Cornell University Veterinary Specialists
ADVANCED CARE + 24-HOUR EMERGENCY

CRITICAL CARE – YEAR IN REVIEW

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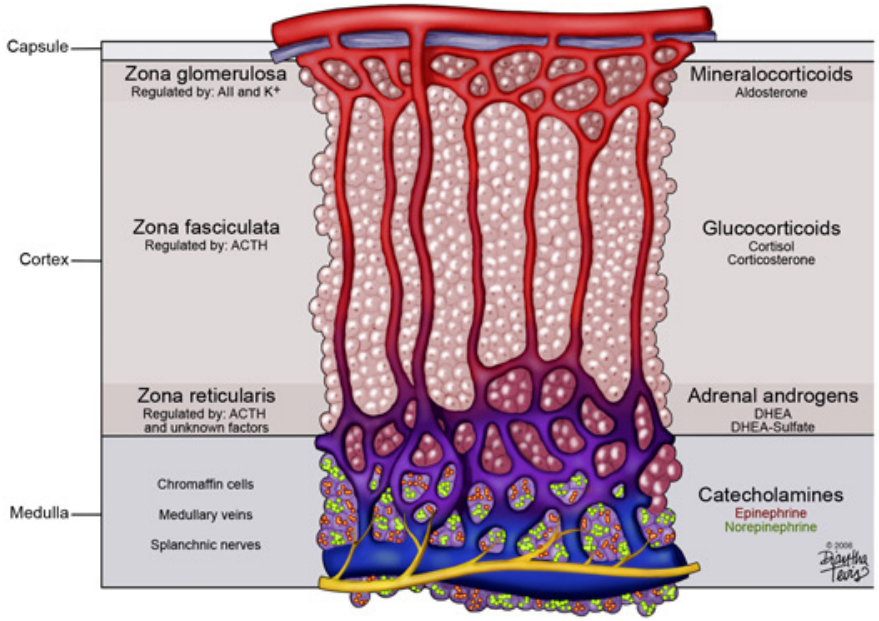
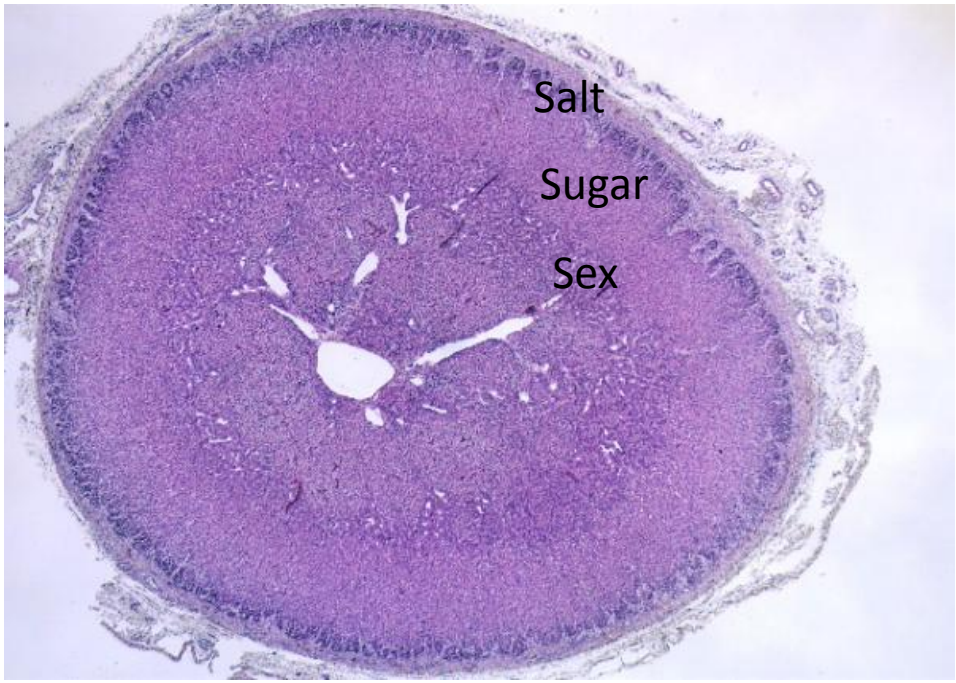
Hypoadrenocorticism –Addison's

- Disease of Adrenal glands





- Blois et al. JAVMA 2011
  - Multiple Endocrine Disease in Dogs- 35 dogs
  - Diabetes and Hyperadrenocorticism 20/35 (57.1%)
  - Hypoadrenocorticism and Hypothyroidism 8/35 (22.9%)
  - Diabetes and Hypothyroidism 10/35 (28.6%)
  - Mean of 14.1 months between diagnosis of 1st and 2nd endocrinopathy

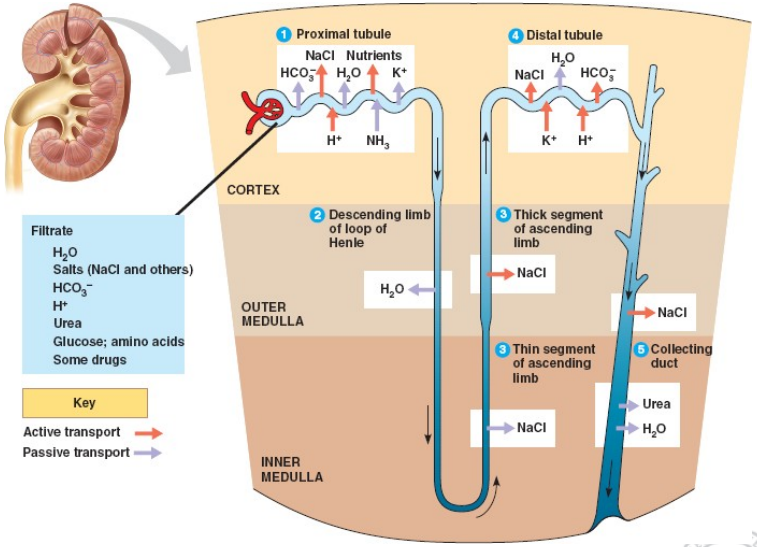
- Wenger et al. Vet Rec 2010
  - Adrenal in Ultrasound
  - Dogs with HA: left adrenal <3.2mm

- Messinger et al JVIM 2009
  - Ionized hypercalcemia in 109 dogs
  - Lymphoma 45%, Anal Sac Adenocarcinoma 3.7%, CRF 14.6%
  - Hypoadrenocorticism 5.5%
- Lennon et al. JAVMA 2007
  - Basal cortisol to rule out HA
  - <1ug/dL: 100%Sensitivity, 98.2% Specificity
  - >2ug/dL: unlikely HA
- Adler et al. JVIM 2007
  - Electrolytes abnormalities with HA
  - <27 Sensitivity

Sugar VS Salt

- Glucocorticoid Deficiency
  - Hypoglycemia
  - Lack of stress leukogram
  - GI signs
    - Vomiting,
    - diarrhea,
    - GI bleeding,
    - Abdominal pain
  - Weight loss
  - Anemia
  - Hypotension

- Mineralocorticoid Deficiency
  - Hyperkalemia
  - Hyponatremia
  - Metabolic acidosis
  - Hypovolemia/Shock



Abnormal Na+ K+ Ratio

- Hypoadrenocorticism
- Chylous effusion
- Pyometra
- Renal Failure
- Heart disease/failure
- Pregnancy
- Gastrointestinal disease
- EDTA contamination

White Blood Cell Count and the Sodium to Potassium Ratio to Screen for Hypoadrenocorticism in Dogs
Seth et al. JVIM 2011

- Veterinary Hospital UPenn
- January 2005-November 2009
- Retrospective
- Control dogs: 110
  - hospitalized, IVF, full bloodwork, baseline cortisol
- Dogs with Hypoadrenocorticism: 53
  - hospitalized, IVF, full bloodwork, ACTH stim

White Blood Cell Count and the Sodium to Potassium Ratio to Screen for Hypoadrenocorticism in Dogs
Seth et al. JVIM 2011

	Normal	Dogs with HA	Control Dogs
Na:K ratio		19.7 (12.0-39.4)	33.1 (20.5-61.6)
HCT (%)	40.3-60.3	46.1 (20.1-68.8)	42.2 (14.1-61.5)
Neutrophils (K/uL)	3.1-14.6	7.75 (2.77-25.90)	9.87 (0.68-53.93)
Lymphocytes (K/uL)	0.9-5.5	2.38 (0.80-8.20)	1.07 (0-6.00)
Eosinophils (K/uL)	0-1.6	0.57 (0-4.00)	0.12 (0-7.00)
Neut:Lym ratio		3.00 (0.76-14.59)	9.51 (1.23-95.15)

Table 3. Sensitivity and specificity of the Na : K ratio or lymphocyte count for predicting hypoadrenocorticism (HA) in dogs with a clinical suspicion of HA.

Na : K ratio	**Sensitivity, %**	**Specificity, %**
<40	100	15
<35	94	35
<28	74	84
<27	70	94
<24	62	96
<20	51	100
Lymphocyte count (cells $\times 10^3/\mu L$)		
>0.75	100	35
>1.0	92	46
>1.2	89	56
>1.4	87	69
>1.6	79	77
>1.8	64	83
>2.0	58	85
>2.2	57	89
>2.4	49	92
>5.0	19	99
>6.0	9	100

Seth et Al, JVIM 2011

CPA - Prognosis

- Kass et al., JVECC, 1992
  - All CPA secondary to G.A. or drug administration
  - One-week survival rate $\leq$ 3% in dogs and cats
- Wingfield et al., JAVMA, 1992
  - 265 cases, 200 dogs/ 65 cats,
  - respiratory arrest or CPA while hospitalized
  - CPA: 4.1% of dogs discharged
    9.6% of cats discharged
  - No neurological outcome reported

CPA - Prognosis

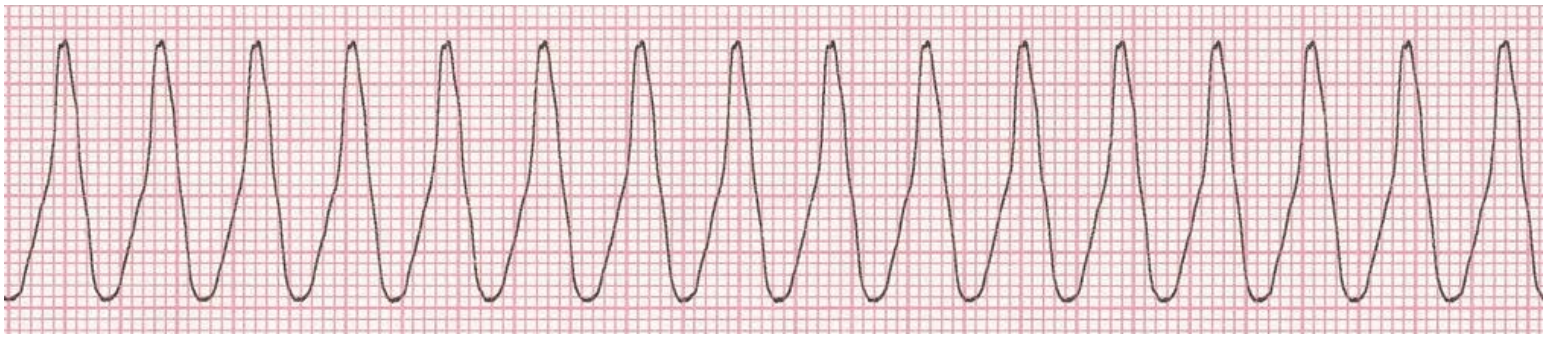
- Waldrop et al., JVECC, 2004
  - 18 successful CPCR in 6 years (15 dogs, 3 cats)
  - 10/18 = anesthesia related
  - 4 patients required PPV for > 7 hours
  - Hospitalization: 5.1 ± 3.7 days
  - 2/18 = discharged with neurologic deficit
    - Blindness, dementia, non-ambulatory

CPA - Prognosis

- Hofmeister et al., JAVMA, 2009
  - 161 dogs and 43 cats with CPA
  - 56% dogs and 44% cats had successful CPCR
    - 6% survived to discharge (12/204)
  - 19 CPA while anesthetized
    - 9/19 survived to discharge

CPA in People - Prognosis

- Out of hospital CPA: 2-8% discharged
  - 97.5%: mild to moderate neurological deficit
  - 2%: severe deficit
- In hospital CPA: 14-20% discharged
- V-fib/V-tach: 10-15 X more likely to survive



Randomized, Blinded Comparison of Epinephrine and Vasopressin for Treatement of Naturally Occuring CPA in Dogs
Buckley et al. JVIM 2011

- Tufts University
- July 2008-May 2010
- 60 dogs
  - 31 dogs –Epinephrine
  - 29 dogs –Vasopressin
- Comparison of
  - Return of Spontaneous Circulation
  - Neurological scoring
  - Discharge from Hospital

Advanced Life Support: Epinephrine

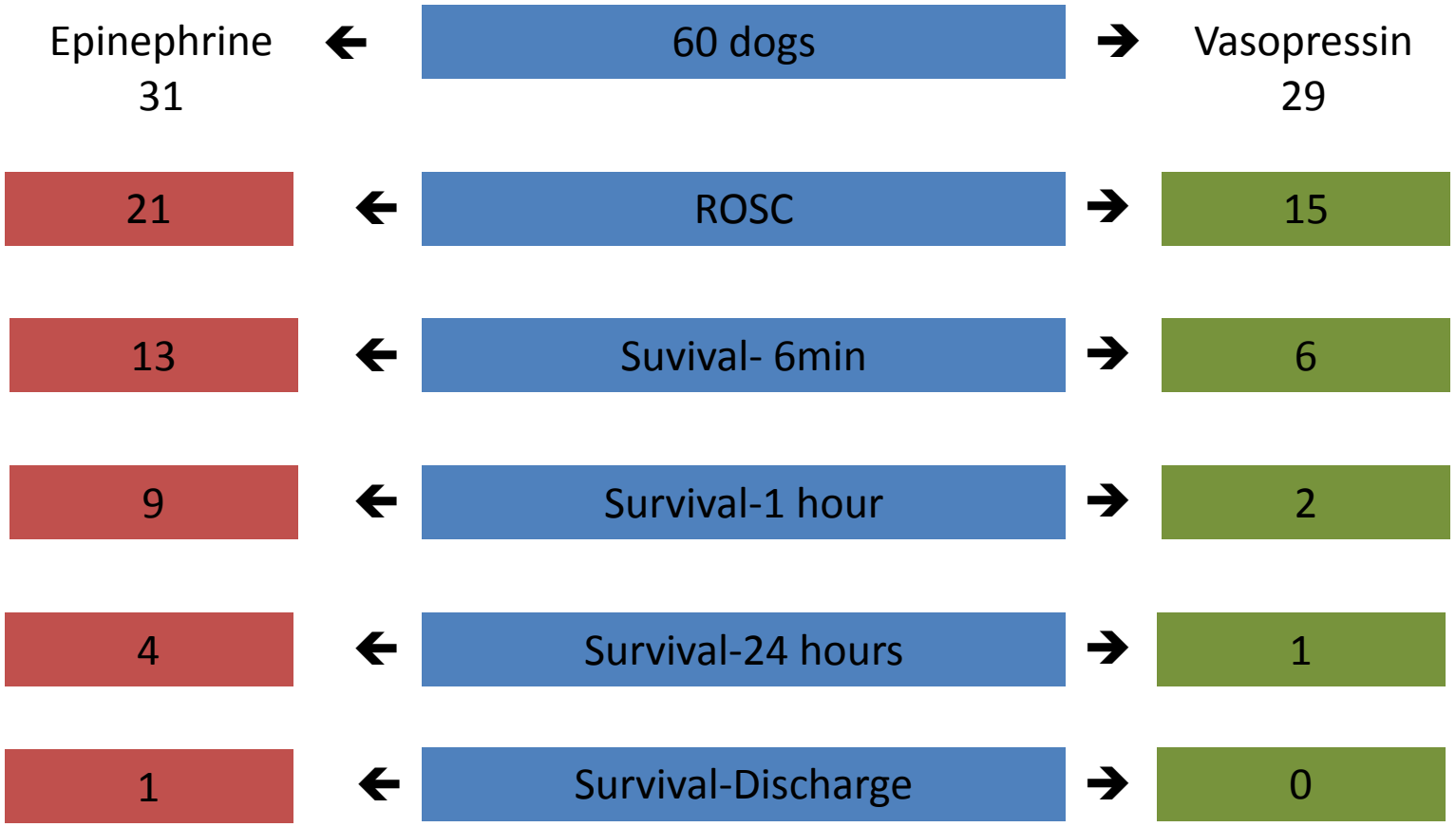
- α_1-adrenergic
- Vasoconstriction
- ↑ MAP, Diastolic pressure, Cerebral and Myocardial Perfusion Pressure

- Low dose (0.01mg/kg)
  - 0.05ml / 10lbs
- Repeat every 3-5 minutes

Advanced Life Support: Vasopressin

- V1-receptor effects
- Non-adrenergic vasoconstriction
- Effective in acidotic environment
- Beneficial? Less deleterious cardiac effect
- 0.8 u/kg once
  - 0.2ml / 10lbs

Randomized, Blinded Comparison of Epinephrine and Vasopressin for Treatement of Naturally Occuring CPA in Dogs
Buckley et al. JVIM 2011



Randomized, Blinded Comparison of Epinephrine and Vasopressin for Treatement of Naturally Occuring CPA in Dogs
Buckley et al. JVIM 2011

- Epinephrine: survival advantage at 1 hour

- Study did not assess difference between subgroups
- Vasopressin group -> twice more DOA
- Epinephrine goup -> 30% more ICU arrest
- Epinephrine group -> 3 X more sinus bradycardia

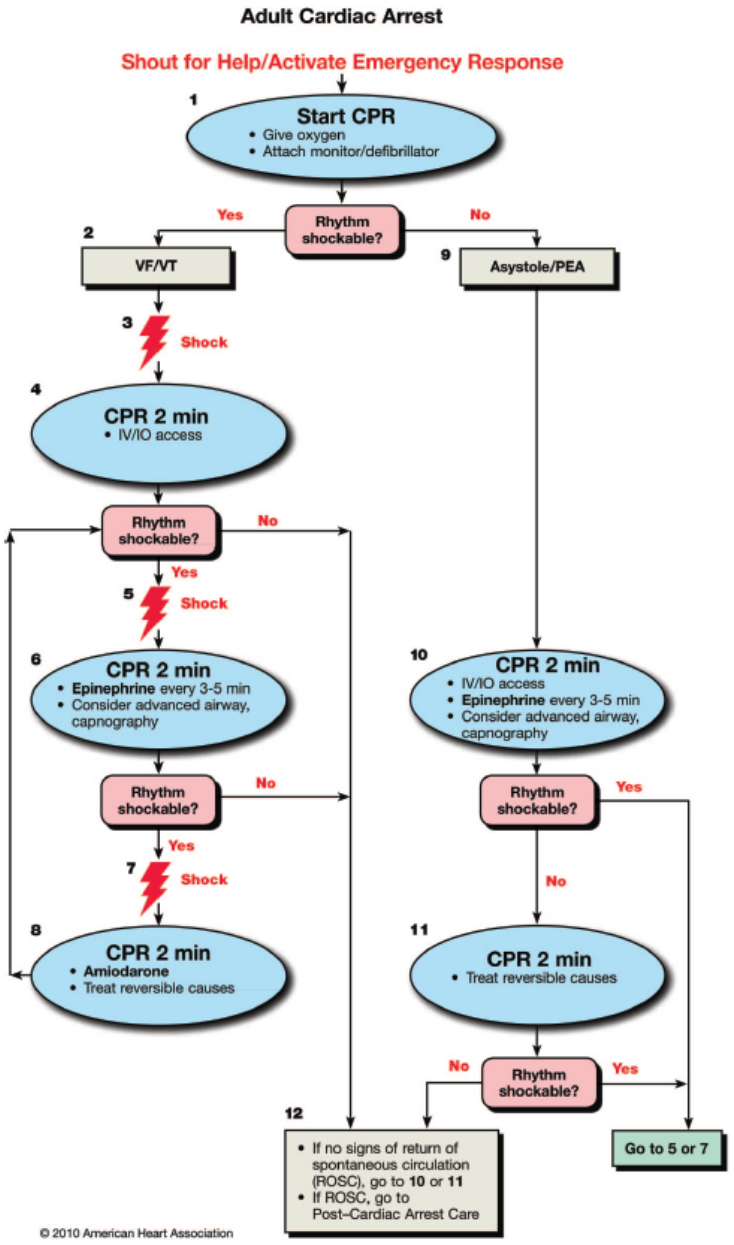


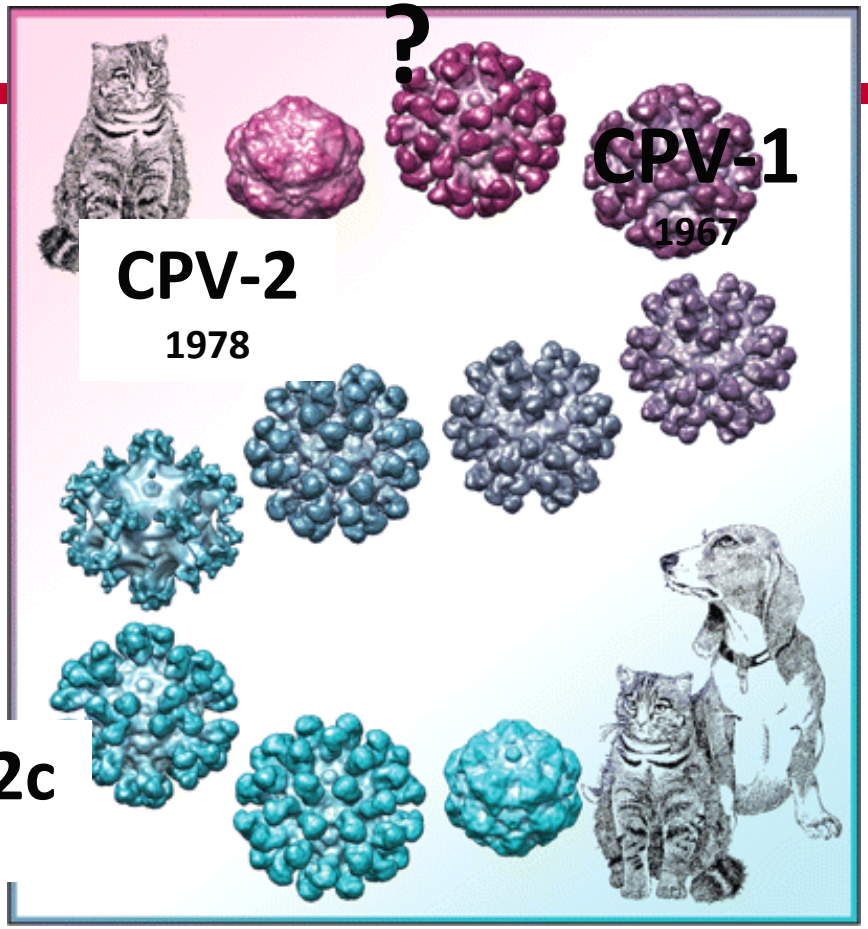
Figure 1. ACLS Cardiac Arrest Algorithm.

Circulation, 2010

RECOVER CPR Initiative

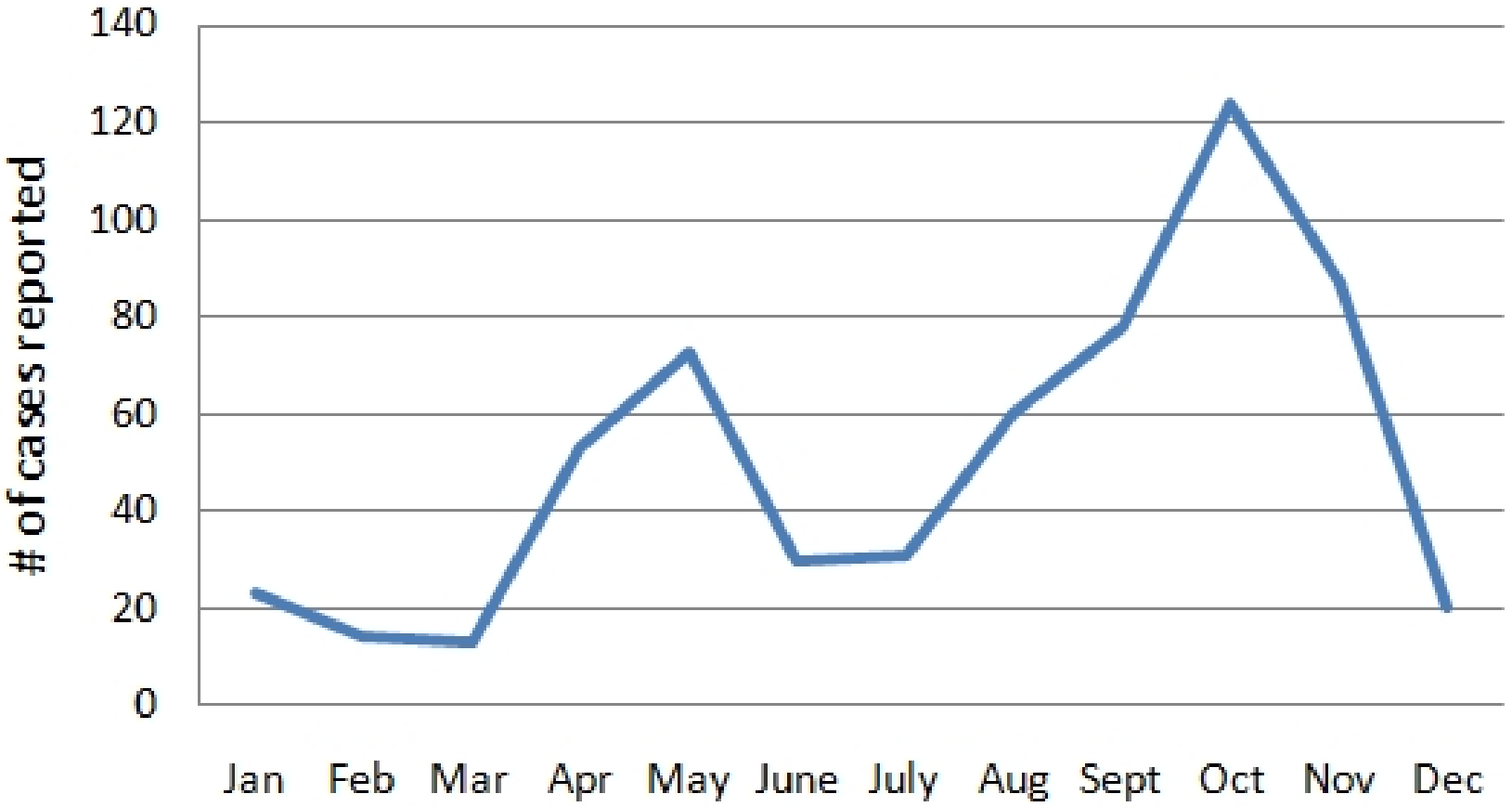
- Reassessment Campaign on Veterinary Resuscitation
- J Vet Emerg Crit Care June 2012
- www.VECCS.org
- 5 Different RECOVER domains
  - Preparedness & Prevention
  - Basic Life Support
  - Advanced Life Support
  - Monitoring
  - Post-Cardiac Arrest Care

- Vasopressin Inj. 20u/ml
  - Cost/ml: $2.00
- Epinephrine Inj. 1mg/ml
  - Cost/ml: $0.34)
- For a 10kg patient
  - Vasopressin: $0.8
  - Epinephrine: $0.034


?
CPV-1
1967
CPV-2
1978
CPV-2a
1980
CPV-2b
1984
CPV-2c
2000

Seasonality of Parvo in Dogs

Includes all cases reported 2007-2011 (as of 2/15/11)

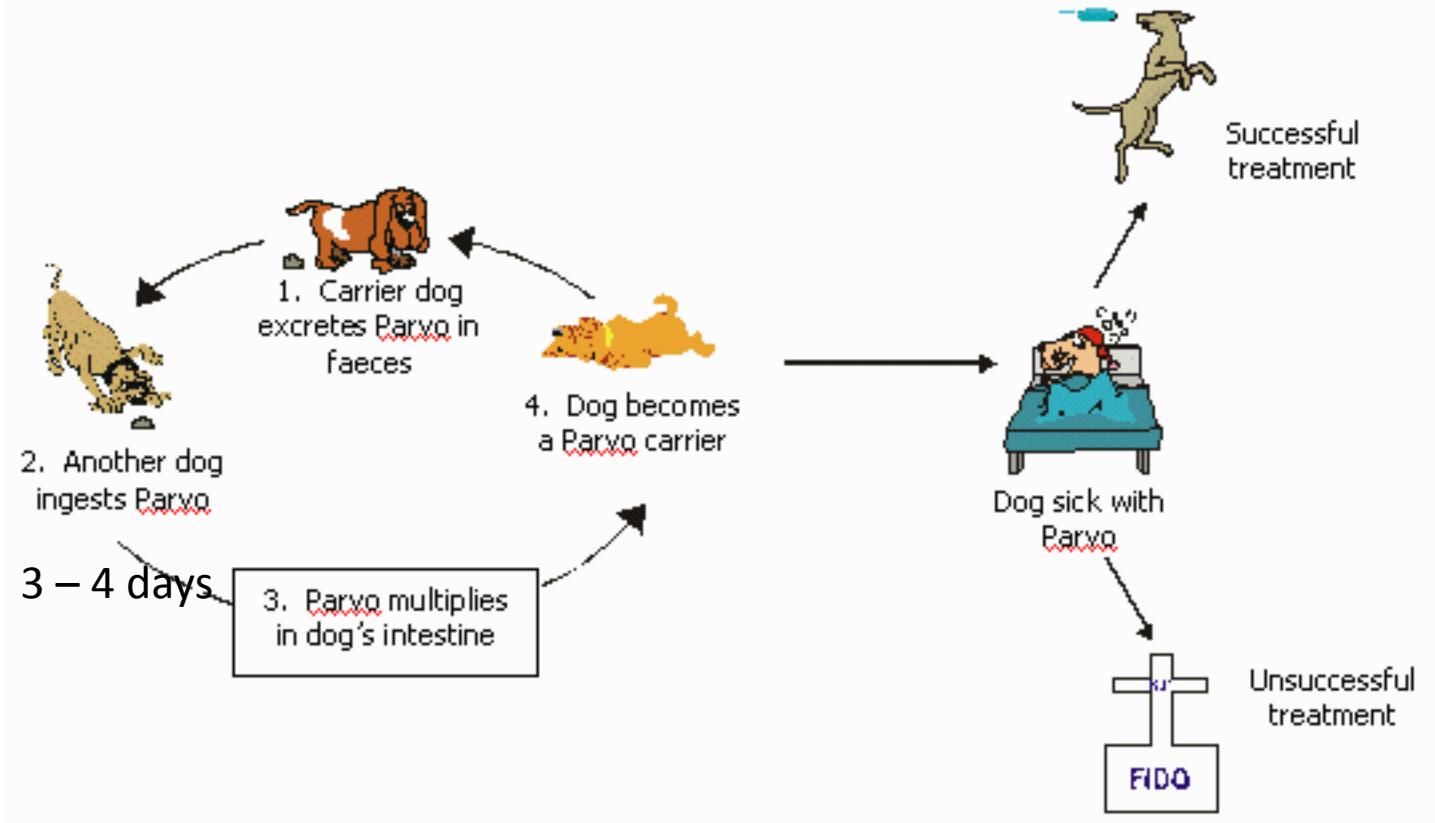


Parvo infections appear to occur most commonly in the spring and fall.

2/15/11 EB

County of Los Angeles Public Health
Veterinary Public Health & Rabies Control

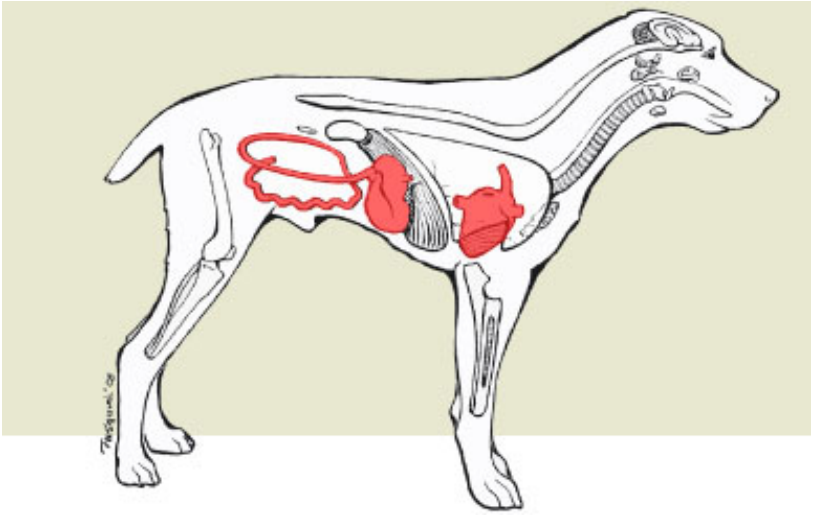
Gemstone Rottweiler



http://gemstonerottweilers.com/parvo.htm

CPV-2a,b,c

- Highly virulent
- 6 wks – 6 months
- $t_{1/2}$ maternal antibody 10 days
- **Vaccination**
- **Diagnostics**
- **Treatment**



Vaccination

Canine parvovirus Type 2 vaccine protects against virulent challenge with Type 2c virus. Vet Microbiol 128(1-2):48-55, 2008.

- 6 vaccinated, 6 controls
- Novibac Intervet Vaccination 8 wks, then 3 wks later
- Oral CPV-2c
- No shedding or clinical signs in vaccinated dogs
- All control dogs developed clinical signs of CPV
- *** Controversial***
  - CPV-2c
  - Worse disease
  - Infects properly vaccinated dogs

Diagnostics

Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- Objectives:
  - Prevalence of CPV strains in dogs with enteritis
  - Compare severity of clinical signs and disease outcomes
  - Sensitivity of ELISA to detect CPV-2b and -2c
  - Outcome home vs. hospitalization therapy
  - Physical or diagnostic prognostic indicators
  - CPV antigen or DNA detection via ELISA* or PCR from pharyngeal swabs

*** IDEXX Parvovirus Fecal Antigen ELISA**

Diagnostics

Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- Materials and Methods:
  - Dogs with history or clinical signs consistent with CPV Aug 2008 – June 2009
  - Informed consent, and compliance with Cornell University IACUC
  - History
  - Fecal swab CPV ELISA
  - Stored fecal sample within 24 hours for CPV ELISA and PCR
  - Pharyngeal swabs from a subset of patients later in study
  - Treatment based on clinician preference, clinical signs, and client $$$

Diagnostics

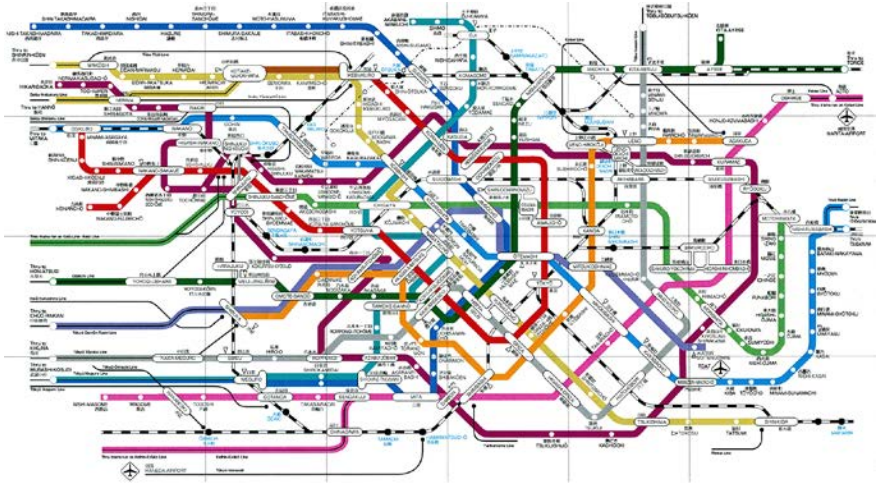
Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- Clinical Severity Score
  - 2 independent reviewers
  - 5 point scale
  - Duration of illness
  - Attitude
  - Ability to ambulate
  - Hydration status
  - Rectal temperature at presentation

Diagnostics

Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- PCR and Genetic Testing
  - ELISA on initial fecal sample/swab
  - PCR and ELISA on 2nd sample obtained within 24 hours
- Statistical Analysis



Diagnostics

Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- Results
  - 72 dogs
  - 53/72 tested positive on initial ELISA
  - 42/53 had 2nd samples obtained within 24 hours of 1st
  - 16/53 had pharyngeal swabs – CPV ELISA and PCR
  - 56/72 positive ELISA or PCR
  - Age range 1 – 36 months
  - Chihuahuas and Pit Bull
  - 25 female , 3 FS; 26 male, 2MN
  - 64.3% had received one vaccination

Diagnostics

Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- Results
  - Age range 1 – 36 months
  - Chihuahuas and Pit Bull
  - 25 female , 3 FS; 26 male, 2MN
  - 64.3% had received one vaccination
  - Median hospitalization 4 days
  - Outcome for 42 of 56 dogs
    - 71.4% recovered
    - 8 euthanized immediately
    - 4 died at home
    - 4 euthanized from worsening despite maximal care
    - 4 euthanized due to financial limitations
    - 14 lost to follow-up

Diagnostics

Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- Results
  - 33 positive by PCR: 9 CPV-2b, and 24 CPV-2c
  - Positive pharyngeal swabs
  - No difference among CPV-2b vs. – 2c infection
    - Median age
    - Infection with either strain if received one vaccination
    - Severity of signs
    - Median leukocyte count
    - Clinical severity scores
    - Length of hospitalization
    - Recovery (either at home or in hospital)

Diagnostics

Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- Sensitivity and Specificity
  - All ELISA positive samples also positive by PCR
  - 6 ELISA negative samples were positive by PCR
  - ELISA: 81.8% sensitivity (probability of true positive)
  - PCR: 100% for both CPV-2b and -2c
  - 100% pharyngeal swabs positive

Diagnostics

Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- Prognostic Variables
- No difference in:
  - Age/Breed/Gender
  - Albumin/Glucose/Leukocyte Count
  - Abdominal pain
  - Vomiting/Diarrhea/Inappetance/Ptyalism
  - Administration of FFP
- Significant: dehydration
  - 10/10 not dehydrated survived
  - 20/31 of dehydrated survived

Diagnostics

Effect of canine parvovirus strain variants on diagnostic tests results and clinical management of enteritis in dogs. JAVMA 241(1):66-72, 2012.

- Conclusions
  - CPV-2c more prevalent than -2b in study population
  - No difference in disease severity or outcome
  - ELISA successful at detection of CPV-2b and -2c
  - Dogs treated at home as likely to survive vs. hospitalization
  - Dehydrated dogs less likely to recover
  - Possible to detect oropharyngeal shedding before fecal shedding

Ancillary Therapies

Clinical evaluation of a single dose of immune plasma for treatment of canine parvovirus infection. JAVMA 240(6):700-704, 2012.

- Background
  - 90% mortality if left untreated
  - Passive immunotherapy for *Clostridium tetani* and *C. difficile*
  - Improved survival, decreased V/D if administered immediately after CPV inoculation
  - Concentrated canine IgG decreased hospitalization in CPV

Ancillary Therapies

Clinical evaluation of a single dose of immune plasma for treatment of canine parvovirus infection. JAVMA 240(6):700-704, 2012.

- Objective
  - Evaluate efficacy of single-dose of CPV-immune plasma as adjunct therapy
  - Reduce viral load?
  - Reduce time to hematologic recovery?
  - Reduce duration of hospitalization?

Ancillary Therapies

Clinical evaluation of a single dose of immune plasma for treatment of canine parvovirus infection. JAVMA 240(6):700-704, 2012.

- Materials and Methods
  - Client-owned dogs with CPV between March 2008 and September 2009, IACUC approval
  - Positive CPV ELISA
  - Clinical signs (V/D, anorexia)
  - < 1 yr of age
  - No vaccine within 1 week of admission

Ancillary Therapies

Clinical evaluation of a single dose of immune plasma for treatment of canine parvovirus infection. JAVMA 240(6):700-704, 2012.

- Materials and Methods
  - Statistics to calculate number of animals needed
  - Pooled antibody rich CPV plasma from recovered patients (mean 1:7000 titers)
  - Double-blinded placebo controlled study: CPV plasma vs. placebo
  - Supportive care treatment
  - PCV/TS, CBC, viremia, Temp, % Wt change , Fever, V/D/regurg, $$
  - Quantitative viral PCR

Ancillary Therapies

Clinical evaluation of a single dose of immune plasma for treatment of canine parvovirus infection. JAVMA 240(6):700-704, 2012.

- Results
  - 14 dogs enrolled, (7 plasma/7 control)
  - 1 dog died 4 days into therapy (control)
  - No significant difference in:
    - **Neutrophil or monocyte counts**
    - **Viral load**
    - **Days hospitalization**
    - **Weight loss**
    - **$$$**

Ancillary Therapies

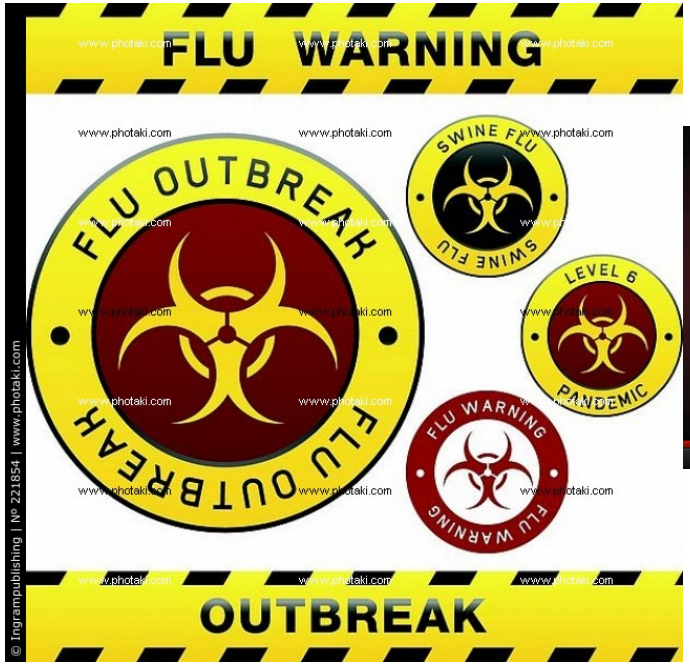
Use of oseltamivir in the treatment of canine parvoviral enteritis. JVECC 20(1):132-142, 2010.

- Prospective randomized placebo-controlled study
- 35 dogs (19 treatment/16 control)
- Standard therapy for CPV +/- Oseltamivir
- No significant difference:
  - Age/gender/breed
  - Clinical severity score
  - Duration of clinical signs/vaccination status
  - Need for colloids/antiemetics
  - Days hospitalization
  - Survival
- Significant changes
  - Weight gain
  - Leukocyte count

Ancillary Therapies

Use of oseltamivir in the treatment of canine parvoviral enteritis. JVECC 20(1):132-142, 2010.

- Significance
  - No adverse effects of treatment with oseltamivir
  - No significant difference in outcome
  - $$$$ Cost of therapy
  - Ethical dilemma?



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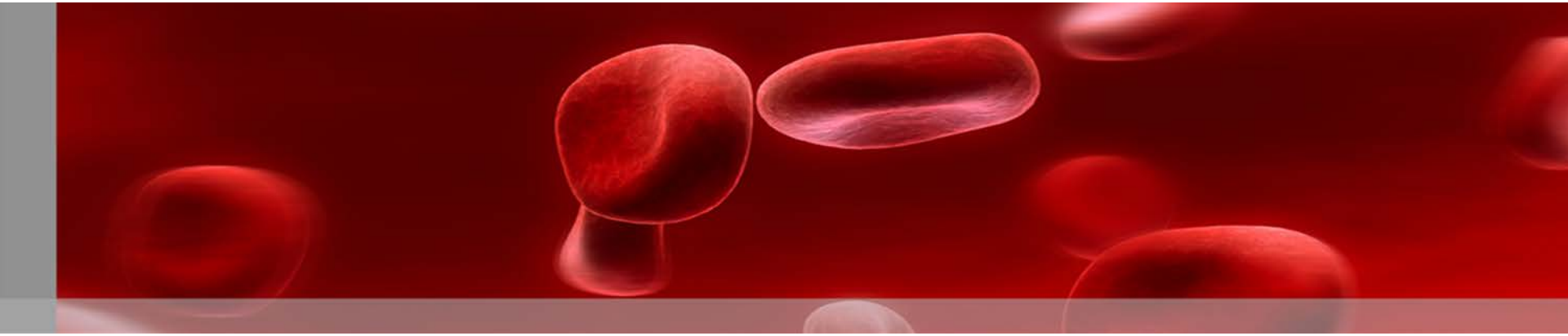
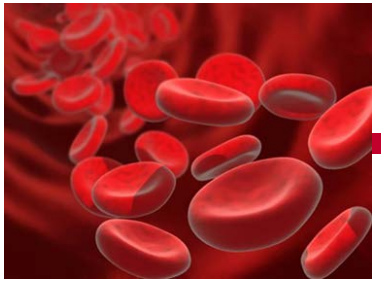
Epsilon Aminocaproic Acid (EACA) - Postoperative Bleeding in Greyhounds



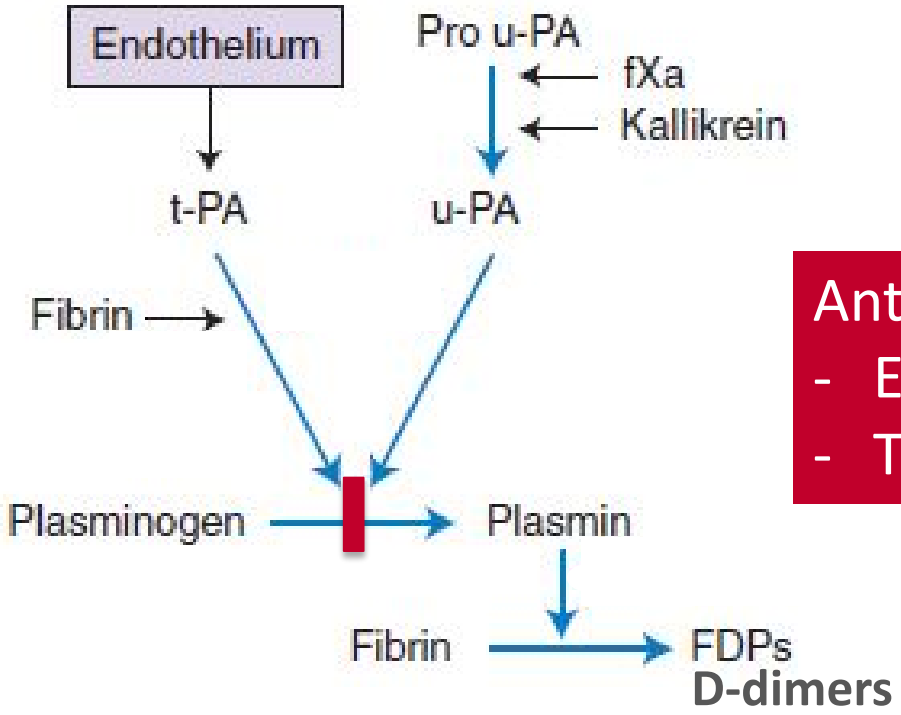
Greyhounds and Bleeding

- > 130,000 RRGs in USA
- High prevalence of postop bleeding
  - 26% following gonadectomy
- Delayed bleeding - within 48-72 hr
- Pathogenesis?
  - Usual coag parameters wnl
  - ↓antiplasmin, ↓antithrombin

⇨ defective fibrinolysis/endothelial dysfunction



FIBRINOLYSIS



Antifibrinolytic agents
- EACA
- Tranexamic acid

J Vet Emerg Crit Care (San Antonio). 2012 Jun;22(3):332-40. doi: 10.1111/j.1476-4431.2012.00735.x. Epub 2012 May 21.

Retrospective evaluation of the effectiveness of epsilon aminocaproic acid for the prevention of postamputation bleeding in retired racing Greyhounds with appendicular bone tumors: 46 cases (2003-2008).

- Retrospective

- 46 RRGs - limb amputation for OSA (2003-2008)
  - 6 dogs – 0 preemptive Rx
  - 15 dogs – FFP at induction
  - 25 dogs – EACA postoperatively

- EACA - 500-1,000 mg (15-40 mg/kg) IV postop diluted in 15 ml 0.9% NaCl over 30 mins
  - 500-1,000 mg PO q8 hr x 5 days

J Vet Emerg Crit Care (San Antonio). 2012 Jun;22(3):332-40. doi: 10.1111/j.1476-4431.2012.00735.x. Epub 2012 May 21.

Retrospective evaluation of the effectiveness of epsilon aminocaproic acid for the prevention of postamputation bleeding in retired racing Greyhounds with appendicular bone tumors: 46 cases (2003-2008).

Postop bleeding

- 13/46 (28%)
- Started 36-48 hrs after surgery
- Widespread within hours; requiring transfusion
- EACA dogs - 4/25 (16%)

  Other dogs - 9/21 (62%)

J Vet Emerg Crit Care (San Antonio). 2012 Jun;22(3):332-40. doi: 10.1111/j.1476-4431.2012.00735.x. Epub 2012 May 21.

Retrospective evaluation of the effectiveness of epsilon aminocaproic acid for the prevention of postamputation bleeding in retired racing Greyhounds with appendicular bone tumors: 46 cases (2003-2008).

- Dogs that did not receive EACA were 5.7 X more likely to bleed
- Bleeding ⟶ 50% ↑ hospital stay
  ≈ 2X cost
- Cost of EACA protocol = $45
- No adverse effects of EACA

Vet Surg. 2012 Jun 19. doi: 10.1111/j.1532-950X.2012.00965.x. [Epub ahead of print]

Epsilon Aminocaproic Acid for the Prevention of Delayed Postoperative Bleeding in Retired Racing Greyhounds Undergoing Gonadectomy.

- Prospective, controlled
- 100 RRGs - OHE/neuter
  - 50 - EACA - 500mg q8h X 3 days
  - 50 - placebo
- Coagulation testing
  - preop, 24h, 48h, 72h
  - PT, aPTT, plat, fibrinogen, D-dimer, antiplasmin, plasminogen
  - Thromboelastography (TEG)
- Bleeding ranked on scale 0-4

Vet Surg. 2012 Jun 19. doi: 10.1111/j.1532-950X.2012.00965.x. [Epub ahead of print]

Epsilon Aminocaproic Acid for the Prevention of Delayed Postoperative Bleeding in Retired Racing Greyhounds Undergoing Gonadectomy.

Postop bleeding:

- Delayed 36-48 hr
- Placebo: 15/50 (30%)

  EACA: 5/50 (10%)
- Odds of bleeding ↑ 19% for 1 kg ↑ BW

Coag testing:

TEG - EACA dogs became “hypercoagulable”

Vet Surg. 2012 Jun 19. doi: 10.1111/j.1532-950X.2012.00965.x. [Epub ahead of print]

Epsilon Aminocaproic Acid for the Prevention of Delayed Postoperative Bleeding in Retired Racing Greyhounds Undergoing Gonadectomy.

- EACA ⇨ ↓ postop bleeding by ↑ clot strength

- Hyperfibrinolysis suggested, but
  - not confirmed by TEG
  - findings in people (D-dimers, fibrinogen) not seen in dogs

EACA - Dogs

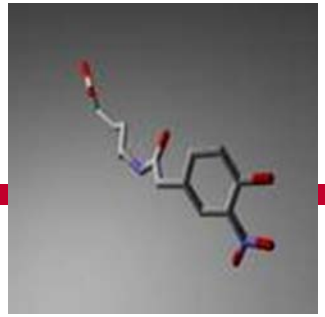
Indicated preemptively to prevent delayed postoperative bleeding in Greyhounds.

- Potential to reduce transfusion need, hospitalization, costs
- Safety profile
- Inexpensive

Dosing protocol?

15-40 mg/kg IV/PO q8h 3-5 days

Other Indications?



- Hyperfibrinolysis
  - 10% of hemodynamically unstable, bleeding human patients
  - Poor prognostic indicator
  - Improved outcomes - tranexamic acid (CRASH-2)
- Universal prohemostatic agent
  - Surgery – CV, spinal, orthopedic, trauma
  - Hemophiliacs

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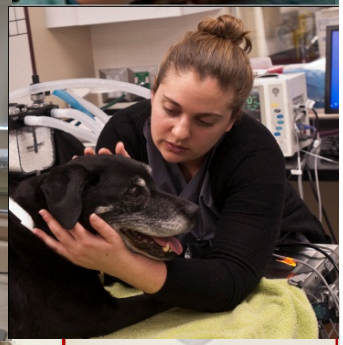
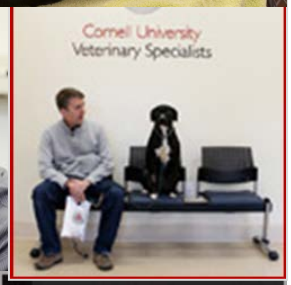
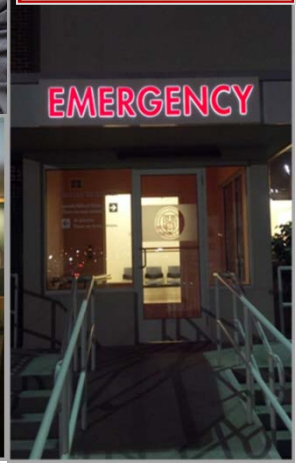


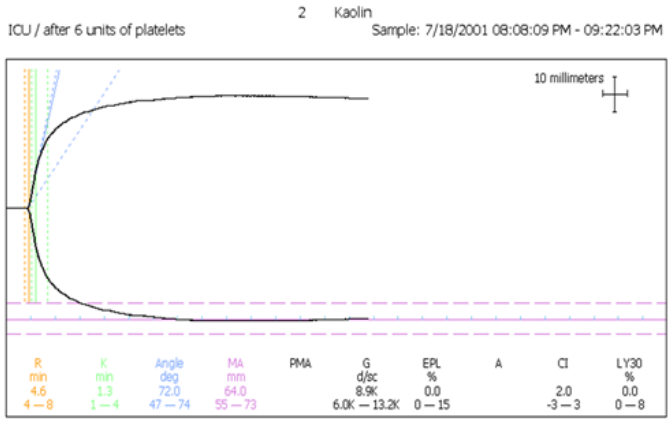


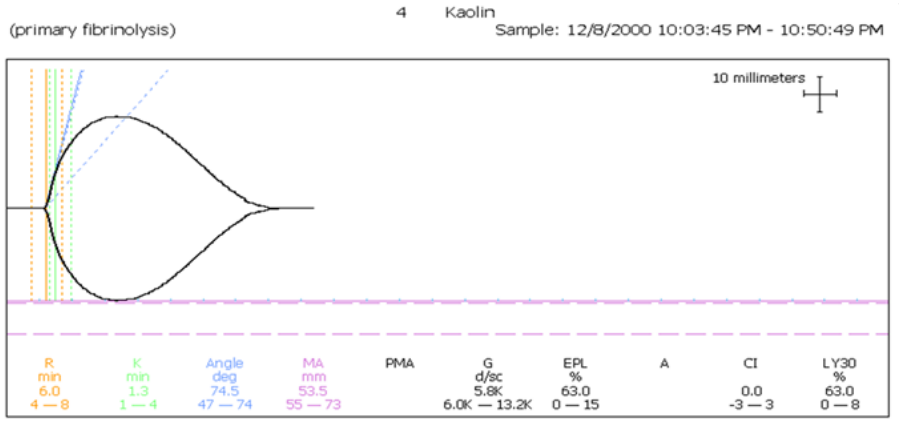



QUESTIONS?

Hyperfibrinolysis

- TEG





- ↑ D-dimer, ↓ fibrinogen = suggestive
- Testing normal, or fails to correct with *appropriate* therapy