Practical Hematology
Treating Coagulopathy

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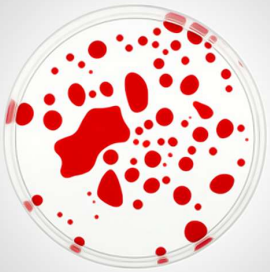

Practical Hematology

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

Assessment of Coagulation

1. Is bleeding appropriate to injury?
   - **Control arterial bleeding with ligation**

2. If not, assess coag status ASAP
   - **Platelet count**
   - **PT, PTT/ACT**
   - **BMBT**
   - **FDPs, d-dimers**
   - **Factor assays & DNA Tests**

Treating Primary Hemostatic Defects

- Simulate primary hemostasis until secondary can kick in
  - **Direct pressure (bandages)**
  - **Topical epinephrine**
  - **cauterize**
- Treat hypovolemia
  - **Colloids and fluids with packed cells or Oxyglobin**
  - **Whole blood transfusion**
- Identify and treat cause
  - **Vasculitis**
  - **Thrombocytopenia <20-50,000/ul**
  - **Platelet function defect**

Treating Primary Hemostatic Defects

- Supportive therapy
  - **Cage rest – avoid injury**
  - **Avoid poking holes in big veins or any arteries**

Tpenia & Vasculitis – Work-Up

- CBC, panel, lytes, UA
  - **Urine P:C ratio if proteinuria on dipstick**
  - **Urine culture if dilute urine**
  - **Anti-platelet-Ab if platelets <50,000/ul**
  - **Bone marrow if severe cytopenias**
- FeLV/FIV in cats, HWAg in dogs
- Coags
  - **PT, PTT/ACT**
  - **BMBT if above normal**
  - **FDPs or d-dimers if PTT elevated**

Tpenia & Vasculitis – Work-Up

- Chest x-rays
  - **Echo if murmur**
  - **Blood culture if endocarditis**
- Abdominal x-rays and/or ultrasound
- Tick panel – save serum
  - **RMSF, Ehrlichia, Borrelia**
- ANA – save serum

1st Round Treatment

- Treat underlying cause
- Doxycycline 5-10 mg/kg PO BID x 3 weeks
  - **If response, may need to treat as long as 6 weeks total**
- Anti-inflammatory prednisone only if chronic infection ruled out by imaging & culture
  - **0.5 mg/lb/day prednisone**

Work-Up 2nd Round

- CBC - If no improvement in thrombocytopenia in 1-2 weeks, do bone marrow if not already done
  - **May find infectious organism or tumor**
  - **Plasma cells – *Ehrlichia* – add prednisone if haven't used yet**
  - **Increased megakaryocytes indicates peripheral destruction or consumption**
    - Coag panel helps sort these 2 things out
    - Look also at the MPV
- If imaging not already done, do it now

2nd Round Treatment

- May need to increase to immunosuppressive prednisone
  - **1-2 mg/lb/day**
  - **Highest dose no longer than 2 weeks**
  - **Primary IMT cases respond within 2-3 days**
  - **Wean off over 2-3 months or more**

3rd Round +

- If first bone marrow showed no increase in megakaryocytes, can repeat in 1-2 weeks
  - **Persistent lack of megakaryocytes when IMT is suspected – antimegakaryocyte Ab assay**
- Repeat diagnostics looking for infection after immunosuppressive therapy for 1-2 weeks
  - **X-rays and ultrasound**
  - **Urine culture**
- If suspecting ITP, may need to add Imuran, and cyclosporine or Danazol
  - **Vincristine 0.02 mg/kg IV q7days**
  - **Begin weaning when platelets reach 100,000/ul**
  - **Decrease one drug every 1-2 weeks, checking CBC**
  - **Wean off drugs over 3-6 months**
- If suspecting infectious disease, can take samples for paired sera

IMT and IMHA – Preventing Relapse

- Gradual and careful weaning off immunosuppressive drugs
  - **Check CBC 1 week after every reduction and prior to the next reduction**
  - **Often takes 3-6 months or more**
  - **May need to stay on drugs long term**
- Minimal exposure to unnecessary drugs
- No vaccination, or rabies only
- Avoid stress as much as possible

von Willebrand Disease

- Treat when bleeding from injury, or perioperatively
- DDAVP (**deamino 8 D-arginine vasopressin**)
  - **Use commercial nasal drops**
  - **1-4 ug/kg SC 30 minutes prior to surgery**
  - **Duration 2 hours**
  - **Works best for Type 1**
- Desmopressin acetate for injection
  - **Same protocol**

von Willebrand Disease

- For active bleeding
  - **Fresh whole blood if significant blood loss or anemia**
  - **Fresh frozen plasma or cryoprecipitate**
    - Smaller volume prevents volume overload
    - Greatly reduces risk of transfusion reaction
  - **Transfusing RBC and von Willebrand Factor to support primary hemostasis**
  - **Platelet transfusion is difficult in practice**
    - Lifespan of transfused platelets is less than 24 hours in fresh whole blood
    - Consider when bleeding into the CNS or life threatening uncontrolled bleeding

von Willebrand Disease

- For active bleeding
  - **Stored whole blood and packed cells contain no appreciable active platelets**
  - **Type 2 and 3 may need 2nd & 3rd transfusion over the next 24-48 hours**

Cryoprecipitate

- Preferred for vWDz, but very expensive
- Prepared from fresh frozen plasma
  - **Supernatant is decanted off during a slow thaw**
  - **White precipitate forms during the thaw**
  - **PPT high in Factor 8, 13, vWF and fibrinogen**
- Contains 5-10x concentration of vWF
- 10% volume of FFP
- 5% volume of whole blood
- Preferred for
  - **von Willebrand Disease**
  - **Hemophilia A (factor 8 deficiency)**
  - **Fibrinogen deficiency – cockers, Kerry Blues**

Congenital Thrombocytopathia

- Treat when bleeding from injury, or perioperatively
- Fresh whole blood transfusion

Platelet transfusion

- Draw immediately prior to transfusion
- Store at room temperature until administered
- Citrate-based coagulant

Platelet Rich Plasma

- Centrifuged with low G force within 6 hours of collection
- 80% of the platelets are harvested
- Suspended in 1/3 of whole blood volume
- Low volume **platelet concentrates** prepared from PRP by a second centrifugation.
- Maintain at room temperature until transfused, as soon as possible

Hemophilia

- Only vitamin K dependent factor deficiency in Devon Rex is treatable
- Restrict activity to avoid trauma
- Avoid surgery, venipuncture, restraint, IM injections.
- Avoid medications that interfere with primary hemostasis
  - **NSAIDs, phenothiazines**
- Transfuse active bleeding or perioperatively
  - **Fresh whole blood if bleeding or anemic**
  - **Plasma if not bleeding or anemic**
  - **Cryoprecipitate preferred for vWDz, fibrinogen deficiency or hemophilia A**

Vitamin K antagonism

- Induce vomiting if known ingestion within several hours
- Activated charcoal and cathartic
- Inject vitamin K 2.5-5 mg/kg
- Then vitamin K 2.5 mg/kg/day PO
  - **Minimum 2 weeks**
  - **Continue until 2 weeks past normal PT**
  - **Recheck PT 2 days after stopping vitamin K**
  - **If elevated again, 2 more weeks vitamin K**

Vitamin K antagonism

- Identify and treat gall bladder, intestinal or nutritional disease that may be contributing
- Avoid drugs that inhibit enzyme that activates vitamin K dependent factors
  - **Vitamin K epoxide reductase**
  - **Sulfonamides and cephalosporins**
- Avoid drugs that decrease protein binding of toxins
  - **Sulfonamides**
  - **Corticosteroids**
  - **Phenylbutazone**
- Avoid drugs that cause thrombocytopenia, thrombocytopathia, etc.

Treating Liver Failure Coagulopathy

- Replace coagulation factors
  - **Plasma 3-5 ml/kg up to every 8 hours**
  - **Transfuse prior to surgery**
  - **Used to incubate with heparin 30 minutes to transfusion, to activate AT3**
    - 50 U/kg added to plasma transfusion
- Or fresh whole blood if anemic or actively bleeding
- Vitamin K 2.5 mg/kg/day as long if PT prolonged

Snake Bite Coagulopathy

- Supportive treatment for snake bite toxicity
- Antivenin accelerates resolution of thrombocytopenia
  - **Must be given within 24 hours of envenomation**
  - **Within 4 hours for maximum effect**
  - **Antivenin will not affect tissue necrosis**
- 2 kinds of antivenin
  - **ACP – contains entire equine IgG to venom**
    - Not effective against Mojave rattlers
    - Half life 60-200 hours
    - 1-5 vials IV, give subsequent vials every 2 hours
    - Measure circumference every 15-30 minutes
    - Continue antivenin until swelling slows or stops

Snake Bite Coagulopathy

- **Fab – contains fragment of ovine IgG to venom**
  - 5x more effective
  - Effective against Mohave rattler and others
  - Shorter half life – must repeat every 18 hours
  - Less likely to cause anaphylaxis or serum sickness
- Premedicate with diphenhydramine
- Skin testing prior to IV administration is controversial – many false positives and negatives
- Thrombocytopenia often resolves within 72 hours
- Heparin and blood products are not likely to help

Snake Bite Coagulopathy

- Serial coags are important because coagulopathy can be delayed
- Serum sickness can occur in 3 days to 3 weeks (immune complex disease)
  - **Fever, joint pain, myalgia, edema, etc.**

Thromboembolism

- Reduce thrombogenesis
  - **Heparin (UF) 200 U/kg SC TID**
    - Prolong PTT to 1.5 x normal
  - **Dalteparin (Fragmin© - LMW heparin)**
    - Dogs 150 U/kg SC TID
    - Cats 180 U/kg q4-6 hrs
  - **Enoxaparin (Lovenox© - LMW heparin)**
    - Dogs 0.8-1 mg/kg TID-QID
    - Cats 1.25 mg/kg q TID
  - **LWMH Monitoring - anti-xA activity at Cornell**
  - **Many argue that heparin therapy helps little if AT3 is low – must give plasma concurrently**

Thromboembolism

- Reduce thrombogenesis
  - **Antiplatelet drugs**
    - Aspirin
      - Cats 5-25 mg/kg PO twice a week
        - » Some use dose as low as 5 mg/cat
      - Dogs 0.5 mg/kg PO BID
    - Clopidogrel (Plavix©)
      - Cats 18.75 mg (1/4 tablet) per cat PO SID
  - **Coumadin – not used much any more**
    - Monitor INR (international Normalization Ratio)
    - Calculate using PTT and coefficients from your lab
  - **Plasma 3-5 ml/kg PRN q8hrs**

Thromboembolism

- Thrombolytic therapy
  - **Risk of reperfusion injury (which can be fatal) is high**
  - **Risk also of smaller emboli causing more problems further downstream**
  - **tPA, streptokinase and urokinase are used**
  - **24-hour monitoring is required to use thrombolytics**

Treating DIC

- Treat the underlying cause
  - **If cause is untreatable, prognosis is dismal**
- Ensure adequate tissue perfusion despite widespread thrombosis
- Replace consumed blood components
- Anticoagulant therapy
  - **Heparin (UF) 50 U/kg SC TID if no gross thrombosis**
    - 200 U/kg SC TID if apparent thrombosis
  - **Dalteparin**

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 5: Hemostatic Abnormalities

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

Acknowledgements

Chapter 63: Bleeding Disorders: Epistaxis and Hemoptysis

- Tracy Gieger
- Textbook of Veterinary Internal Medicine, eds Stephen J Ettinger and Edward C Feldman, 6th Ed 2005

Chapter 64: Petechiae and Ecchymoses

- Mary Beth Callan
- Textbook of Veterinary Internal Medicine, eds Stephen J Ettinger and Edward C Feldman, 6th Ed 2005