Practical Hematology
Non-Regenerative Anemias

Wendy Blount, DVM

Practical Hematology

1. **Anemia 101**
2. **Blood Loss Anemia**
3. **Hemolysis**
4. **Non-Regenerative Anemias**
5. Transfusion Medicine
6. Polycythemia
7. Bone Marrow Disease
8. Coagulopathy
9. Central IV Lines
10. Leukophilia
11. Leukopenias
12. Splenic Disease

Non-Regenerative Anemia

1. **Absolute Reticulocyte Count**
   - Non-regenerative <50,000/ul
2. **Corrected Percent Reticulocytes**
   - <0.5% is non-regenerative

In theory, it would be nice to consider the EPO level, but there is not commercial lab offering that assay right now

Non-Regenerative Anemia

3. **Consider the erythropoietin (EPO) level**
   - The lower the HCT, the higher the EPO level should be
   - Renal disease can be associated with inappropriately low EPO levels
   - EPO level high with bone marrow disease

Non-Regenerative Anemia

- **EPO has four effects on bone marrow:**
  1. Stem cells differentiate to erythroid
  2. Decreases RBC maturation time
  3. Increases Hb per RBC
  4. Stimulates release of reticulocytes from bone marrow to blood

Mild Non-Regenerative Anemia

Mild to moderate NRA often resolves when the primary problem is treated
- RBC morphology rarely helpful - usually normocytic normochromic

Endocrinopathy – corrects 3-4 months after correction of endocrinopathy
- Hypothyroidism – most common
- Addison's Disease
- (Growth hormone deficiency)

Moderate and treatable Inflammatory Disease

Anemia of Renal Disease

Lack of EPO, blood loss anemia, IDA or all 3

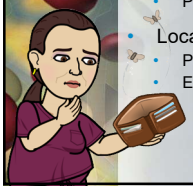
- **Bone Marrow**
  - Erythroid hypoplasia if EPO low
  - Erythroid hyperplasia if recent GI ulcer bleeding
  - Increased hemosiderin if ACID
  - Or decreased iron stores if IDA
- **Iron Panel**
  - Usually normal, but IDA also possible
- **EPO levels**
  - Normal to modestly reduced
  - Lower in cats with CRF than in dogs
  - **Respond well to EPO therapy**
- **Uremic toxins suppress bone marrow activity (including PTH)**
  - Also supplement calcitriol??

Treatment of Anemia of Renal Disease

- Treat renal disease
- Human recombinant erythropoietin (extralabel)
  - 100 U/kg SC 3x weekly until PCV low-normal, then 1-2x weekly
  - Procrit®, Epogen®
  - Correct iron deficiency first if present
    - Either do a renal panel or try a short course of iron supplementation
  - Reserve for HCT <25% in dogs and <20% in cats
  - Sudden severe anemia while taking EPO may mean antiEPO antibodies have developed (25%)
    - Called secondary PRCA
    - Transfuse and stop EPO
  - Takes a few weeks to a few months for antibodies to develop, if they do at all
  - Darbopoietin – only 10% secondary PRCA

Treatment of Anemia of Renal Disease

- Cost of EPO
- GoodRx – with coupon
  - Procrit® - 2 vials (1ml) 20,000 units/ml - $1,100.00
  - Epogen® - 4 vials (1ml) 10,000 units/ml - $675.00
  - Search this week showed coupon for $50/vial
- Covetrus 028881
  - Procrit® - 4 vials (1ml) 20,000 units/ml - $440.66
- Local Pharmacy – if they will split packages
  - Procrit® - 1 vial (1ml) 20,000 units/ml - $500.00
  - Epogen® - 1 vial (1ml) 10,000 units/ml - $175.00



Treatment of Anemia of Renal Disease

Calcitriol Therapy

- PTH released in response to hyperphosphatemia ➔ nephrotoxic, marrow suppression & other morbidities
- Calcitriol reduces PTH

1. ***Confirm CRF*** – creat >2
2. ***If hyperphosphatemic, start AIOH*** at 30-90mg/kg/day
   - Titrate dose until phos <6 mg/dl
   - Also feed low phosphorus diet
3. Get ***baseline PTH*** (MSU)
4. Determine ***starting calcitriol dose***:
   - creat 2-3 mg/dl – calcitriol 2.5-3.5 ng/kg/day (prevent PTH elevation)
   - creat >3 mg/dl – calcitriol 3.5 ng/kg/day (reduce PTH)

Treatment of Anemia of Renal Disease

Calcitriol Therapy

5. ***Serum Calcium*** – Day 7, Day 14 if creat <3 and then q6 months in all cases
   - If hypercalcemic, d/c calcitriol for 1 week and recheck, to see if too much calcitriol is the cause
   - Not enough calcitriol can also cause hypercalcemia
6. ***Monitor BUN, creat, phos*** q1-3 months
7. ***Recheck PTH*** in 4-6 weeks
   - If still high, increase calcitriol by 1-2 ng/kg/day
   - Repeat until PTH normal
   - Do not exceed 6.6 ng/kg/day unless iCa^{++} measured
   - Try pulse dosing if >5 ng/kg/day is needed (double the dose, given QOD)
8. ***Assess clinical benefit*** – improved appetite, activity level, stabilization of CRF numbers

Anemia of Chronic Liver Disease

Compounded by coagulopathy and blood loss, especially in cats

- **RBC Morphology**
  - Abnormal lipid metabolism – acanthocytes, target cells, leptocytes, codocytes
  - Microcytosis in dogs with PSS
- **Bone Marrow -** variable
  - ± Erythroid hypoplasia due to reduced synthesis of nutrients for hematopoiesis
- **Iron panel**
  - Increased hepatic iron, ± low serum iron
  - Normal TIBC, UIBC
- **EPO levels** - variable

Iron Deficiency Anemia

- **Iron metabolism**

1. Absorbed from food in the GI tract
2. Held on intestinal epithelial cells by ferritin
   - Sloughed or absorbed, based on need
3. Absorbed into blood and carried by transferrin (measured as TIBC)
4. Stored in the tissues as soluble ferritin (mostly in the liver) or insoluble hemosiderin (mostly in the bone marrow)

Rattler, 10 month Pyrenees: History

- 3 day history of bloating and one day of lethargy with pale gums
- On monthly Heartgard®
- Adopted at 6 months of age from Shelter
- Lives in a 20-acre farm
- Spends most of his time in a Large dog pen

Rattler - Physical Exam

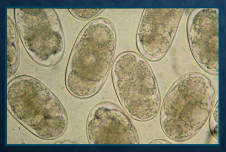
- T 100F, HR 180, RR 65, white gums
- Body condition 3/5
- Rectal exam: dark brown stool noted
- Abdomen distended with fluid wave
- Grade 2-3/6 systolic heart murmur

Rattler - Initial Thoughts

- Does anemia explain the pallor, or is there primary heart disease? Or both?
- Is dark stool melena?
- What kind of fluid is in the belly?
- Does anemia explain the murmur, tachycardia and tachypnea? Cardiovascular disease? Respiratory Infection?

Rattler - Diagnostics

- PCV / TS: 9% / 3.4 g/dl / clear serum
- CBC: HCT 8%, neutrophils 17.6K, plate 120K
- Chemistry: alb 1.0. glob 1.6, bili 0.2
- Fecal flotation



Rattler - Diagnostics

GlobalFAST®

- *TFAST*® - No pneumothorax, No pleural effusion, No pericardial effusion
  - LA normal size, RV & LV mildly enlarged
- *VetBLUE*® - No interstitial or alveolar fluid at lung periphery
- *AFAST*® - Ascites - AFS 4/4
  - Volume replete (no hypovolemia, no right sided volume overload)
  - Abdominocentesis – pure transudate (chart)
  - DDx – liver dz, hypoproteinemia

Rattler - Treatment

- Transfusion 500cc whole blood
- Panacur 50 mg/kg PO SID x 3 weeks, repeat in 2 weeks

Recheck 1 week:

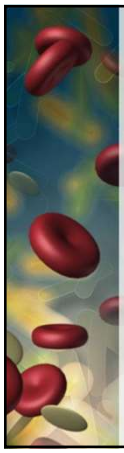
- Exam – vitals, check ascites, check heart murmur
- Fecal flotation & cytology
- PCV ± chemistries
- Further diagnostics if not resolving

Rattler - Recheck

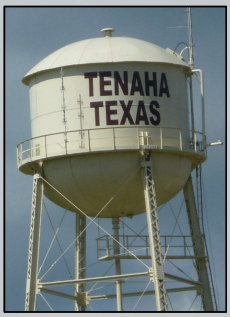
- Exam – ascites resolved, murmur & pallor still present
- Fecal flotation – negative; cytology – normal (no RBC)
- PCV – 16%, TP 4.0, platelets 100K/ul

Further Diagnostics:

- Reticulocytes 63,000/ul
- Non-regenerative to mildly regenerative anemia
- Neutrophils normal
- Fasting and 2 hour post-prandial bile acids normal

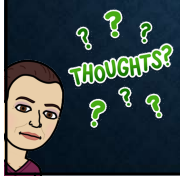


Merry Holmes Vann
Cold Spring TX



Rattler - More Thoughts

- Why did he have severe hookworms when on Heartgard?
  - Shelter dog – overwhelming exposure
  - Husbandry – small area of ground – reinfection
  - Resistance to Pyrantel at low doses
- Why is his regenerative response so poor?
  - Bone marrow disease
  - Ehrlichiosis or other tick borne dz
  - Other chronic inflammatory dz
  - IDA



Rattler - Plan

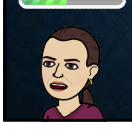
- Doxycycline 5-10 mg/kg PO BID x 3 weeks
- Recheck CBC, retics 1 week
- Iron?
  - Right thing for IDA
  - Wrong thing for everything else on the list

Recheck 2

- PCV 15%, retics 40,000/ul
- Non-regenerative anemia
- Platelets normal
- Fecal flotation & cytology normal

Rattler – More Thoughts

- *Further pursue tick borne disease* – treat with prednisone and/or do bone marrow
  - some tick borne diseases will not resolve without corticosteroids
- *Pursue IDA* – treat with iron and/or do iron panel
- *Lymphoma* or *toxic bone marrow arrest* are less likely but possible
  - Bone marrow would reveal



Rattler – Bone Marrow Aspirate

- White cell line normal
- Maturation appears normal in the red cell line
- M:E is 4:1, indicating erythroid hypoplasia
- Normal megakaryocytes
- Rare iron stores
- Consistent with IDA

Rattler – Iron Panel (KansasSU)

- Iron 19 mcg/dl (98-220 mcg/dl) – very low
- UIBC 402 mcg/dl (110-370 mcg/dl) - high
- TIBC 421 mcg/dl (249-496 mcg/dl) – high normal
- Iron % saturation 4.5% (28-62) – very low

Consistent with Iron Deficiency Anemia

Rattler – Treatment

- Iron dextran 15-20 mg/kg IM once (max 300 mg)
  - (cats 50 mg/cat)
  - 60% absorbed in 1-3 days
  - 90% absorbed in 1-3 weeks
  - Then oral or monthly injections if needed

Iron Deficiency Anemia

- **Blood Smear**
  - Microcytic, hypochromic RBC
  - nRBC, schistocytes, target cells, dacryocytes
- **CBC**
  - Decreased MCV (<60fl), MCH
  - Decreased MCHC (<32 g/dl)
  - Thrombocytosis (may be >1,000,000/ul)
- **Iron panel (KSU)**
- **Bone marrow**
  - Depleted iron stores
  - mild erythroid response
- **EPO levels**
  - increased

Iron Deficiency Anemia

- Low **serum iron (SI)** - <60 ug/dl
- Low **ferritin** (soluble tissue storage protein)
- Low **transferrin saturation** - <20%
  - Transferrin is plasma protein that transports iron-ferritin complex (aka TIBC)
  - Normally 20-60% saturated
- Normal to increased **UIBC** (unbound iron binding capacity)
- Normal to increased **TIBC** (total iron binding capacity) aka transferrin

TIBC - SI = UIBC

Transferrin saturation = SI / TIBC

Iron Deficiency Anemia

- **Treatment – weeks to months**
  - **Iron dextran (see Rattler's case)**
  - **Ferrous sulfate**
    - 11 mg/kg PO daily
    - Give with a meal, but no dairy, antacids or eggs
    - Colors stool black (can't monitor for melena)
    - **Most oral vitamins + iron do not have nearly enough iron**
  - **If any problems in response, repeat iron panel**

Iron Deficiency Anemia

- The most common causes of iron deficiency anemia are chronic GI blood loss and flea anemia
- Anemia varies from mild to severe
- Poikilocytosis and hypochromasia are typical
- Hypoproteinemia often present
- Anemia won't budge until iron is supplemented, even if chronic blood loss is corrected
- Rapid improvement within a week or two supplementing iron
- Mother's milk contains little iron
  - Neonates susceptible to non-regenerative IDA due to parasitism
- Iron supplementation is rarely needed unless there is chronic external blood loss and/or CRF

Differential Diagnosis

Microcytic anemia (low MCV)

- **Microcytic but not hypochromic**
  - Akita, Shiba Inu, Chow chow
  - Puppies
  - **Dyserythropioesis of Springer Spaniels** (polymyopathy, cardiac)
  - Chloramphenicol toxicity
  - Copper deficiency (Cu required for Fe to enter RBC)
  - Chronic liver disease (especially PSS)
- **Iron deficiency anemia -** Hypochromic

Anemia of Chronic Inflammatory Disease

- The most common anemia in small animals
- Can develop within 7-10 days
- Iron is sequestered in the macrophages, so not available for RBC production
  - Physiologic metabolic response to deprive infectious organisms of iron
  - Apolactoferrin secreted by neutrophils
  - Chelates iron, especially at low pH of inflammation
  - Macrophages have lactoferrin receptors that internalize the chelated iron
  - Results in diversion of iron from ferritin (soluble) to hemosiderin (insoluble)

Anemia of Chronic Inflammatory Disease

- Activated macrophages remove RBC from circulation
- Fever shortens RBC lifespan
- Depletion of small proteins (transferrin)
- Iron panel
  - **SI**
  - **Ferritin**
  - **Transferrin/TIBC**
- Bone marrow
  - **Increased hemosiderin in macrophages**
  - Lack of marked erythroid response
  - Myeloid hyperplasia

Iron Panel distinguishes between IDA and ACID in cats with severe NR anemia

Anemia of Chronic Inflammatory Disease

- EPO levels
  - Normal to decreased
- Treatment
  - **Treat underlying problem**
  - Iron administration is of little help, and can make matters worse:
    - Chronic overdose - liver failure, GI distress/fibrosis
    - Acute overdose - pulmonary edema, shock
    - Repeated transfusion can cause chronic overdose
  - EPO administration of little help

Non-Regenerative IMHA (NRIMHA)

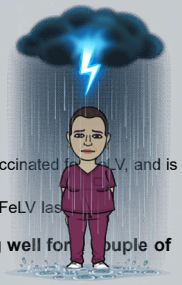
- Bone marrow
  - Maturation arrest at stage attacked by antibodies
  - May see other bone marrow problems: dyserythropoiesis, hematophagocytic syndromes, myelofibrosis, bone marrow necrosis
  - Can do immunologic staining for definitive diagnosis
- Etiology
  - Immune mediated destruction of erythroid stem cells later than PRCA
- Treatment
  - Immunosuppression as for IMHA

Pure Red Cell Aplasia (PRCA)

- **Severe anemia – PCV <10-20%**
  - Sometimes spherocytes and stomatocytes
- **Bone marrow**
  - Nearly absent erythroid precursors
- **Etiology**
  - FeLV, FIV, parvovirus infection
  - Immune mediated destruction of earliest erythroid stem cells
- **Treatment**
  - Immunosuppression as for IMHA

Caly

Caly



2 yr old SF DLH

- FeLV+ since a kitten
- Indoor cat
- Other indoor cat "Molly" vaccinated for FeLV, and is currently FeLV negative
- Littermate "Bandit" died of FeLV last

Caly has not been feeling well for a couple of weeks

Another vet who knows that cat is FeLV+ did bloodwork and found that Caly was neutropenic (2,100/ul) and anemic (PCV 22%) and was told there was nothing else that could be done

She is here for a second opinion

Caly

Exam – T-101.7°F

- Generalized lymphadenopathy

CBC – WBC 2,400/ul (segs 1,400/ul – lymphs 1,000/ul – monos 400/ul), PCV 20%

Reticulocyte count – 0.5%

Mira Vista Histoplasma Antigen (urine) – negative

Lymph Node Cytology (3 nodes)

- heterogeneous population of lymphocytes
- 85% mature to 15% immature cells
- 0-3 neutrophils/HPF
- Dx - reactive lymph nodes

Caly

Tx

- prednisone 10 mg PO SID x 2 weeks
- Clavamox 62.5 mg PO BID x 14 days
- Recheck CBC 2 weeks, sooner if not doing well

2 week recheck

- Feeling great, lymphadenopathy resolved
- PCV 24%
- **FeLV IFA –** positive (National Vet Lab)
- Prednisone 5 mg PO SID x 2 weeks
- Then 5 mg PO SID x 4 weeks
- Recheck 4-6 weeks, or sooner if not OK

Caly

Day 60 recheck

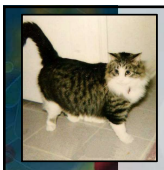
- Feeling great, CBC normal
- Prednisone 2.5 mg PO SID x 4 weeks
- Recheck 30 days, or sooner if not OK
- Owner wants to start multivitamin with herbal immunostimulant

Day 90 recheck – CBC normal

- Stopped prednisone

Day 120 recheck – CBC normal

- Recheck 6 months or sooner if not doing well

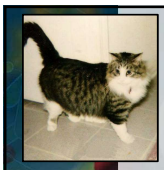


Caly

Caly does well for 1 year

- Not feeling well, enlarged lymph nodes
- No fever
- **CBC** – PCV 9%, **panel** - WNL

Shudder



Caly

Caly does well for 1 year

- Not feeling well, enlarged lymph nodes
- No fever
- **CBC** – PCV 9%, **panel** - WNL
- **Lymph node cytology -** predominantly small lymphocytes with mildly increased numbers of macrophages, plasma cells and plasmacytoid lymphocytes
- **Dx** – reactive lymph node
- **Transfusion** – 60cc whole blood
- Next day - PCV 22% - she feels great
- **Thoracic radiographs, abdominal ultrasound** including FNA cytology liver & Spleen - NSAF

Caly

- **Reticulocyte count** (pre-transfusion) – 0.4%
- **Bone Marrow**
  - Cytology – increased rubriblasts (11%), and prorubricytes (64%); reduced rubricytes, metarubricytes & reticulocytes (25%).
  - Histopathology – no evidence of neoplasia
  - Dx – myeloid dysplasia
- **Tx:**
  - Erythropoietin 100U SC MWF
  - Prednisone 10mg PO SID x 2 weeks
  - Azithromycin 50mg PO SIX x 2 weeks
- **Recheck 2 weeks –** or sooner if not OK

Caly

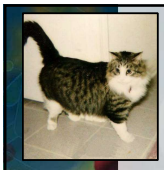
2 week Recheck – doing well

- **CBC -** WNL
- **Tx:**
  - Erythropoietin 100U SC 2x weekly
  - Prednisone 10mg PO SID x 2 weeks
  - Then 5 mg PO SID x 4 weeks
- **Recheck 2 weeks –** or sooner if not OK

4 week Recheck – doing well

- **CBC –** PCV 23%
- **Tx:** Erythropoietin 100U SC 2x weekly
  - Prednisone 20mg PO SID x 4 weeks
  - Then 10 mg PO SID x 4 weeks
- **Recheck 2 weeks –** or sooner if not OK

Attendee
City TX



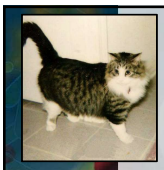
Caly

6 week Recheck – doing well

- **CBC –** WNL
- **Tx:** Erythropoietin 100U SC 2x weekly
  - Prednisone 20mg PO SID x 2 weeks
  - Then 10 mg PO SID x 4 weeks
- **Recheck 3 weeks –** or sooner if not OK

9 week Recheck – doing well

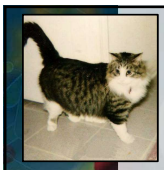
- **CBC –** WNL
- **Tx:** Erythropoietin 100U SC 2x weekly
  - Prednisone 10mg PO SID x 3 weeks
  - Then 5 mg PO SID x 4 weeks
- **Recheck 4 weeks –** or sooner if not OK



Caly

13 week Recheck – doing well
- **CBC –** WNL
- **Tx:** Erythropoietin 100U SC 2x weekly
  - Prednisone 5mg PO SID x 4 weeks
- **Recheck 4 weeks –** or sooner if not OK

17 week Recheck – doing well
- **CBC –** WNL
- **Tx:** Erythropoietin 100U SC 1x weekly
  - Prednisone 5mg PO SID x 4 weeks
- **Recheck 4 weeks –** or sooner if not OK



Caly

21 week Recheck – doing well
- **CBC –** WNL
- **Tx:** stop erythropoietin
  - Prednisone 5mg PO SID x 4 weeks
- **Recheck 4 weeks –** or sooner if not OK

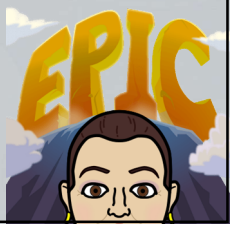
25 week Recheck – doing well
- **CBC –** WNL
- stop prednisone

Did well for 1 year

Caly

- Stopped Epogen® after 4 months
- weaned off prednisone over 5 months
- Every CBC done during this time (q3-4 weeks) was normal

Did well for 1 year



Caly

4½ years old – not feeling well
- **CBC –** PCV 10%
- **Retics and bone marrow** confirm maturation arrest again and ruled out neoplasia
- **No response to:**
  - 2 Transfusions
  - Prednisone, erythropoietin
  - Baypamun®
  - Staphylococcus A protein
  - Transfer Factor®
- **Euthanized 2-1/2 years after first sign of FeLV related illness**

Feline Leukemia

- **Causes anemia in numerous ways**
  - ACID by susceptibility to pathogens
  - Pure red cell aplasia
  - Aplastic pancytopenia (NRIMHA)
  - Hemolytic anemia due to hemoplasmas
  - IMHA
  - Myelodysplasia
  - Myelofibrosis
  - Hemophagocytic syndrome

You can't treat FeLV anemia intelligently without a bone marrow sample

- **Hemogram**
  - Often macrocytic (>52 fl), normochromic
  - Megaloblastic rubricytes
  - **Usually non-regenerative**

Treating FeLV Anemia

- **If myelodysplasia** (pancytopenia possible)
  - EPO 100 U/kg SC 3x weekly until PCV low-normal, then 1-2x weekly
  - Prednisone 1-2 mg/lb/day, and taper over 60-90 days or more
  - Relapse common with taper – go slow
- **If regenerative anemia**
  - Prednisone 1-2 mg/lb/day, and taper over 60-90 days or more
  - Doxycycline 5-10 mg PO BID x 3 weeks
- **Antibiotics for infection, or if Neutrophils <1000-1500/ul**
- **Check for & treat histoplasmosis** (form)

Treating FeLV Anemia

- Can live 2-4 years
- If lymphoma, prognosis worse
- Acts of desperation
  - Various herbal immunostimulants
  - Baypamun®
  - Immunoregulin®
  - Feline Interferon (Verbagen Omega®)
  - Interferon (RoferonA®)
  - Transfer Factor®
  - BCG

CleoCatra

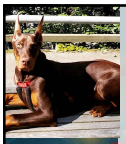
- Bone Marrow Dysplasia
- FeLV negative, FIV negative
- No response to all of the things done for Caly

Aplastic Anemia

- **Pancytopenia**
  - often preceded by leukocytosis for several weeks
  - Neutropenia first
  - then thrombocytopenia
  - then anemia
- **Etiology**
  - Estrogen toxicity
    - Iatrogenic
    - Sertoli cell or granulosa cell tumor
  - Drugs
    - AZT, antineoplastics, azathioprine, phenylbutazone, sulfas, fenbendazole, quinidine, thiacetarsemide, phenobarbital, cephalosporins
    - Cats – propylthiouracil, methimazole, griseofulvin
    - Dobermans –
    - Dogs with bute toxicity rarely recover

Aplastic Anemia

- **Etiology**
  - Chloramphenicol causes mild, reversible nonregenerative anemia in dogs
  - Infection
    - Ehrlichia (also immune mediated)
    - Bacterial endotoxins, Aflatoxin B
    - Parvovirus
  - DIC (bone marrow necrosis)
  - Idiopathic
- **Bone marrow**
  - Hypocellular bone marrow despite spicules, except plasmacytosis
  - May have myelonecrosis
  - Often need **bone marrow histopath** to confirm



Ruger

3yr male Doberman – 88 lbs

CC: decreased appetite and energy, gradually coming on for about 2 weeks; treated for a skin infection with SMZ 1 month ago.

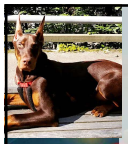
Exam: no clues

CBC: HCT 26%, segs 1,110/ul, lymphs 600/ul, monos 90/ul, platelets 82K/ul

Panel, lytes, UA: no clues

TVMDL PCR Tick Panel: all 12 negative ($60)

Ehrlichia canis, chaffeensis, ewingii
Rickettsia rickettsii *Anaplasma phagocytophilum*
Borrelia burgdorferi, hermsii, parkeri, turicatae
Babesia gibsoni, canis, caballi



Ruger

Tx: doxycycline 200mg PO BID x 14 days, with food
Recheck one week, teach owner to take temp
dispense amoxicillin and ciprofloxacin, to be started in case of fever; Yunnan Bai Yao to be given in case of petechiae, bruising or any other bleeding.

Week 1: no change, no fever

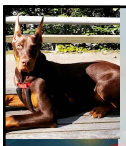
CBC: HCT 22%, segs 1,040/ul, lymphs 432/ul, monos 0/ul, platelets 63K/ul

Thoracic rads, Abdominal US: no clues

Liver, Spleen cytologies: no clues (BMBT 1 minute 4 sec)

Bone Marrow Cytology: erythroid and myeloid hypoplasia, inadequate megakaryocytes, mild to moderate plasma cells (aplastic anemia with plasma cells), moderate marrow necrosis

Tx: continue doxycycline for at least 2 more weeks
prednisone 20mg PO BID until recheck in 1 week

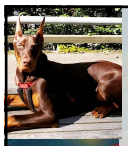


Ruger

Week 2: feeling better, no fever

CBC: HCT 18%, segs 820/ul, lymphs 600/ul, monos 150/ul, platelets 52K/ul

Tx: continue doxycycline for at least 1 more week
prednisone 40mg PO BID until recheck in 1 week
amoxicillin 1000mg PO BID x 14 days
recheck 1 week
if no improvement in CBC, do another bone marrow cytology, if owner wants to continue
transfusion and/or EPO if indicated by anemia
vincristine if platelets<10-15K/ul
Neupogen if segs <500/ul



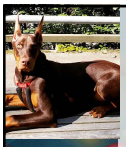
Ruger

Week 3: energy back to normal, no fever, peeing a river, eating everything is sight, keeps the owner up panting all the time and staring at him

CBC: HCT 19%, segs 980/ul, lymphs 640/ul, monos 120/ul, platelets 58K/ul
BMBT: not done

Bone Marrow Cytology: erythroid and myeloid hyperplasia in the cell lines that has not yet reached the mature blood cells, adequate numbers of small megakaryocytes

Tx: prednisone 40mg PO BID one more week if the owner can take it
amoxicillin 1000mg PO BID x 7 more days
recheck 1 week



Ruger

Week 4: same as last week.

CBC: HCT 25%, segs 5,320/ul, lymphs 1,320/ul, monos 300/ul, platelets123K/ul

Tx: Wean off prednisone over 3-4 months
30 mg PO BID x 3 weeks, recheck CBC 1 week in
20 mg PO BID x 3 weeks, recheck CBC 1 week in
15 mg PO BID x 3 weeks, recheck CBC 1 week in
10 mg PO BID x 3 weeks, recheck 1 week in
10 mg PO SID x 3 weeks, recheck 1 week in
If CBC OK, stop
Recheck CBC in 1 week, 2 weeks after that, 30 days after that, 60 days after that, 90 days after that, then 1-2x yearly for awhile
Ruger recovered and did not relapse (No more SMZ!)

Aplastic Anemia

- **Treatment**
  1. Discontinue bone marrow toxins
  2. Doxycycline 5-10 mg/kg PO BID x 3 weeks
     - If improved but not recovering, 6 weeks total
  3. 1 week later - if that fails, antiinflammatory
     - Prednisone 0.5 mg/lb/day
     - If not effective after 1-2 weeks, increase to 2 mg/b/day x 1-2 weeks & start azathioprine
     - Then as for IMHA
  4. Prophylactic antibiotics if segs <1-1,500/ul
  5. Avoid injury that can risk bleeding
  6. Transfuse to buy time for bone marrow response, if needed
  7. Vincristine, EPO or GCSF (Neupogen) as needed

WBC recover first, then platelets, then RBC

Aplastic Anemia

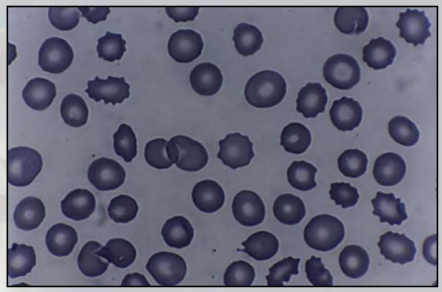
- **"Panic Numbers"**
  - Weekly rechecks until near normal range
  - If stable and above panic numbers, continue treatment
  - If numbers falling or below panic thresholds, add/increase immunosuppression

1. PCV <15% K9 <12% fel - transfuse, start EPO
2. Neutrophils 1,000-1,500/ul – amoxicillin x 14d
3. Neutrophils <1,000/ul – amoxi + quinolone
4. Neutrophils <500/ul – start GCSF, treat sepsis
5. Platelets <50K/ul at risk for hemorrhage
   - If no vasculitis, often don't bleed until <10K/ul
6. Platelets <10-15K/ul – vincristine 0.02 mg/kg IV

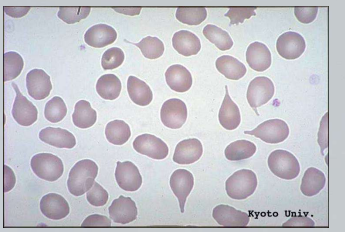
Myelophthisic Disease

- **Bone marrow has been replaced by something else**
  - Tumor cells
  - Fungal granuloma
  - Fibrous tissue, fat
  - Bone (osteopetrosis)
- **Hemogram**
  - Normocytic, normochronic anemia
  - nRBC

Myelophthisic Disease



Myelophthisic Disease



- Budding fragmentation, dacryocytosis
- Large platelets or megaplatelets
- Degenerative left shift

Myelophthisic Disease

- **Myelofibrosis**
  - neoplasia
  - Chronic severe hemolytic anemia
    - Congenital anemia
  - Idiopathic myelofibrosis
    - Nonregenerative anemia and thrombocytosis
    - Organomegaly due to EMH
    - Left shift in all 3 cell lines
  - Can not diagnose on bone marrow aspirate
    - Need bone marrow core biopsy

Myelophthisic Disease

- **Bone Marrow Neoplasia**
  - May or may not be associated with **leukemia**
    - Neoplastic cells in peripheral blood
  - Neoplastic cells often found elsewhere
    - Liver, spleen, lymph nodes
  - Myeloproliferative neoplasia
    - Granulocytes and monocytic
    - "non-lymphoid leukemia"
  - Lymphoproliferative Neoplasia
  - Clinical Signs
    - Bone pain
    - Fever, infection, leukopenia
    - Anorexia, lethargy, vomiting, diarrhea
    - May progress to anemia and thrombocytopenia

Myelodysplasia

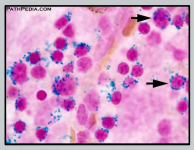
- **Also known as….**
  - Refractory anemias
    - RARS – Refractory Anemia with Ringed Sideroblasts
    - RAEB – Refractory Anemia with Excess Blasts
  - Refractory Cytopenias
    - RCMD – Refractory Cytopenias with Multilineage Dysplasia
  - Preleukemia (**can progress to acute leukemia**)
  - Subacute leukemia
  - Dysmyelopoiesis (due to toxicity)
  - Myelodysplastic Syndrome (MDS)

Myelodysplasia

- **Many blast cells in the affected line (5-20%)**
- **But they don't mature in the usual way, due to acquired genetic mutation**
  - maturation arrest – atypical (dysplastic) morphology of RBC precursors
  - Hyperplastic bone marrow with 5-20% blasts
- **Etiology**
  - drug induced - chloramphenicol
  - FeLV, FIV
  - Idiopathic, immune mediated

Myelodysplasia

- **Siderocytes, Sideroblasts**
  - Contain Pappenheimer bodies – iron granules
  - Resembles basophilic stippling
  - Prussian Blue stains Pappenheimer bodies, but not RNA of basophilic stippling
  - RARS – Refractory Anemia with Ringed Sideroblasts
- **Treatment**
  - EPO
  - Corticosteroids (DepoMedrol®)



Congenital Dyserythropoiesis

- **English Springer Spaniels**
  - Bone marrow - dyserythropoiesis
  - Polymyopathy
  - Cardiac disease
  - Hemogram – poikilocytosis
    - spherocytes, schistocytes, dacryoctyes, codocytes, vacuolated RBC
- **Giant Schnauzers**
  - Vitamin B12 malabsorption
  - Chronic non-regenerative anemia and neutropenia
  - Hemogram – anisocytosis, MCV normal, poikilocytosis
    - macrocytes, schistocytes, acanthocytes, elliptocytes, keratocytes, hypersegmented segs, giant platelets
- **Poodles**
  - Dyserythropoiesis (PK deficiency like disease), hemolysis, macrocytosis

Folate Deficiency

- **hemogram**
  - Macrocytosis (increased MCV)
- **B12 deficiency anemia not observed in dogs and cats, except Giant schnauzers**
- **Etiology folate deficiency**
  - Distal small intestinal disease
  - Prolonged TMPS administration
- **Treatment**
  - Treat small intestinal disease
  - Supplement folate if giving TMPS for more than 30 days

Macrophage Proliferative Disorders

- **Hemophagocytic Syndrome**
  - Benign proliferation of macrophages
  - Causes cytopenias
  - Idiopathic or secondary to chronic antigenic stimulation:
    - IMHA, ITP – Evan's Syndrome
    - Chronic infection
    - Myelodysplastic syndromes
    - neoplasia
- **Malignant Histiocytosis**
  - Aggressive histiocytic neoplasia that results in death within weeks to months

Non-Regenerative Anemias

- Take much longer to respond than regenerative anemias
  - Often 3-4 weeks or more
  - Some can take 6 months or more to completely respond
  - Prepare to transfuse
  - IDA is the exception – 10-14 days
- Highly regenerative anemias can respond as quickly as 3-5 days, if blood loss or hemolysis is stopped

Curtis Wilson
Beaumont TX

Summary

PowerPoints - .pptx, .pdf 1 slide per page, .pdf 6 slides per page

Client Handout – Iron Deficiency Anemia

Drug Handouts

- Calcitriol
- Cyanocobalamin
- Doxycycline
- Erythropoietin
- Folate
- Iron
- Methylprednisolone
- Prednisone

Summary

Laboratory Information

- *KSU* – Comparative Hematology Sub Form
- *MSU* – Endocrinology Submission Form
- *MSU* – Endocrinology Test Fees
- *MSU* – Endocrinology Reference Ranges
- *MSU* – Endocrinology Testing Schedule
- *MiraVista* – Fungal Submission Form
- *Mira Vista* – Test Samples
- *Mira Vista* – Fungal Test Chart
- *NVL* – Slide Prep for FeLV IFA
- *NVL* - FeLV IFA Submission Form

Acknowledgements

Chapter 2: The Complete Blood Count, Bone Marrow Examination, and Blood Banking

- Douglass Weiss and Harold Tvedten
- Small Animal Clinical Diagnosis by Laboratory Methods, eds Michael D Willard and Harold Tvedten, 5th Ed 2012

Chapter 3: Erythrocytes Disorders

- Douglass Weiss and Harold Tvedten
- Small Animal Clinical Diagnosis by Laboratory Methods, eds Michael D Willard and Harold Tvedten, 5th Ed 2012

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Chapter 59: Pallor

- Wallace B Morrison
- Textbook of Veterinary Internal Medicine, eds Stephen J Ettinger and Edward C Feldman, 6th Ed 2003

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