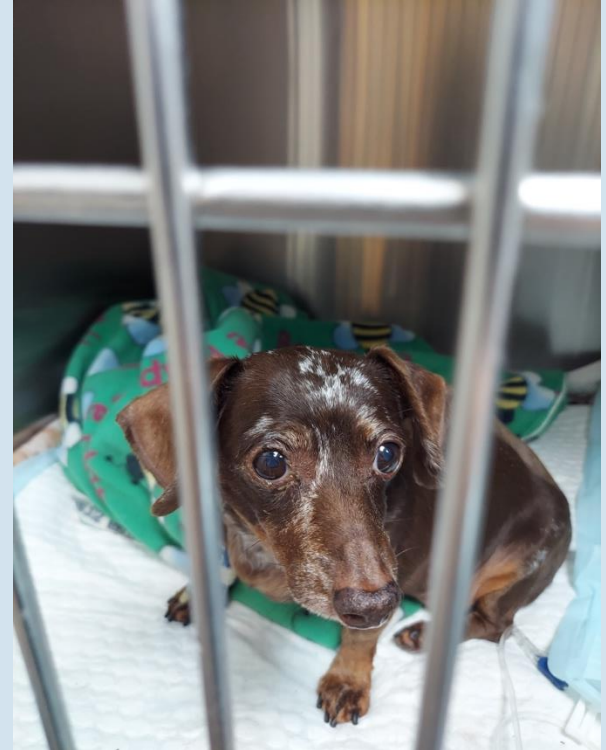
Treatment in Humans

03

Iron Usage in Veterinary
Medicine

04

Inducing Seizures



(Smith, 2022)

02 Treatment in Humans

- Oral. Versus Intravenous (Moon, T., Smith, A., Pak, T. *et al.*)
 - Consistent increase of hemoglobin levels
 - No difference between oral or intravenous pre-operative therapy
 - Predisposed for anemia, iron supplementation is recommended pre-operation
 - Colorectal cancer, uterine disease, sickle cell anemia



(Tsang 2011)

Background Literature

01

Iron-Induced Epilepsy

02

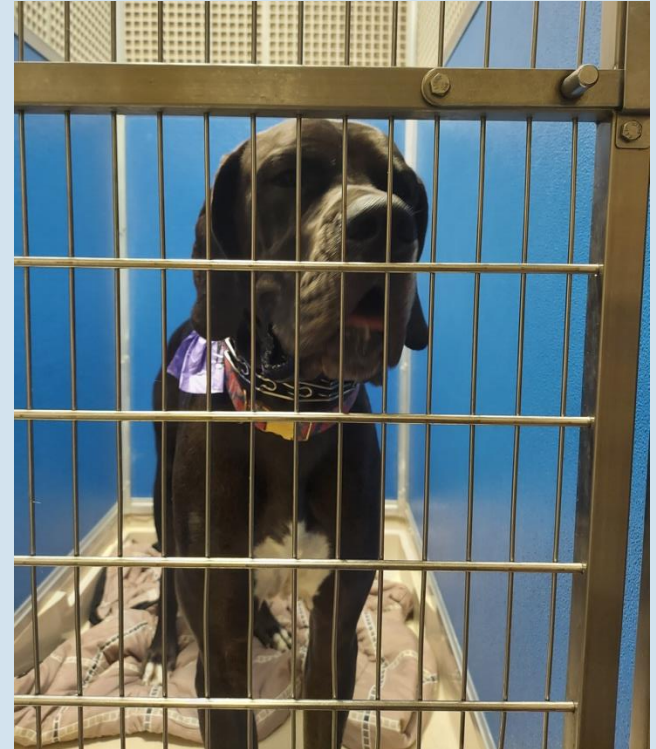
Treatment in Humans

03

**Iron Usage in Veterinary
Medicine**

04

Inducing Seizures



(Smith, 2022)

03

Iron Usage in Veterinary Medicine

- Ingestion of $>60\text{mg/kg}$ is considered potentially serious (Agraham)
 - $20\text{-}60\text{mg/kg}$ can damage intestinal tract
 - $<20\text{mg/kg}$ approved
- Not suggested for healthy canines
- Prescribed for iron deficiency anemia, chronic blood loss, and kidney disease (Richards, T., Baikady, R. R., Clevenger, B.)
- Iron levels above 13g/dL to be considered for surgery



(Smith, 2022)

Background Literature

01

Iron-Induced Epilepsy

02

Treatment in Humans

03

Iron Usage in Veterinary
Medicine

04

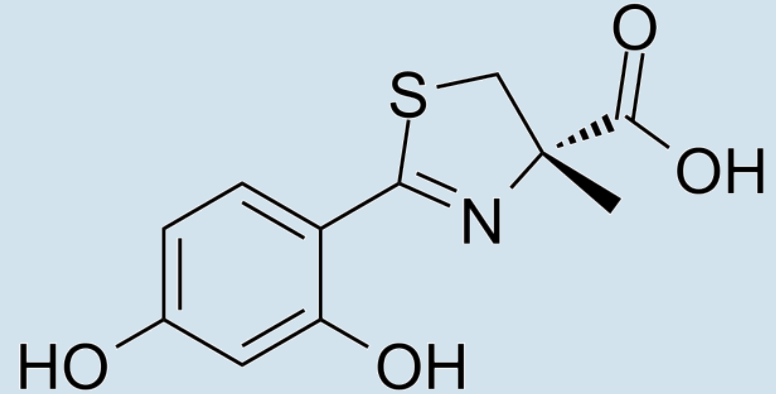
Inducing Seizures



(Smith, 2022)

04 Inducing Seizures (2)

- Deferitrin
 - Desferrithiocin-derived hexadentate iron chelator
 - Promotes iron excretion through urination
 - Sanofi Genzyme Corporation
 - Tested efficacy on male Beagles (conventional)
 - Dosage: 150μmols/kg
 - In solution with sterile water
 - Given orally in gelatin capsules



(Deferitrin molecule)

Lacuna

(as of November 8th, 2022)

PubMed.gov

anemia and epilepsy



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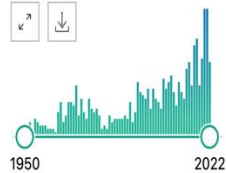
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RESULTS BY YEAR



TEXT AVAILABILITY

- ☐ Abstract
- ☐ Free full text
- ☐ Full text

ARTICLE ATTRIBUTE

- ☐ Associated data

ARTICLE TYPE



Association of Anemia With Epilepsy and Antiepileptic Drugs.

1

Padda J, Khalid K, Syam M, Kakani V, Kankeu Tonpouwo G, Dhakal R, Padda S, Cooper AC, Jean-Charles G.

Cureus. 2021 Nov 7;13(11):e19334. doi: 10.7759/cureus.19334. eCollection 2021 Nov.

PMID: 34909297 [Free PMC article.](#) [Review.](#)

Epilepsy is a disorder that causes unprovoked seizures regularly. It affects between 1% and 3% of the population. ...Further studies and clinical trials are warranted to prove a clear association between **epilepsy** and hematologic disease, which will improve quality o ...



Choline-related-inherited metabolic diseases-A mini review.

2

Wortmann SB, Mayr JA.

Cite

J Inherit Metab Dis. 2019 Mar;42(2):237-242. doi: 10.1002/jim.d.12011. Epub 2019 Jan 25.

PMID: 30681159 [Free PMC article.](#) [Review.](#)

Share

The broad phenotypic spectrum ranging from malodor, intellectual disability, to **epilepsy**, **anemia**, or congenital myasthenic syndrome is presented, highlighting the central role of choline within human metabolism....



Pharmacokinetics and Tolerability of Multiple Doses of Pharmaceutical-Grade

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anemia and epilepsy in Canines



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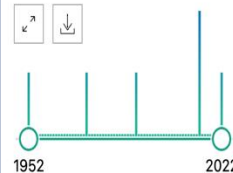
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RESULTS BY YEAR



TEXT AVAILABILITY

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- ☐ Full text

ARTICLE ATTRIBUTE

- ☐ Associated data

ARTICLE TYPE



Retrospective evaluation of systemic hypertension in **dogs** with nonassociative (primary) immune-mediated hemolytic **anemia** (December 2016 to April 2019): 26 cases.

1

Hall GBF, Stoye DQ, Thomas EK, Culshaw GJ.

Cite

J Vet Emerg Crit Care (San Antonio). 2022 Mar;32(2):229-235. doi: 10.1111/vec.13128. Epub 2022 Jan 25.

PMID: 35080103

SETTING: University teaching hospital. ANIMALS: Twenty-six clinical **dogs** presenting to the ICU with nonassociative (primary) IMHA and a control group of 23 clinical **dogs** with idiopathic **epilepsy** hospitalized in the ICU for seizure treatment or monitoring.



Phenobarbitone-induced haematological abnormalities in idiopathic epileptic **dogs**: prevalence, risk factors, clinical presentation and outcome.

2

Bersan E, Volk HA, Ros C, De Risio L.

Cite

Vet Rec. 2014 Sep 13;175(10):247. doi: 10.1136/vr.102158. Epub 2014 May 16.

PMID: 24836432

Share

The aim of this retrospective study was to assess prevalence, risk factors, clinical presentation and outcome of phenobarbitone induced haematological abnormalities (PBIHA) in **dogs**. The medical

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NIH

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Canine iron for epilepsy

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3 results

Page 1 of 1

RESULTS BY YEAR

Year	Results
1996	0
2022	3

TEXT AVAILABILITY

☐ Abstract

☐ Free full text

☐ Full text

ARTICLE ATTRIBUTE

☐ Associated data

ARTICLE TYPE

☐ 1

Comparison of Serum Trace Nutrient Concentrations in Epileptics Compared to Healthy Dogs.

Cite

Share

Vitale S, Hague DW, Foss K, de Godoy MC, Selmic LE.
Front Vet Sci. 2019 Dec 19;6:467. doi: 10.3389/fvets.2019.00467. eCollection 2019.
PMID: 31921923 **Free PMC article.**
Idiopathic **epilepsy** (IE) is a common cause of seizures in **dogs**. There are several investigations regarding serum concentrations of trace nutrients, including copper, selenium, zinc, manganese, and **iron** in human epileptics and animal models. However, research ...

☐ 2

Measurement of Neutrophil Gelatinase-Associated Lipocalin Concentration in Canine Cerebrospinal Fluid and Serum and Its Involvement in Neuroinflammation.

Cite

Share

Meyerhoff N, Rohn K, Carlson R, Tipold A.
Front Vet Sci. 2019 Sep 18;6:315. doi: 10.3389/fvets.2019.00315. eCollection 2019.
PMID: 31620456 **Free PMC article.**
A commercially available Enzyme-linked Immunosorbent Assay (ELISA) for detection of **canine** NGAL was validated for use in **canine** CSF. Concentration in CSF and serum of **canine** patients suffering from steroid- responsive meningitis- arteriitis (SRMA), Meningoenc ...

Lacuna

If oral iron consumption pre-operation for preventing post-operation epilepsy is beneficial to humans, would this same treatment be beneficial for canines?

Hypothesis

In major abdominal surgery in canines, pre-operational oral intake of iron will prevent the occurrence of post-operational epilepsy and will maintain the levels of hemoglobin between 14-20 grams/deciliter.

Specific Aim

- Investigate the influence of pre-operative oral consumption on hemoglobin levels in canines
- Evaluate occurrence of late epilepsy in canines included in the study

Methodology: Ranges



Time Frame

- Deferritin Dosage: 30 days
- Iron Dosage: 31st day
- CBC Conduction:
 - Weekly 60 days
 - Monthly 3 years



Subjects

- Male Beagles (Conventional)
- Same family lineage
- No genetic predisposition for anemia



Sample Size

- 45 Total
 - 15 Negative Control Group
 - 15 Positive Control Group
 - 15 Experimental Group



Dosages

- Deferritin Dosage: 150 μ mol/kg
- Iron Dosage: 15mg/kg

Methodology: Grouping

Negative Control

- 15 sample size
- Given sugar pill (placebo)
- Expected:
 - Normal Iron Levels (14-20g/dl)
 - No Seizure Occurrence

Positive Control

- 15 sample size
- 150 μ mol/kg Deferitritin dosage
- Expected:
 - Lowered Iron Levels (<12g/dl)
 - Seizure Occurrence signifigant

Experimental Group

- 15 sample size
- 150 μ mol/kg Deferitritin dosage
- 15mg/kg iron dosage
- Expected:
 - Before iron dosage, iron level <12g/dl
 - After iron dosage, iron level between 14-20 g/dl
 - Low seizure occurence

Methodology: Guidelines



Administration

- Deferitritin:
 - Gel capsule
 - 150 μ mol/kg, sterile water
- Iron:
 - table
 - 15mg/kg



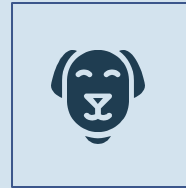
Post-Trial Period Results

- Every month after initial completion, CBC is conducted
- Seizure occurrence must be reported by owner and canine be brought in for CBC



Sample Collection

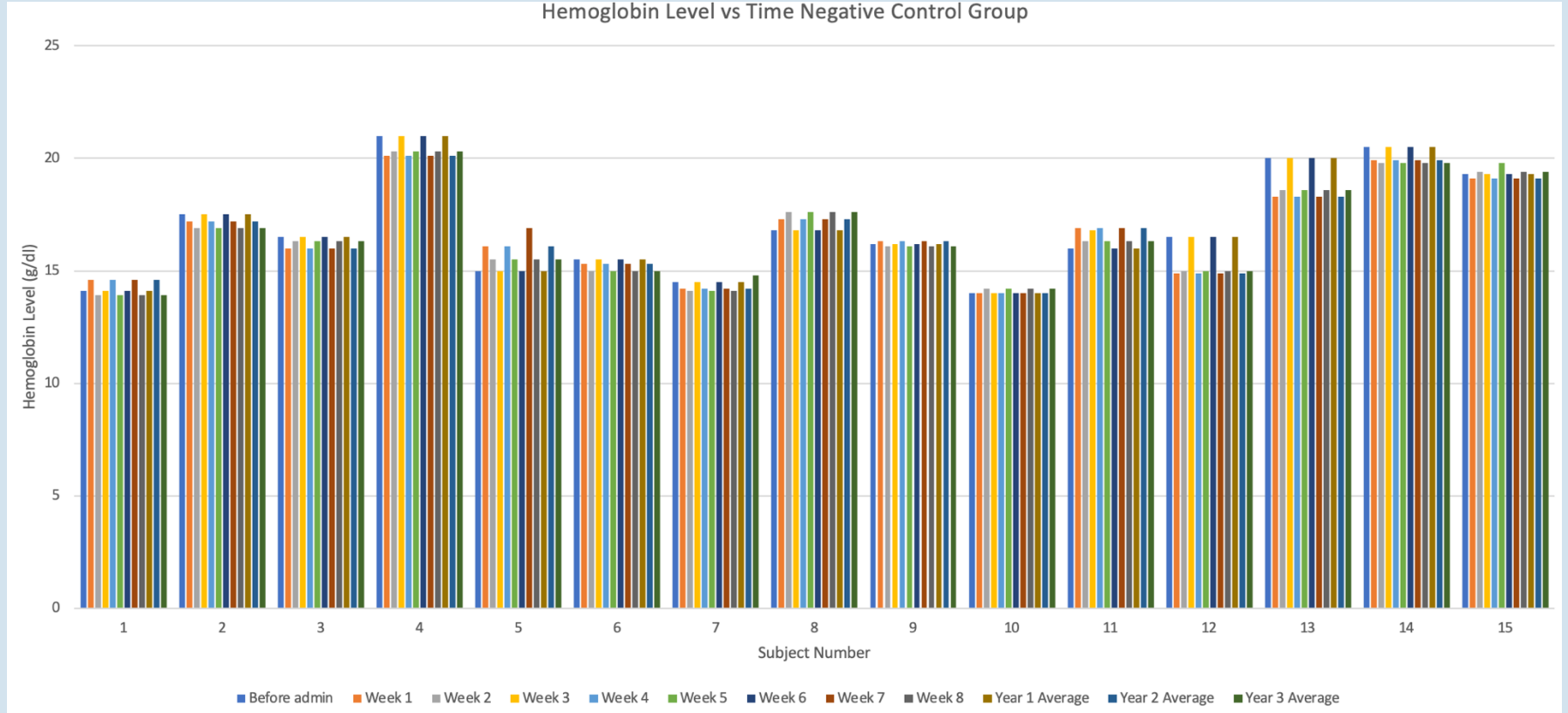
- Complete Blood Count
- Before Deferitin dosage, weekly during Deferitin dosage time period
- Before iron dosage, day after iron dosage, weekly after iron dosage for collection period



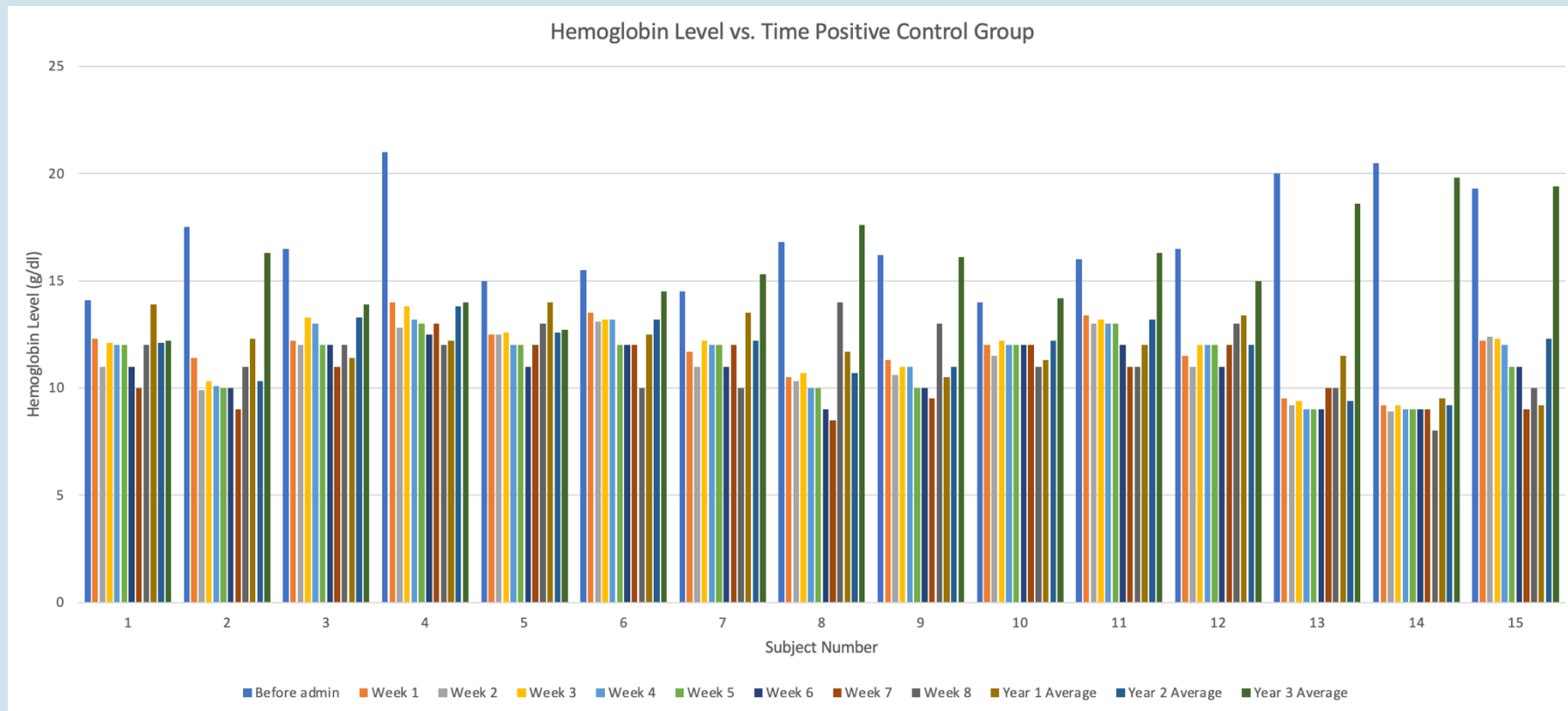
Result Evaluation

- Blind experiment:
 - Evaluator is not made aware of what group canine is in
- SPSS Statistical Software

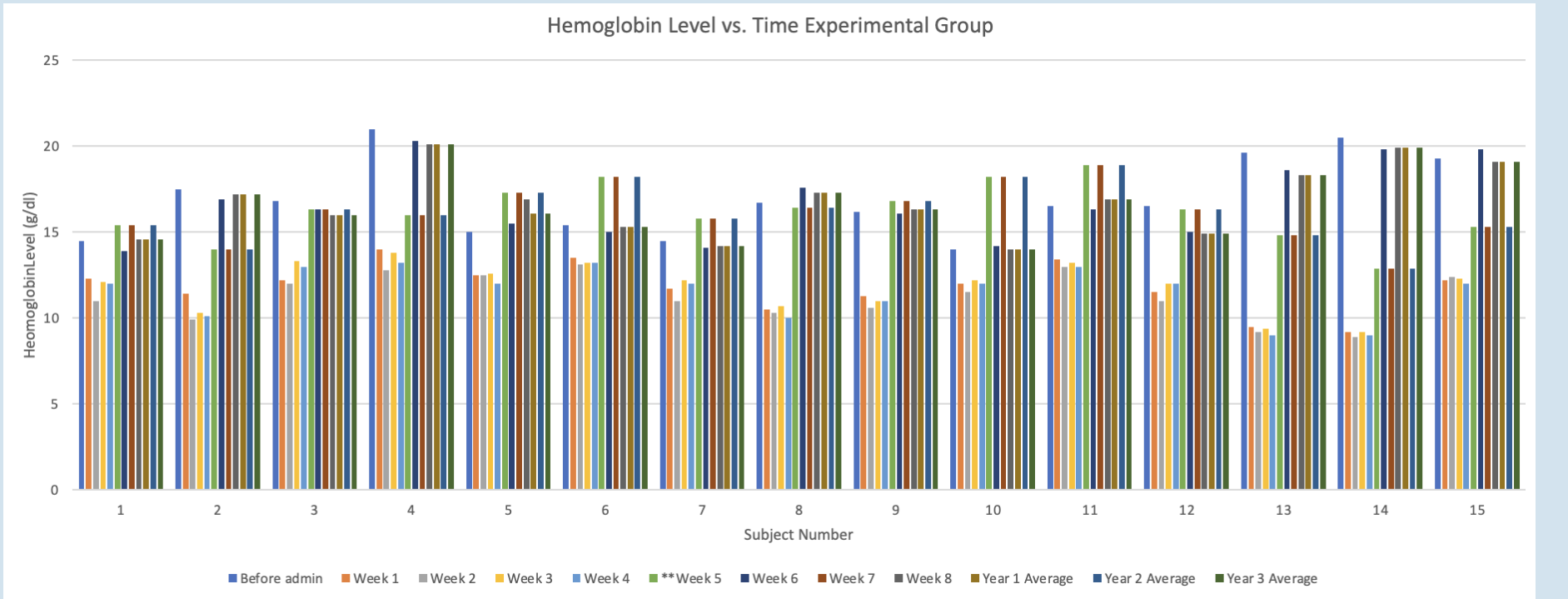
Expected Results: Negative Control



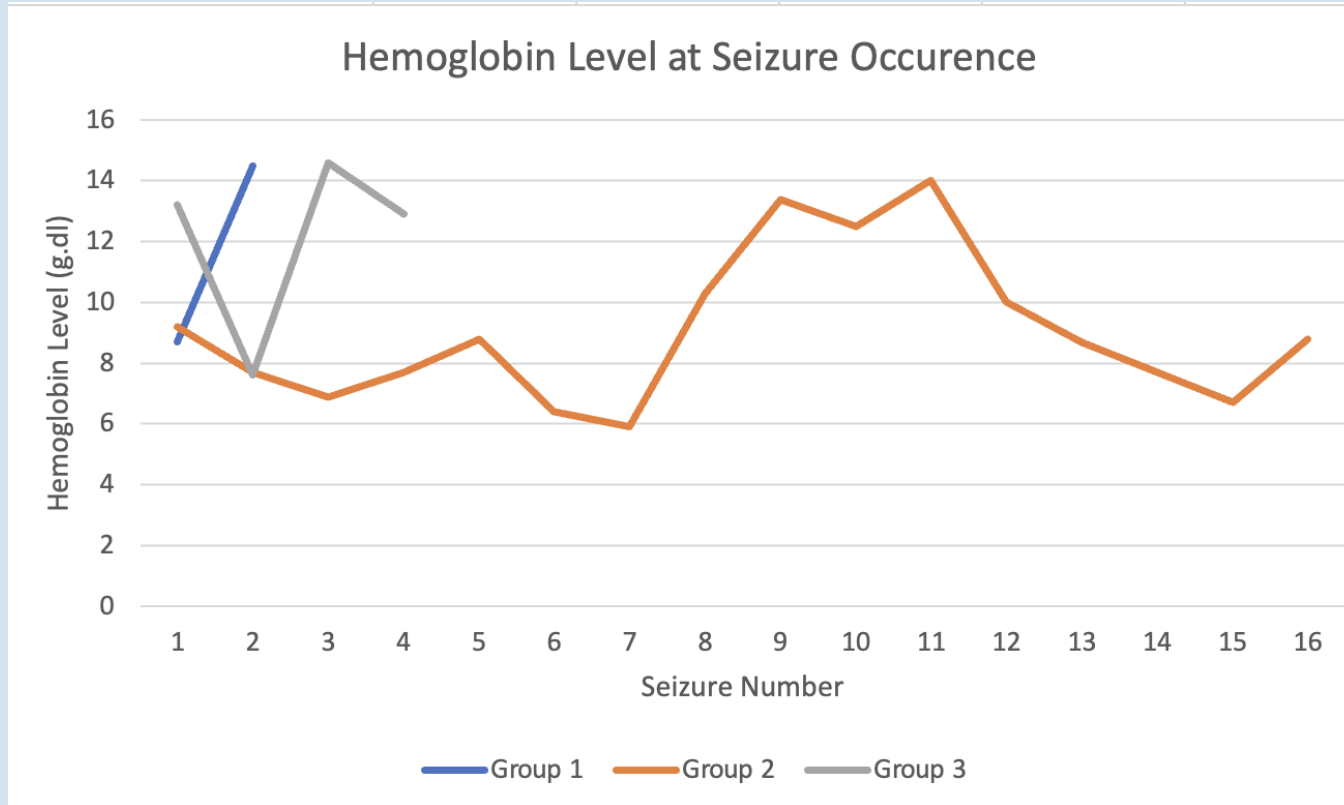
Expected Results: Positive Control



Expected Results: Experimental Group



Expected Results: Comparison



Discussion and Future Studies

Dosage

What is the best dosage of iron for prevention of post-operative epilepsy?

Sex

Should canines in heat or menstruating be treated with similar methods?

Administration

Does intravenous administration of iron differ from oral consumption in canines?

Feline

Could this study be conducted for the prevention of post-operative epilepsy in felines?

Post-Consumption

Will a combination of pre-operative and post-operative iron consumption have better results?

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Image Citations

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Does anyone have any questions?

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