Effect of desmopressin acetate administration on primary hemostasis in Doberman Pinschers with type-1 von Willebrand disease as assessed by a point-of-care instrument

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Objective—To evaluate primary hemostasis following administration of desmopressin acetate (DDAVP) to Doberman Pinschers with type-1 von Willebrand disease (vWD).

Animals—16 nonanemic Doberman Pinschers with type-1 vWD.

Procedure—Closure time (CT), defined as time required for occlusion of an aperture by a platelet plug assessed within the point-of-care instrument, plasma von Willebrand factor (vWF) concentration, and buccal mucosal bleeding time (BMBT) were determined before and 1 hour after administration of DDAVP (1 µg/kg, SC).

Results—Baseline closure times measured with adenosine diphosphate ([ADP-CT], 108 to > 300 seconds; reference range, 52 to 86 seconds) and epinephrine ([EPI-CT], 285 to > 300 seconds; 97 to 225 seconds) as platelet agonists were prolonged in all dogs. Following DDAVP administration, ADP-CT (59 to 186 seconds) was significantly shortened from baseline, but there was no decrease in EPI-CT. Although mean plasma vWF concentration increased significantly after DDAVP administration, only 1 dog had an increase of > 35 U/dL. There was no correlation between increase in plasma vWF concentration and shortening of the ADP-CT. Baseline BMBT was prolonged in 12 of 14 dogs, with significant shortening of BMBT after DDAVP administration in 6 of 7 dogs. In vitro replacement of vWF-deficient plasma with plasma from an unaffected dog shortened the ADP-CT, whereas in vitro addition of DDAVP had no effect.

Conclusions and Clinical Relevance—Administration of DDAVP to Doberman Pinschers with type-1 vWD resulted in improved hemostatic function, as assessed by the point-of-care instrument and shortening of BMBT, despite minimal increase in plasma vWF concentration. (*Am J Vet Res* 2002;63:1700–1706)

Desmopressin acetate (DDAVP), a synthetic analogue of the neurohypophyseal hormone arginine vasopressin, has been used to control bleeding in a variety of hemostatic disorders, but most commonly **von Willebrand disease (vWD)**, in humans and dogs. In humans, administration of DDAVP results in a 2- to 5-fold increase in plasma **von Willebrand factor (vWF)** concentration in clinically normal individuals, as well as those with type-1 vWD,[1-3] whereas the effect of DDAVP on vWF concentration in clinically normal dogs and dogs with type-1 vWD is much less dramatic, with an approximate 50% increase above baseline in some but not all dogs tested.[4-6] Because the increase in bleeding time and plasma vWF concentration have not been found to be reliable indicators of response to DDAVP in dogs, there is a need for a means to evaluate objectively changes in primary hemostasis in response to treatment.

A recently introduced point-of-care primary hemostasis function analyzer[a] evaluates in vitro platelet adhesion and aggregation by simulating high shear blood flow at an injured blood vessel wall. This instrument allows simple and accurate detection of vWD and intrinsic platelet function defects (ie, thrombopathia) in humans[7-12] and dogs.[13,14] The purpose of the study reported here was to evaluate improvement in primary hemostasis following administration of DDAVP to Doberman Pinschers with type-1 vWD using this point-of-care instrument, and to determine whether such an improvement was associated with an increase in plasma vWF concentration, shortening of the **buccal mucosal bleeding time (BMBT)**, and control of surgical or spontaneous bleeding.

Materials and Methods

Animals—Blood was collected from 16 client-owned Doberman Pinschers with type-1 vWD diagnosed on the basis of plasma vWF concentration < 35 U/dL (equals 35% of a pooled normal control) as determined by use of a validated ELISA.[15,b] Dogs with vWD ranged in age from 6 months to 11 years and included 9 males (2 sexually intact, 7 castrated) and 7 females (1 sexually intact, 6 spayed). None of the dogs received blood component treatment or DDAVP during the month prior to our study. Response to DDAVP was evaluated perioperatively in 5 dogs undergoing cervical disc fenestration, ovariohysterectomy, subcutaneous mass removal, castration, or cranial cruciate ligament repair, in association with diagnostic procedures in 4 dogs (oral biopsy [n = 1], myelogram [1], and arthrocentesis [2]) and during episodes of spontaneous oral or gastrointestinal surface bleeding in 2 dogs. In addition, 5 Doberman Pinschers with vWD, but without clinical signs, were tested. Blood was also collected from 1 healthy dog with normal primary hemostatic function, as assessed by the point-of-care instrument for in vitro plasma replacement studies. The study protocol was approved by the Committee for the Use of Client Owned Animals in Research at the University of Pennsylvania, and informed owner consent was obtained.

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Blood sample collection and DDAVP testing—All blood samples (4.5 mL) were obtained with minimal trauma via cephalic, saphenous, or jugular venipuncture (20-gauge needle) and collected directly into evacuated tubes containing one-tenth the volume of 3.8% sodium citrate as the anticoagulant.[c] Platelet count (reference range, 150,000 to 400,000 platelets/µL) and PCV (reference range, 38 to 55%) were within the reference range for all dogs at the time of testing of primary hemostasis.

After obtaining baseline citrated blood samples for assessment of primary hemostasis by use of the point-of-care instrument[a] and measurement of plasma vWF concentration, DDAVP[d] at a dose of 1 µg/kg was administered SC,[4,5] and citrated blood samples were collected 1 hour later for repeat testing. An aliquot of blood was stored at room temperature (approx 21°C) for < 1 hour prior to testing with the point-of-care instrument, and the remainder was centrifuged (1,000 × *g* for 5 minutes); the plasma was separated and frozen at -70°C until measurement of vWF concentration by ELISA. To assess the reproducibility of a dog's response to DDAVP, this procedure was repeated in 2 dogs at 8 to 12 months after initial testing. For patients undergoing surgical or diagnostic procedures or experiencing spontaneous bleeding, the need for blood component therapy and subjective assessment of extent or control of bleeding following DDAVP administration were recorded.

Assessment of primary hemostasis—The point-of-care instrument[a] was used according to the manufacturer's instructions and has been described in detail elsewhere.[13,16,17] Briefly, the system consists of a microprocessor-controlled instrument and disposable test cartridges. Fresh (< 1 hour, kept at room temperature [approx 21°C]) citrated blood (800 µL) is placed in the sample reservoir of a disposable test cartridge with a membrane containing collagen (2 µg of equine fibrillar collagen type-1) and **adenosine diphosphate** (**[ADP]**; 50 µg) or **epinephrine** (**[EPI]**; 10 µg of epinephrine bitartrate). Following incubation of a sample in the reservoir at 37°C for approximately 3 minutes, blood is aspirated through a central aperture (diameter, 150 µm) in the membrane under a steady vacuum that creates high shear conditions through a capillary. In response to stimulation by collagen and ADP or EPI and the shear stresses at the aperture, platelets adhere and aggregate on the collagen surface surrounding the aperture and form a plug that ultimately occludes the aperture. The instrument monitors blood flow through the aperture and reports the time required for full occlusion of the aperture as the **closure time (CT)** in seconds; CT is indicative of primary hemostasis in the sample. The cutoff time of the instrument is typically set at 300 seconds; thus, if the aperture remains open at 300 seconds, CT is reported as > 300 seconds.

An instrument self-test was performed daily prior to evaluating blood samples to ensure proper functioning and cleaning of the automated system. **Adenosine diphosphate-closure time (ADP-CT)** was determined before and after DDAVP administration in all 16 dogs; **epinephrine-closure time (EPI-CT)** was measured before and after DDAVP administration in 14 and 9 dogs, respectively. All blood samples were evaluated with each agonist in duplicate.

Determination of buccal mucosal bleeding time—Buccal mucosal bleeding time was determined before DDAVP administration in 14 dogs and also 1 hour after DDAVP administration in 7 dogs by use of a 2-bladed (5-mm long, 1-mm deep), spring-loaded device[e] to incise the upper lip mucosa (reference range, ≤ 3.6 minutes) as previously described.[18,19]

In vitro plasma replacement studies—To determine the effect of replacing plasma from a vWF-deficient dog with plasma from a healthy dog with normal primary hemostatic function, as assessed by the point-of-care instrument, platelet poor plasma was prepared from fresh citrated blood from each of 2 Doberman Pinschers with vWD and a healthy dog by centrifugation at 1,000 × *g* for 5 minutes. After removing the platelet poor plasma (supernatant), an equal volume of plasma from a healthy dog was added to the samples from the vWF-deficient dogs and gently mixed with the cellular portion. Closure times, measured with ADP as the platelet agonist, and plasma vWF concentrations were determined before and after plasma replacement.

In vitro addition of DDAVP—To determine the effect of in vitro addition of DDAVP to citrated whole blood from vWF-deficient dogs, DDAVP at final concentrations of 0.0125, 0.025, and 0.05 µg/mL were added to citrated whole blood samples from 5 Doberman Pinschers with vWD and incubated at room temperature (approx 25°C) for 1 hour, after which time the ADP-CT and plasma vWF concentration were determined.

Statistical analyses—Differences in ADP-CT, EPI-CT, plasma vWF concentration, and BMBT before and after DDAVP administration were analyzed by use of a paired *t*-test. Closure times of > 300 seconds were assigned a value of 300 for calculations. Similarly, if a BMBT test had been stopped and the result recorded as > X minutes, the BMBT was assigned a value of X for calculations. Linear regression analysis was performed, and the Pearson correlation coefficients were calculated to determine whether there was a relationship between shortening of the ADP-CT and change in plasma vWF concentration after DDAVP administration, shortening of the ADP-CT and shortening of the BMBT after DDAVP administration, and change in plasma vWF concentration and shortening of the BMBT after DDAVP administration. Results were considered significant at $P < 0.05$.

Results

Reference ranges for CT for healthy dogs have been previously established in our laboratory; ADP-CT and EPI-CT ranged from 52 to 86 and 97 to 225 seconds, respectively.[13] The baseline ADP-CT and EPI-CT were prolonged in all 16 Doberman Pinschers with vWD, ranging from 108 to > 300 and 285 to > 300 seconds, respectively, when compared with the reference ranges (**Fig 1**). One hour following an SC injection of DDAVP, the ADP-CT was significantly ($P < 0.001$) shortened from baseline (values before DDAVP administration) in all 16 dogs and ranged from 59 to 186 seconds. Only the sample from the dog with the shortest baseline value of 108 seconds had an ADP-CT (59 seconds) after DDAVP administration that was within reference range. Response to DDAVP, as assessed by shortening of the ADP-CT, was reproducible in the 2 dogs tested again at 8 to 12 months. In both dogs, the baseline ADP-CT was > 300 seconds. The ADP-CT after DDAVP administration was 95 and 110 seconds for the first dog and 125 and 140 seconds for the second dog. There was no significant ($P = 0.18$) shortening of the EPI-CT after DDAVP administration, which remained measurably unchanged (> 300 seconds) in 7 of 9 dogs and only decreased to 161 and 216 seconds in the other 2 dogs.

Doberman Pinschers with vWD had baseline plasma vWF concentration ranging from 0 to 24 U/dL. Although there was a significant ($P = 0.02$) increase in

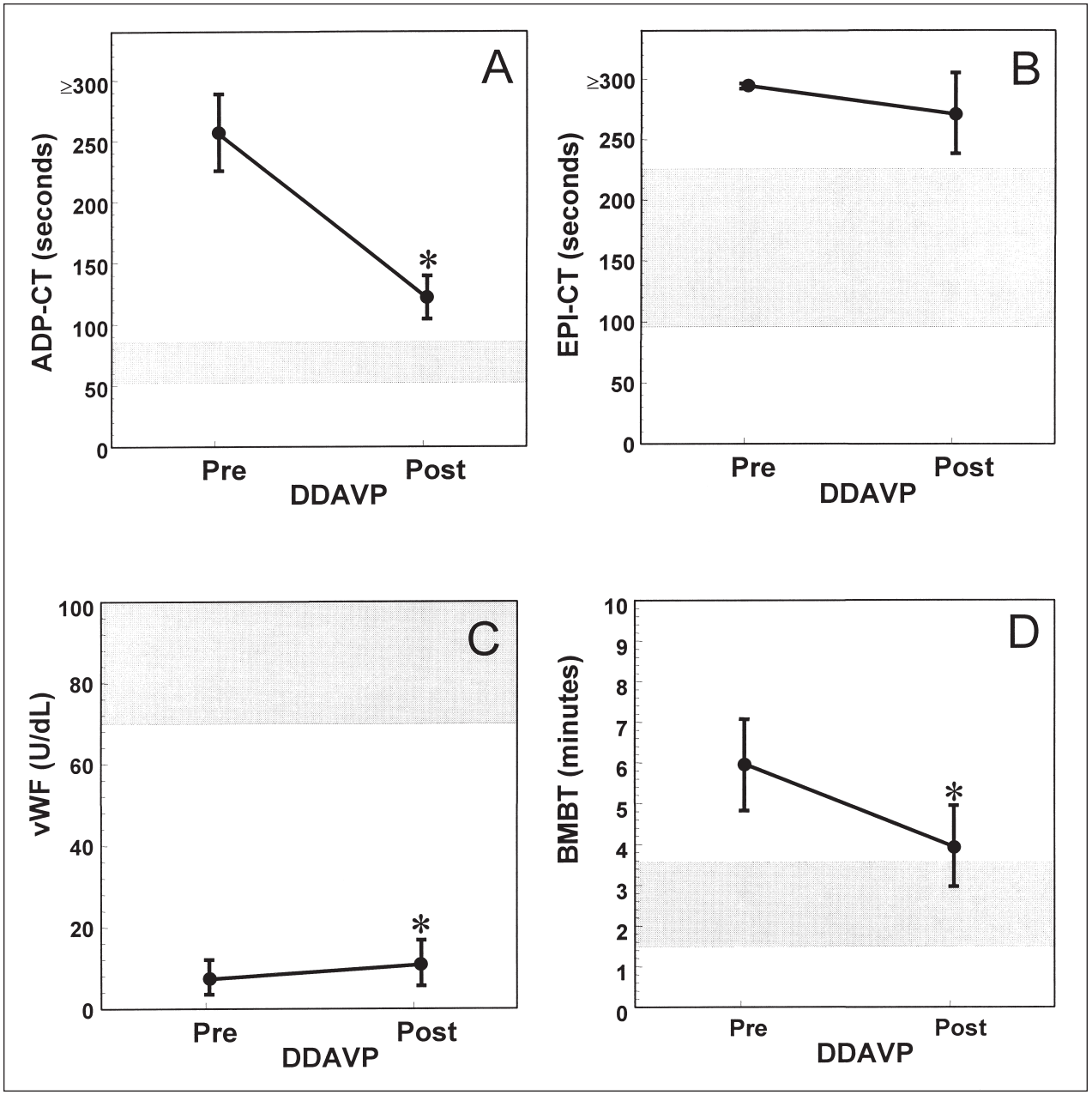

Figure 1—Mean (± SD) changes in variables of primary hemostasis in Doberman Pinschers with type-1 Von Willebrand disease before (Pre) and 1 hour after (Post) administration of desmopressin acetate (DDAVP; 1 µg/kg, SC). A—Closure time as determined with the point-of-care instrument using the adenosine diphosphate cartridge (ADP-CT). B—Closure time as determined with the point-of-care instrument using the epinephrine cartridge (EPI-CT). C—Plasma von Willebrand factor (vWF) concentration. D—Buccal mucosal bleeding time (BMBT). Shaded areas represent reference range values. *Significantly ($P < 0.05$) different from baseline or values before DDAVP administration.

mean plasma vWF concentration 1 hour after DDAVP administration, there was no change in plasma vWF concentration following DDAVP administration in 9 dogs, and increases in the remaining 7 dogs ranged from 38 to 138% (mean ± SD, 77 ± 33%; median, 67) above the baseline measurement (Fig 1). The plasma vWF concentration after DDAVP administration was > 35 U/dL in only 1 dog (40 U/dL) and in the other dogs ranged from 0 to 29 U/dL (12 ± 11 U/dL; median, 11). However, analysis by linear regression revealed no significant correlation ($P = 0.88$, $r = 0.04$) between the increase in plasma vWF concentration and shortening of the ADP-CT after DDAVP administration.

Buccal mucosal bleeding times were prolonged (4 to > 10 minutes) in 12 of 14 dogs at baseline, and there was a significant ($P = 0.02$) shortening of the BMBT observed after DDAVP administration, with shortening by 2 to > 6 minutes evident in 6 of 7 dogs tested (Fig 1). The BMBT after DDAVP administration ranged from 2.8 to 6 minutes, and 3 dogs had BMBT within the reference range. The correlation ($P = 0.08$, $r = 0.64$) between shortening of the ADP-CT and BMBT after DDAVP administration was not significant; however, the number of dogs to compare was small, and the termination of the baseline BMBT at various time points (eg, > 6 minutes or > 8 minutes) by different

clinicians makes it difficult to accurately determine the true degree of shortening of the BMBT after DDAVP administration. There was no correlation ($P = 0.85$, $r = 0.08$) between the increase in plasma vWF concentration and shortening of the BMBT after DDAVP administration.

The 5 Doberman Pinschers with vWD given DDAVP and undergoing surgical procedures did not have excessive bleeding or require any blood products, cryoprecipitate, fresh-frozen plasma or packed RBC, during or following surgery, despite the fact that blood type-compatible components were readily available. Similarly, the 4 dogs that received DDAVP prior to diagnostic procedures did not have an increased bleeding tendency or require blood components during or following these procedures. One dog with oral bleeding from an undifferentiated sarcoma and 1 dog with gastrointestinal bleeding and inflammatory bowel disease received fresh-frozen plasma (10 mL/kg) 1 hour following administration of DDAVP because of persistent bleeding, and the bleeding continued despite administration of plasma.

In vitro replacement studies in which plasma from 2 vWF-deficient dogs (plasma vWF concentrations, 1 and 7 U/dL) was removed and replaced with an equal volume of plasma from a healthy dog (plasma vWF concentration, 57 U/dL) resulted in shortening of the ADP-CT in both dogs, with the baseline ADP-CT of > 300 seconds decreasing to 69 and 97 seconds. After replacement, plasma vWF concentrations in the 2 reconstituted samples were 60 and 47 U/dL, respectively.

In vitro addition of DDAVP (0.0125 to 0.05 µg/mL citrated blood), at a concentration expected to exceed the in vivo plasma concentration after DDAVP administration, and incubation for 1 hour had no effect on ADP-CT (baseline mean, 242 seconds; with DDAVP, 261 seconds) in samples from 5 Doberman Pinschers with vWD. Plasma vWF concentration baseline mean, 4 U/dL; with DDAVP, 1 U/dL remained unchanged after incubation with DDAVP in samples from 2 dogs in which it was measured.

Discussion

von Willebrand disease is the most common hereditary bleeding disorder in dogs and occurs in > 70 breeds. The prevalence of type-1 vWD in the Doberman Pinscher has been estimated to be as high as 70%.[20] A splice site mutation seems to be responsible for the vWF deficiency in Doberman Pinschers.[21] Affected dogs appear to be at risk when their vWF concentration is < 35 U/dL[21] and may have severe, uncontrolled bleeding following surgery or trauma or spontaneous mucosal surface bleeding. Cryoprecipitate and, if cryoprecipitate is not available, fresh-frozen plasma are the mainstay of treatment during episodes of severe bleeding, but may also be administered prophylactically to dogs with vWD expected to have excessive bleeding or undergoing surgery where bleeding would be difficult to control. Desmopressin appears to have successfully prevented or controlled surgical and spontaneous bleeding in dogs with vWD, but not all vWF-deficient dogs may respond to DDAVP. In our study, administration of DDAVP to Doberman Pinschers with type-1 vWD resulted in improved hemostasis, as assessed by the point-of-care instrument, and shortening of the BMBT despite minimal increase in plasma vWF concentration.

Because there is a variable response to DDAVP in humans with vWD, a test dose of DDAVP has been recommended prior to relying on this medication for control of bleeding.[22-25] The point-of-care primary hemostasis function analyzer has been evaluated in humans to identify quickly potential "responders" to DDAVP. Infusion of DDAVP (0.3 µg/kg, IV) to human patients with type-1 vWD resulted in normalization of CT in all patients with both the ADP and EPI cartridges, as well as normalization of the bleeding time in most patients at 3 minutes to 4 hours after injection.[7,26] In our study, a noticeable shortening of the ADP-CT was observed in all 16 Doberman Pinschers with vWD 1 hour following administration of DDAVP (1 µg/kg, SC). Although DDAVP led to normalization of ADP-CT in only 1 dog of our study, there was a significant shortening of ADP-CT, with the decrease ranging from 49 to ≥ 203 seconds (mean and median of 135 and 128 seconds, respectively). However, unlike in humans, there was no significant shortening of the EPI-CT after DDAVP administration. Results of a previous study[13] assessing the point-of-care instrument for identification of primary hemostatic disorders in dogs indicate that the reference range for EPI-CT in healthy dogs is broad (97 to 225 seconds), compared with the ADP-CT (52 to 86 seconds). In that study,[13] the EPI-CT was > 300 seconds in 5 apparently healthy dogs without clinical evidence of bleeding or history of ingestion of nonsteroidal antiinflammatory drugs, suggesting that the EPI cartridge may not be useful in dogs. On the basis of results of previous optical aggregometry studies,[27-29] EPI does not consistently induce platelet aggregation in dogs but rather acts to potentiate platelet aggregation by other agonists. Therefore, whether using the point-of-care instrument for identifying dogs with vWD or assessing their response to DDAVP in vitro, use of the ADP cartridge rather than the EPI cartridge is recommended.

In humans with vWD, shortening of the CT following DDAVP administration was generally paralleled by a several-fold increase in plasma vWF concentration.[7] In contrast, there did not appear to be a clear association between shortening of the ADP-CT and increase in plasma vWF concentration in the dogs of our study. The increase in plasma vWF concentration observed following administration of DDAVP to the Doberman Pinschers of our study is similar to the approximately 50% increase over baseline reported in previous studies.[4-6] Overall, the mean increase in plasma vWF concentration over baseline was 34% in our study. However, plasma vWF concentration did not increase at all in 9 dogs, and in the remaining 7 dogs, the mean increase was 77% above the baseline measurement and only 1 dog reached > 35 U/dL, which is considered to be adequate for normal hemostasis. Although there was not a relationship between shortening of the ADP-CT and an increase in vWF concentration, there was an apparent association between shortening of the ADP-CT and shortening of the BMBT after DDAVP adminis-

tration. Shortening of the BMBT 30 to 120 minutes after DDAVP administration has also been previously reported in Doberman Pinschers with vWD, despite a relatively minimal change in plasma vWF concentration.[5]

Although assessed subjectively, administration of DDAVP appears to have resulted in control of surgical bleeding in the dogs of our study, without the need for administration of blood components. However, it is also possible that these dogs may not have bled excessively even without DDAVP, because a prolonged BMBT and the degree of vWF deficiency do not necessarily predict the extent of surgical bleeding, and an untreated control group was not included in our study. In the 2 dogs with spontaneous mucosal surface bleeding as a result of an oral undifferentiated sarcoma and severe lymphoplasmacytic enteritis, vWD likely exacerbated the bleeding tendency, but DDAVP alone and in combination with fresh-frozen plasma was insufficient to control the bleeding as the underlying disease persisted.

The mechanism by which DDAVP improves primary hemostasis in dogs is not completely understood and was not addressed in our study. Although the beneficial hemostatic effects of DDAVP in humans with vWD and hemophilia A have been mainly attributed to increases in plasma concentrations of vWF and factor VIII, respectively, it is recognized that DDAVP is efficacious in hereditary and acquired thrombopathias in human patients who have concentrations within reference range or even high concentrations of vWF and factor VIII, such as in patients with uremia.[22,30-34] It has been proposed that favorable hemostatic effects of DDAVP may be mediated by increased platelet adhesion to the vessel wall as a result of the abluminal secretion of vWF toward the subendothelium; heightened coagulability attributable to increased concentrations of factor VIII, a rate-accelerating factor in the process of fibrin formation; and the fresh appearance in plasma of ultralarge vWF multimers.[22] The appearance of large multimers of vWF has been found in the plasma of humans following administration of DDAVP, and the larger multimers may be more hemostatically effective by supporting, to a greater degree, platelet adhesion to the vascular subendothelium and inducing platelet aggregation under conditions of high shear forces.[35] Likewise, an increase in the higher molecular weight forms of vWF in the plasma has been proposed in Doberman Pinschers with vWD[5] and healthy Beagles[36] in response to DDAVP. The vWF multimer analysis was not performed in our study, but the plasma vWF concentrations remained low.

In vitro addition of DDAVP, at concentrations estimated to be similar to or greater than plasma concentrations in vivo, to citrated whole blood from Doberman Pinschers with vWD had no beneficial effect on primary hemostasis as assessed by the ADP-CT. There was no increase in plasma vWF concentration found in blood samples incubated with DDAVP, which may be explained by canine platelets having negligible amounts of vWF and vWF-producing endothelial cells being obviously absent in this test situation. Evaluation of the in vitro effects of DDAVP on the function of human platelets revealed failure to induce either platelet aggregation or surface expression of activation-dependent antigens; however, DDAVP greatly inhibited platelet aggregation response to vasopressin and increased maximal extent of platelet aggregation induced by collagen and ADP, indicating that DDAVP interacts directly with platelets and facilitates their activation via other agonists.[37]

Removal of plasma from a citrated blood sample from 2 vWF-deficient dogs and replacement with an equal volume of plasma from a healthy dog with normal primary hemostasis, as assessed by the point-of-care instrument, led to shortening of the ADP-CT. Although it would have been preferable to have a healthy dog with a within-reference range plasma vWF concentration (≥ 70 U/dL) for the plasma replacement studies, the plasma vWF concentration was measured on batched samples after the studies were performed, and the dog was selected on the basis of an ADP-CT that was within reference range, a result immediately available. The finding of a normal ADP-CT with a plasma vWF concentration of 57 U/dL supports our notion that the point-of-care instrument mainly identifies dogs at increased risk of bleeding, that is, dogs with plasma vWF concentration < 35 U/dL. Because an abnormal result (ie, prolonged CT) from the point-of-care instrument used in our study does not differentiate between vWD and an intrinsic platelet function defect (it is assumed that patient is determined to have a platelet count and PCV within reference range prior to testing), the ability to shorten or correct the prolonged ADP-CT by replacing an affected dog's plasma with that of a healthy dog would lend support for a diagnosis of vWD rather than a thrombopathia. Because there is typically a several-day delay from sample submission to determination of plasma vWF concentration via ELISA, in vitro replacement of plasma as described above may facilitate an earlier diagnosis of vWD with the point-of-care instrument.

Our study focused on evaluation of the effects of DDAVP on primary hemostasis in Doberman Pinschers with type-1 vWD. Other breeds of dogs with vWD were not studied, so it is uncertain whether other dogs with vWD will respond similarly. In addition, there were no patients in our study in which the ADP-CT was evaluated after receiving cryoprecipitate or fresh-frozen plasma from either a regular blood donor or one who had been treated with DDAVP prior to blood donation to determine the effects of blood component treatment on primary hemostasis. Results of studies[7,26] in humans with vWD have indicated a variable effect of vWF concentrates and cryoprecipitate on shortening of the CT, depending on the type of vWD, with those patients having type-1 vWD with platelet vWF concentrations within reference range having the greatest shortening of the CT. Cryoprecipitate has been observed to have a greater effect on CT than vWF concentrates, an effect attributed to the large proportion of high molecular weight multimers of vWF present in cryoprecipitate, but not the vWF concentrates.[f] The variable response to vWF concentrates and cryoprecipitate in shortening the CT among the many forms of vWD described

in humans has been attributed mainly to the platelet concentration of vWF; normalization of plasma vWF concentration but failure to correct the platelet vWF deficiency leads to normalization of the von Willebrand ristocetin cofactor activity, yet has minimal effect on CT.[7,26] The point-of-care instrument is reported to be particularly sensitive to platelet vWF[7,26]; however, interestingly, healthy dogs with negligible platelet vWF concentration,[38,g] as well as DDAVP-treated Doberman Pinschers with vWD, have measurable ADP-CT that are similar to (or even shorter than) the reference ranges established for clinically normal humans. Addition of purified canine vWF to the blood of a dog with type-3 vWD resulted in finite ADP-CT at 10% vWF, and 30% vWF was in the reference range.[14]

The point-of-care instrument not only allows for rapid and sensitive assessment of primary hemostasis in dogs, but it provides an objective assessment of improvement in primary hemostasis in Doberman Pinschers with type-1 vWD following administration of DDAVP. Because all dogs with vWD, whether Doberman Pinschers or other breeds, may not respond to DDAVP, a test dose may be considered with measurement of the ADP-CT before and after DDAVP administration, prior to a surgical procedure. The response to DDAVP appeared to be similar in the 2 Doberman Pinschers tested at a later time point, but more dogs would need to be retested to document reproducibility and predictability. Although the dogs of our study had shortening of the ADP-CT following DDAVP administration and did not require blood transfusion support, we cannot conclude from our study that a positive response to DDAVP will eliminate the need for cryoprecipitate or other blood components for a particular patient. Cryoprecipitate and compatible RBCs should still be made available, even for dogs with an improvement in primary hemostasis following DDAVP administration.

[a]PFA-100, Dade Behring Inc, Miami, Fla.
[b]vWF Zymtec, DMS Laboratories Inc, Flemington, NJ.
[c]Vacutainer, Becton-Dickinson, Rutherford, NJ.
[d]DDAVP rhinal tube, Rhône-Poulenc Rorer Pharmaceuticals Inc, Collegeville, Pa.
[e]Simplate II R, Organon Teknika Corp, Durham, NC.
[f]Chang AC, Jacobs H, Weinstein MJ, et al. The correlation of closure time and von Willebrand factor activity of factor VIII concentrates (abstr). *Blood* 1998;92:184a.
[g]Meyers KM, Wardrop KJ, Helmick CM, et al. Immunohistochemical detection of von Willebrand factor in vascular endothelium but not platelets from plasma deficient VIIIR: AG deficient and control dogs and species differences in platelet VIIIR:AG (abstr). *Fed Proc* 1987;46:424.

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