



## HEMOPHILIA A (FACTOR VIII DEFICIENCY)

Case Report  
Ann Della Maggiore, DVM

REVIEWED BY  
THERESA ORTEGA, DVM, DACVIM

### Signalment:

“Caleb”  
7mo MC Chihuahua

**History:** Caleb presented for marked post operative hemorrhage following a routine canine castration on 9/27/08. A regional exploratory surgery was performed by the primary veterinarian following the initial surgery; ligations were visualized and noted to be secure in place. A bandage was placed and Vitamin K, ampicillin, acepromazine, and ketoprofen were administered. Caleb was discharged to the owners with Clavamox drops, acepromazine and ketoprofen syrup. At home, Caleb was very active; the owner administered acepromazine 2.5mg by mouth and placed Caleb in a crate. Two hours later, he was taken out of the crate and bleeding was noted through the bandage around his incision site. No other known medical conditions, no prior bleeding episodes, coughing sneezing, vomiting, or diarrhea had been noted. No change in water intake, urination, or bowel movements. No known toxin exposure (rodenticides or anti-coagulants).

**Clinical Exam:** On exam Caleb was depressed, and hypothermic (99.7). Mucous membranes were pale and there was significant scrotal and prescrotal swelling and ecchymosis, with dried blood around incision site. A small amount of hemorrhagic fluid was noted on incision; he was not actively bleeding. No petechiation or ecchymosis were noted away from the surgical wound.

### Laboratory findings:

9/27/08 Initial PCV/TS: 25%, 4.4 g/dL, PT 12 sec, PTT 131sec, BMBT within 1 min formed clot  
9/28/08 12am PCV/TS: 19%, 3.6 g/dL, blood smear 5-8 platelets per high powered field  
7am PCV/TS: 25%, 3.5 g/dL (post pRBC transfusion)  
9/29/08 5am PCV/TS: 39%, 6.2 g/dL (post plasma and pRBC transfusion)  
10/01/08 Cornell Animal Health Diagnostics Center: Hemophilia panel: APTT: 28.0 sec (RR 10-17), PT: 14.0 sec (RR 11-16), Factor VIII:c activity 1% (RR:50-200), Factor IX:c activity 166% (RR:50-150)

\*Note: Severe hemophilia is characterized by factor VIII:c activity < 2%

**Diagnostic findings:** Brief emergency ultrasound showed no free abdominal fluid.

**Diagnosis:** Hemophilia A (Factor VIII deficiency)

**Treatment/Management:** At initial presentation Caleb, received a 30ml/kg IV bolus of Normosol R over 20 minutes for volume resuscitation and then was started on Normosol R qs 20meq/L KCL IV at twice maintenance to correct dehydration over the next 24 hours. Initial laboratory results showed no coagulation defects (PT, PTT, And BMBT were normal). During volume resuscitation, Caleb's anemia progressed; he was cross matched and transfused with 40 ml packed RBC over a four hour period. Post transfusion his IV fluids were decreased to 14ml/hr. On 9/28, Caleb's PCV was 25%; another transfusion was started and 50 ml of packed RBC were given over 3.5 hours. Increased ecchymosis, swelling, and bleeding from the incision site were noted. Blood was pulled for a Hemophilia panel and shipped to the Cornell Diagnostics center. Fresh frozen plasma was started and 60mls were transfused over several hours. The scrotal site remained swollen, and continued to ooze blood throughout the day. The right scrotal area and right inguinal area developed an asymmetrical swelling. On 9/29, Caleb's scrotal ecchymosis and swelling progressed, but scrotal bleeding ceased. Caleb was weaned off IV fluids, and started on tramadol for pain.

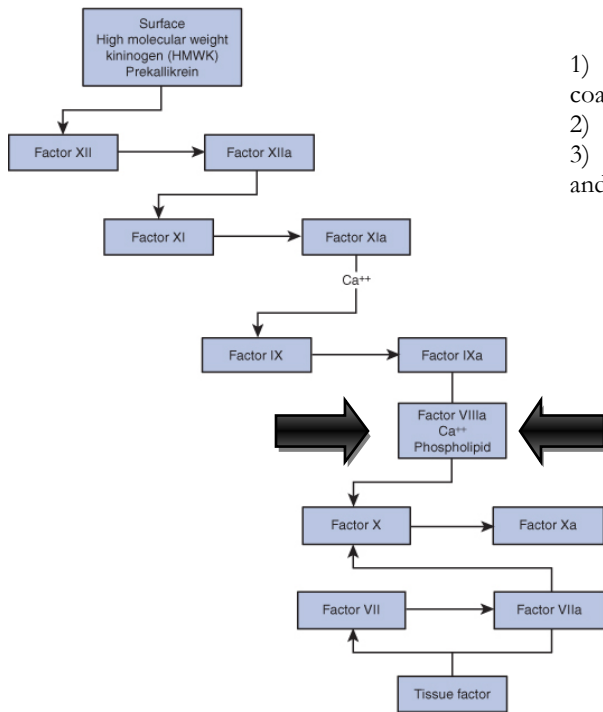
**Follow-up care:** At the time of discharge Caleb's bleeding had stopped, packed cell volume remained steady, and ecchymoses were resolving. The owner was directed that throughout Caleb's life it is imperative to monitor for bumps, swellings, or bruising that might signal another bleeding event. Any trauma could lead to further complications; therefore if bleeding is ever suspected to apply pressure and contact a veterinarian. The owner was also advised to invest in cryoprecipitate which she would keep frozen, and if Caleb was to have another bleeding episode she would take it to her veterinarian for administration. Follow up care was provided by the primary veterinarian. Phone discussion 3 months after discharge revealed that Caleb was doing well, and had not had further bleeding episodes to date.

### Discussion:

Hemophilia A is considered the most common congenital coagulopathy seen in domestic animals, and was first reported over 60 years ago [1,2,3]. It is an X chromosomal recessive inherited trait, and is most widely documented in dogs, specifically the German Shepherd [1]. Hemophilia A is a deficiency in functional factor VIII due to a spontaneous mutation in a gene on the X chromosome. Hemophilia A in humans is the result of decreased production of factor VIII or production of a dysfunctional factor VIII. This

change usually occurs due to a base substitution or deletion [1, 3]. This is an X chromosomal recessive trait; usually males are affected and females are asymptomatic carriers of the defective gene. Interestingly, one of the first recognized signs of Hemophilia A in dogs is the occurrence of large hematomas in the scrotum following castration[1].

Factor VIII interacts with calcium, phospholipid and factor IX within the coagulation pathway to activate Factor X. It also plays an important role in the stabilization of the hemostatic plug and fibrin formation (figure 1) [1,2]. Without factor VIII, the speed in which factor X is produced is greatly reduced and the stability of the hemostatic plug is compromised. The initial platelet plug forms, but the fibrin reinforcement is delayed or absent leading to rebleeding [1,2]. Typical signs include bleeding into body cavities, and large hematomas [1,2]. Screening tests for Hemophilia A include a prolonged activated partial thromboplastin time (APTT) and a normal prothrombin time (PT). Definitive diagnosis is made by demonstrating a deficiency in factor VIII by a specific assay [1,2,3]. Spontaneous bleeding is expected to occur when factor activity is less than 5% [2]. Factor VIII specific assay may not be able to differentiate between carrier females and clear (unaffected) females. Therefore pedigree analysis should be performed to determine carrier status and breeding recommendations should be made[3].



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Figure 1

**Figures:**

- 1) Intrinsic and extrinsic coagulation cascade
- 2) Caleb at discharge
- 3) Caleb's ecchymosis and scrotal swelling



Figure 2



Figure 3

Hemophilia animals require diligent supportive care during an episode of bleeding; therapy should be directed toward supporting hemostasis (bandages, cautery, confinement to prevent over activity). Depending on the severity of the bleeding, exogenous coagulation factors should be provided (cryoprecipitate, fresh frozen plasma, or fresh whole blood- dependent on which is clinically indicated). Cryoprecipitate contains concentrates of Factor VIII ten times higher than that found in plasma, and allows smaller volumes to be transfused to achieve the same effect as plasma [1]. Human factor VIII is available, although difficult to acquire in veterinary institutions due to high demand in human hospitals. Ideally Human factor VIII could be transfused; good therapeutic effects are seen when factor VIII levels are increased to 15 to 30 U/dL. Unfortunately, factor VIII transfusions have been shown to induce factor VIII inhibitors [4]. Desmopressin (DDAVP) has been studied in humans and is suspected to cause release of factor VIII from storage sites within the hepatocyte. The clinical efficacy of this increase has not been fully studied, and potential side effects include vasodilation, water retention, hyponatremia, and thrombosis [5]. More recent studies have used the canine model to study hemophilia A in humans. Adenoviral vectors expressing human factor VIII have been shown to correct the Factor VIII defect within 48 hours. The effects last for one to two weeks before dogs begin making antibodies to human Factor VIII [6]. Since many of these treatment options are experimental, the recommended treatment involves limiting trauma/activity, avoiding medications that will alter homeostasis (ie NSAIDS, phenothiazines) [5], and exogenous coagulation factors as needed.

**References:**

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