*Dove*Lewis®

Third Thursday Rounds

January 21, 2021

Use of Immunosuppressant Therapy in Dogs and Cats

Presented by
Ladan Mohammad-Zadeh
DVM, DACVECC

DoveLewis

Third Thursday Rounds

Virtual Third Thursday: Attendee FAQ's

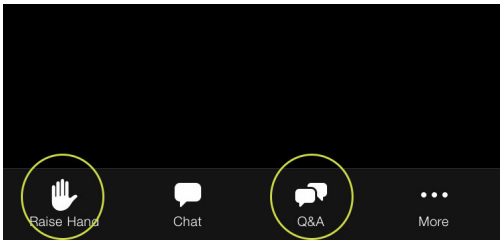
Do I need to create my own Zoom account to attend?
No. You can access the webinar through the link in your confirmation email. Click the link that says, "Click Here to Join" at the time of the lecture.

Is there someone to help if I have trouble accessing the lecture?
Yes. Please reach us at contact@atdove.org if you're experiencing difficulties joining the meeting. During the lecture, you can use the "Raise Hand" function and someone will be able to help you.

Is attendance tracked?
Yes. As you register for the Zoom meeting, you will be asked to enter your information. Attendance is tracked for RACE records.

Is this lecture RACE approved?
Yes. This lecture is RACE-Approved for one Interactive-Distance CE credit. You will receive an emailed certificate of attendance within one business day after the event.

Will I be able to ask questions?
Yes. If you have questions during the lecture, please use the Q&A function to submit your question. We will save questions for the end of the lecture.



Will I be able to talk?
No. All attendees will be in listen-only mode. If you have a question or need help, the Q&A or Raise Hand function.

Will the presenter or other attendees be able to see me?
No. All attendees will only have the capability to listen to the presenter.

How will I get my certificate?
You must register by using the Zoom link to prove attendance. You will receive an emailed certificate of attendance within one business day after the event.

Do I have to answer the poll questions?
No. The poll questions are optional, but we encourage you to try!

Can I record the lecture?
No. The lecture will only be recorded by DoveLewis, and will likely be available on atdove.org at a later date.

For more support, please email *contact@dovelewis.org*

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Lecture Notes

Use of Immunosuppressant Therapy in Dogs and Cats

Outline

- Importance and consequences of immune mediated disease
- Review of commonly used immunosuppressant drugs in canine and feline
- Review of recent literature evaluating use of these drugs in patients

Immune Mediated Disease

- Immunity essential for a healthy functioning body
- Balance between immune response and attenuating response
- Certain diseases result from a loss of balance favoring a state of hyperimmune response

Immune Mediated vs. Autoimmune

- Immune mediated encompasses true auto-immune
- Avoiding using the term "autoimmune" allows for other etiologies
    - Environmental factors, drug therapy, infectious disease, neoplasia act as triggers
- Autoimmune
    - Must be identification of an "auto-antigen"
- Examples of disease is veterinary patients
    - Immune mediated hemolytic anemia
    - Immune mediated thrombocytopenia
    - Inflammatory bowel disease
    - Immune mediated polyarthritis
    - Atopic dermatitis
    - Steroid responsive meningitis/arteritis
    - Autoimmune disease
        - Lupus, pemphigus

Why does it matter?

- Systemic inflammation
- Local inflammation
- End organ damage
- Increased morbidity and mortality

Glucocorticoids

- At immunosuppressive doses down regulates macrophage ability to present antigens, suppress TH1 cell function and induces T cell apoptosis and some patients B cell antibody disruption
- Advantages – quick onset (2-4 day), both anti-inflammatory effects, suppresses humoral and cell mediated pathways, very inexpensive
- Disadvantages – well known side effects

Use of Immunosuppressant Therapy in Dogs and Cats

Azathioprine

- Purine analogue that renders DNA/RNA it is incorporated into non-functional
- Decreases T-cell function
- Disadvantages
- Myelosuppression, hepatic necrosis, pancreatitis, delayed onset of action (days to weeks)
- Dose – 2 mg/kg q 24 hr dogs only
- Use in cat discouraged due to risk of myelosuppression

Mycophenolate

- Inhibits purine synthesis pathway which is critical step specific to T-cell and B cell proliferation and antibody production
- Dose 10 mg/kg q 12 hrs
- Theoretically adverse side effects similar to azathioprine but…
- Clinically patients seem to tolerate better
- Newer drug, less use overall in patient population?

Cyclosporine

- Polypeptide originally derived from Norwegian soil fungus
- Wide variety of actions
- Inhibits T cell activation and proliferation
- Attenuates some inflammatory cytokines
- Decreases actions of natural killer cells, macrophages, eosinophils and mast cells
- It is a first line agent for transplant patients in human medicine
- Little risk of bone marrow suppression in human or animal models

Need to measure levels?

- Routinely done in human and veterinary patients being managed for organ transplant rejection
- Trough whole blood levels 400-600 ng/mL used as therapeutic target
- References also cite 200-400 ng/mL
- Lack of access to this test
- Lack of correlation between clinical efficacy and blood levels across multiple diseases processes

Chlorambucil

- Chemotherapeutic agent whose immunosuppressive properties have not been evaluated in veterinary patients
- Alkylating agent that interferes with DNA replication
    - CYTOTOXIC
- Used mostly for GI inflammatory disease that is poorly responsive to steroids
- Most predictable side effect is myelosuppression, q2 – 4 week CBC monitoring

Use of Immunosuppressant Therapy in Dogs and Cats

Adjunct therapies

- Vincristine
  - Decreases phagocytosis of platelets
  - Induces thrombopoiesis
  - Microtubule assembly is altered in these platelets but does not appear to be clinically relevant
- IVIG
- These drugs are typically only used ONCE during course of treatment
- Little evidence to suggest they positively impact long term outcome

Drug Potpourri

- Leflunamide
  - Pyrimidine synthesis inhibitor
- Methotrexate
  - Inhibits folate production → decrease purine production
- Tacrolimus
  - Similar to cyclosporine
  - Limited to topical use
- Lomustine (CCNU)
  - Alkylating chemotherapeutic agent
- Not considered first line agents

One Drug or Two?

- Argument for single agent therapy (prednisone)
  - Cost
  - Efficacy
- Potential challenges when two agents started at the beginning of disease course
  - If patient has side effects early on…
  - If patient responds well early on…
  - If patient does not respond after a few weeks…

How Long Before Taper?

- IMHA, ITP
  - Spherocytosis, regeneration
  - Platelet counts normalize
- IBD with PLE
  - Albumin level
- Meningitis, IMPA
  - Ideally monitor for cytologic resolution of inflammation
  - Usually treatment guided by clinical signs

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Use of Immunosuppressant Therapy in Dogs and Cats

Taper Schedule

- 4 weeks therapy prior to beginning taper or 2 weeks beyond normalization
- Taper prednisone completely first
- Similar dose reduction/schedule for second agent
- No physiologic reason for most second agents to be tapered
    - Can be stopped cold turkey
    - Taper may better identify a lowest effective dose if long term therapy is needed

Examples of Use in Literature

- Limited search results to last 10 years
- Limited scope of disease to IMHA, ITP, IMPA, PLE
- Found mostly small retrospective studies
- ACVIM consensus statement on IMHA (2018)

Discussion and relevance of the following research studies:

- Treatment of canine idiopathic immune-mediated haemolytic anaemia with mycophenolate mofetil and glucocorticoids: 30 cases (2007 to 2011). Wang, Smith JR, Creevy KE Journal of Small Animal Practice (2013) 54, 399–404
- Treatment of presumptive primary immune-mediated thrombocytopenia with mycophenolate mofetil versus cyclosporine in dogs. Cummings FO, Rizzo SA . Journal of Small Animal Practice (2017) 58, 96–102
- Comparison of the efficacy of prednisone and cyclosporine for treatment of dogs with primary immune-mediated polyarthritis Rhodes AC, Vernau W, Kass PH, Herrera MA, Sykes JE. J Am Vet Med Assoc. 2016;248:395–404
- Comparison of a chlorambucil-prednisolone combination with an azathioprine-prednisolone combination for treatment of chronic enteropathy with concurrent protein-losing enteropathy in dogs: 27 cases (2007–2010). Dandrieux J.R.S., Noble PM, Scase TJ, Cripps PJ, Alexander, German AJ. J Am Vet Med Assoc. 2013;242(12):1705-1714

Conclusions

- Very limited number of immunosuppressant agents that are FDA approved for veterinary use
- Steroids are considered first line agent for majority of immune mediated conditions
- Choice of second agent is largely based on anecdotal evidence
- Opinion should be taken as dogma
- Have a taper and monitoring plan in place
- Understand which side effects to look for depending on which medication is being used
- Be ready to change treatment if no response to therapy
- Client education

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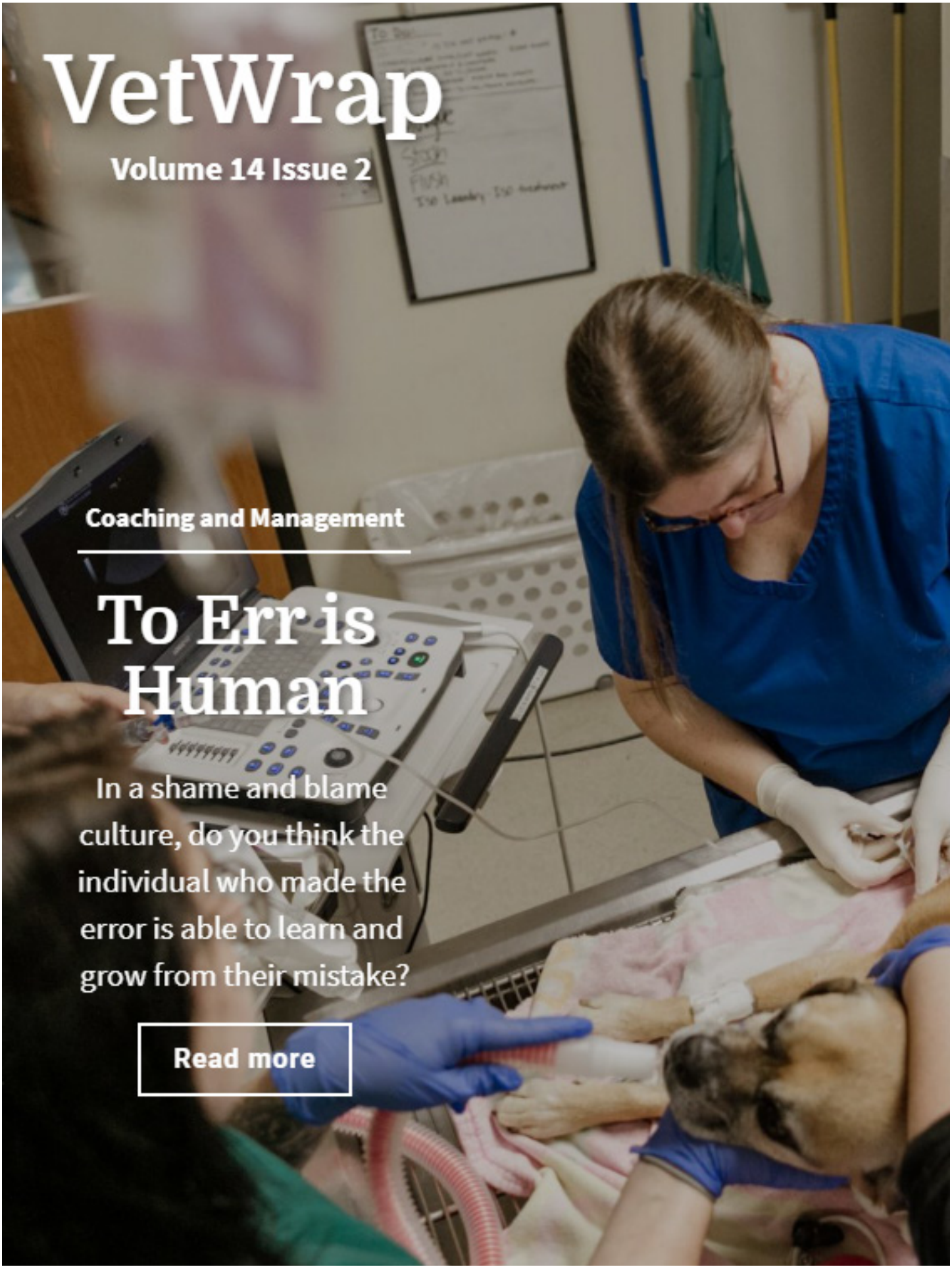

VetWrap

Volume 14 Issue 2

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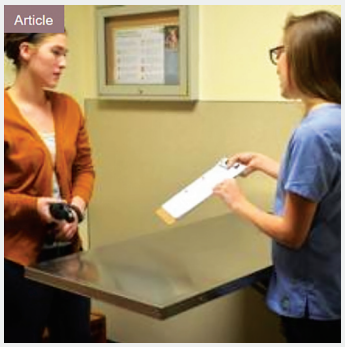

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