

**Practical
Hematology**
Diagnosing
Coagulopathy

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Practical Hematology

1. Determining the cause of anemia
2. Treating regenerative anemias
 - Blood loss
 - Hemolysis
3. Treating non-regenerative anemias
4. Blood & plasma transfusions in general practice
5. Determining the causing of coagulopathies
- 6. Treating coagulopathies in general practice**
7. Finding the source of leukocytosis
8. Bone marrow sampling

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**
 - **MBT**
 - **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/uI**
 - **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/uI**
 - **Bone marrow if severe cytopenias**
- FeLV/FIV in cats, HWAg in dogs
- Coags
 - **PT, PTT/ACT**
 - **MBT 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 Thrombocytopenia

- 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, thrombocytopenia, 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 Mojave 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**