Reference values for activated coagulation time in cats

Jeff D. Bay, DVM; Michael A. Scott, DVM, PhD; Jerry E. Hans, DVM

Objective—To establish reference values for activated coagulation time (ACT) in cats by use of jugular venipuncture and direct collection of blood into ACT vacuum tubes.

Animals—100 clinically normal cats that were to have elective surgery performed at a private practice.

Procedure—Collection of 3 blood samples for ACT measurement was attempted for each cat at the time of elective surgery: sample 1, obtained before sedation; sample 2, tube 1 of 2 consecutive samples obtained from a single venipuncture of the contralateral jugular vein after sedation with acepromazine and ketamine hydrochloride; and sample 3, tube 2 collected immediately following collection of sample 2 without removing the needle from the vein. Venipuncture quality was rated subjectively on a 3-point scale.

Results—Median ACT were 95 seconds for each sample group. The middle 95% of values ranged inclusively from 55 to 185 seconds (sample 1), 65 to 135 seconds (sample 2), 45 to 145 seconds (sample 3), and 55 to 165 seconds overall (samples 1, 2, and 3). Significant differences in ACT values were not detected between sample groups. Significant relationships between ACT and venipuncture quality or sex of cat were not detected.

Conclusions and Clinical Relevance—With the ACT protocols used, clinically normal cats had ACT of < 65 seconds. The ACT in cats does not appear to be significantly affected by sex, sedation with acepromazine and ketamine, or by moderately traumatic venipunctures. These results refute widespread statements that ACT should be < 65 seconds in healthy cats. Cats with ACT repeatedly > 165 seconds should be further evaluated for hemostatic disorders. (Am J Vet Res 2000;61:750–753)

The activated coagulation time (ACT) test is used to assess coagulation of whole blood via contact activation. The ACT has been widely used to monitor heparinization of human patients1-3 and has been assessed for similar use in dogs4,5 and cats.6 However, the ACT test has usually been recommended as part of a simple, inexpensive, and rapid in-clinic hemostatic screening profile for any congenital or acquired disorder involving intrinsic or common coagulation pathways.1,7-9 Prolonged ACT may be present in patients with hemophilia,10,11 vitamin K deficiency or antagonism,12-14 hepatic failure, and consumptive coagulopathies.15 Evidence for any of these disorders, therefore, can be quickly and inexpensively gathered in-clinic, without waiting for results of more expensive testing by outside laboratories.

Several procedures have been developed to measure ACT, and recent procedures with relatively small blood volume requirements have been applied to dogs.16 Most commonly, however, a standard volume of blood (2 ml) is collected into preheated commercial test tubes (ACT tubes) containing siliceous (diatomaceous) earth as an activator of coagulation. Mixing of blood with siliceous earth activates the intrinsic coagulation pathway. Tubes are maintained at 37 or 38 C until the endpoint of the test, when a clot first begins to form. Time from blood contacting siliceous earth until the first definite sign of a clot is the ACT.

Expected ACT for cats are widely reported as < 65 to 75 seconds,17-26 but those reports are largely based on a single study of 22 cats from which samples were collected via jugular catheters.8 In contrast to these reports, but consistent with the authors’ experience, 3 veterinary reference textbooks27-29 indicate that ACT in cats may be similar to those of dogs (70 to 120 and 60 to 125 seconds), although no data are available. The primary purpose of the study reported here was to establish reference values for ACT in cats, using a clinically relevant method of direct jugular venipuncture, with collection of blood into vacuum tubes. Secondary objectives were to evaluate effects of acepromazine and ketamine hydrochloride sedation on ACT, because chemical restraint of cats may sometimes be necessary for successful jugular venipuncture; to determine if ACT of consecutive samples collected from single venipuncture sites differ significantly, because a 2-tube collection method would theoretically be helpful in minimizing any procoagulant effects of traumatic collection; and to determine if venipuncture quality significantly affects ACT.

Materials and Methods

Animals—One hundred cats of various ages that were to undergo elective surgery or dental prophylaxis were tested after obtaining owner consent for 3 jugular venipunctures. Age, sex, breed, and weight were recorded for each cat. Physical examination of all cats indicated they were free of...
any clinical disease that may influence hemostasis. None of the cats had signs of hemostatic disease.

ACT—Evacuated glass ACT tubes* were used for collection of blood. Two milliliters of blood were drawn by jugular venipuncture through 1-in, 22-gauge, single-use vacuum tube needles into tubes preheated in a 37°C heating block. Quality of each venipuncture was graded as 1 (blood was collected easily), 2 (some difficulty with venipuncture), or 3 (traumatic venipuncture). Partial samples and samples collected slowly because of poor blood flow were not used. A timer was started when blood first contacted siliceous earth in the tube. After samples were obtained, tubes were inverted 5 times and immediately placed back into the heating block. At 45 seconds, tubes were briefly removed every 10 seconds and gently tipped to assess for clotting. Time to formation of the first definite sign of clotting was recorded as the ACT. An initial incubation period of 45 seconds was used in place of the typically described 60 seconds24 because of the reported short ACT in cats2 and because ACT < 60 seconds have been reported in clinically normal dogs.28 Following the first ACT measurement (sample 1), cats were sedated with a mixture of acepromazine and ketamine, administered IV (0.08 and 8 mg/kg of body weight, respectively) or IM (0.2 and 20 mg/kg, respectively), and the same procedure was immediately repeated using the contralateral jugular vein (sample 2). In addition, when blood flow permitted, a second sample (sample 3) was collected from the same venipuncture site to compare results between the 1- and 2-tube collection methods.

Statistical analyses—Relationship between ACT and quality of venipuncture was assessed by use of the Spearman rank correlation for nonparametric data. The Wilcoxon signed rank test was used to compare differences in ACT with the various collection conditions (sample 1 vs sample 2 and sample 2 vs sample 3). A Kruskal-Wallis test was used to determine whether ACT varied significantly by sex of cat. Values of \( P < 0.05 \) were considered significant.

Results

Five cats were eliminated from the study because a sufficient quantity of blood was not obtained or rate of blood flow during collection was too slow for all 3 samples. Of the 95 cats tested, 44 were sexually intact males, 4 were castrated males, 42 were sexually intact females, and 5 were spayed females. Domestic shorthair (n = 64) and domestic longhair (24) cats predominated, but Siamese (4), Siamese mixed-breed (1), Maine Coon (1), and Persian (1) cats were also tested. Body weights ranged from 1 to 6.25 kg (median, 3.25 kg) in the 92 cats for which body weights were recorded. Procedures to be performed included castration, ovariohysterectomy, oenorchectomy, and dentistry. Because cats used in this study were undergoing elective surgical procedures, most of them were young. Ages ranged from 3 months to 7 years (mean and median, 15 and 7 months, respectively). Five cats had flea allergy dermatitis (1 was severe), 1 cat was thin, 1 had psychogenic alopecia, and 1 had positive FeLV test results.

For most cats, all 3 ACT samples were not obtained because of difficulties in drawing blood from some uncooperative cats or because of the difficulty in maintaining adequate blood flow with the vacuum tube collection system in some instances. Therefore, data were analyzed by sample group, rather than by differences among samples for individual cats.

The median ACT values were identical for each sample group despite minor differences in the distributions of the values (Table 1). Differences in ACT between sample 1 and sample 2 (without sedation vs with sedation) and between sample 2 and sample 3 (1- vs 2-tube collection) were calculated (Wilcoxon signed rank test). Because of missing data in each sample group, there were 26 and 55 usable pairs of differences, respectively. Significant differences in ACT were not detected between sample 1 and sample 2 (\( P = 0.42 \)) or between sample 2 and sample 3 (\( P = 0.14 \)).

When ACT were grouped according to venipuncture quality, the group with the most traumatic venipunctures had the lowest median ACT (Table 2). However, a significant relationship was not detected between ACT and venipuncture quality in this population, as determined by the Spearman rank correlation (\( r_s = -0.030 \)).

Because of the small number of spayed females (n = 5) and castrated males (4) in the study population, ACT for all females were compared with those of all males in each sample category (sample 1, sample 2, and sample 3), without regard to neuter status. Neither consistent nor significant differences were detected using the Kruskal-Wallis test (\( P = 0.52, 0.08, \) and 0.77, respectively).

Discussion

We are aware of only 1 study in which ACT reference values were determined in cats.24 Methods used for blood collection in that study, however, were not those
used most commonly in a clinical setting, and results were not consistent with our clinical observations. We determined ACT reference values on the basis of data obtained from 95 cats using blood collected via jugular venipuncture through vacuum tube needles. Using the central 95% of ACT values for each sample collection method, cut-offs for high values among sample groups could be suggested for each method. However, distributions were similar (Table 1), and significant differences in ACT were not detected among the groups. Therefore, we suggest that 165 seconds, the upper limit of the central 95% of all 177 ACT combined, is a reasonable cut-off for high ACT values in cats.

Using this proposed upper reference limit, 6 ACT were prolonged in 4 cats in this study. These prolonged ACT did not appear to be associated with venipuncture quality, because ACT values > 165 seconds were observed in each of the 3 venipuncture quality categories. One of these cats consistently had ACT > 165 seconds (245, 185, and 185 seconds) but had no clinical evidence of a hemostatic disorder before or after onychectomy was performed. This cat may have had a deficiency of factor XII, but further testing was not performed. Factor XII deficiency, the most common congenital coagulation disorder in cats, results in delayed activation of the intrinsic coagulation cascade in vitro without clinically detectable hemostatic abnormalities.31 This disorder is usually discovered as a prolongation of ACT or activated partial thromboplastin time during coagulation testing for other reasons.

Problems that may be encountered with ACT measurement in cats include difficulties in obtaining blood from uncooperative cats and difficulties in maintaining adequate blood flow with a vacuum tube collection system. Sedation of the cat may alleviate some of these difficulties. Comparing ACT between unsedated (sample 1) and sedated (sample 2) groups of cats revealed that sedation with acepromazine and ketamine had no significant effect on the results. Furthermore, ACT values were within 1 inspection interval (10 seconds) of each other in more than two-thirds of the 55 cats for which both sample 2 and sample 3 ACT values were measured (data not shown). These findings suggest that a 1-tube collection method is generally adequate for measuring ACT. Further support for this conclusion was the lack of a significant relationship between ACT and venipuncture quality. However, the shortest median and individual ACT were seen in quality 3 samples, and there was greater dispersion of ACT in the quality 3 group despite there being fewer samples (Table 2). Therefore, it is possible that the ACT may be shortened by traumatic venipuncture in some cats.

In studies in humans, it has been demonstrated that differences in sex may influence coagulation, with women having higher clotting factor concentrations and mildly shorter clotting times than men.32-34 To our knowledge, relationships between sex and coagulation have not been evaluated in cats. In our comparison of ACT between male and female cats in this population, significant differences were not found.

In humans, clotting factors increase in concentration with advancing age. Concentrations of coagulation inhibitors also increase with age, but to a lesser extent.35-38 Clotting activity appears to be favored, however, as evidenced by increases in coagulation activation markers in older humans.39,40 Whether the described changes would affect ACT in humans is unknown. The study population reported here overrepresents young cats, so it is possible that ACT in older cats may differ mildly from those of the cats in this study. To our knowledge, however, a relationship between age and coagulation has not been reported in cats.

Results of this study are directly applicable to clinical settings, because data were generated in a private practice with client-owned cats, using widely available, inexpensive materials. However, results are only applicable to the method used. Syringe collection (versus vacuum tube collection), differences in the initiation and timing of clot inspection, differences in incubation temperatures, and individual operator variations may alter results. With the protocols used herein, ACT of ≤ 165 seconds should be considered normal in cats. Cats with ACT repeatedly > 165 seconds should be further evaluated for specific disorders of the intrinsic or common coagulation pathways.

References


