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Diurnal Variations of Blood Pressure in Cats

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ABSTRACT. Blood pressure (BP) was analyzed invasively using the telemetry system in unanesthetized, unrestrained healthy adult mongrel cats. After surgical implantation of a telemetry transmitter, BP was transiently elevated due to the invasive nature of the surgery, but it was gradually decreased. BP was largely stabilized seven to ten days postsurgery. Once BP was settled, systolic, diastolic and mean BPs[2] were obtained at 5-min intervals in individual cats. Hourly averages of these BP values revealed a diurnal variation with two peaks at 8:00 and 19:00. We also found that BP was significantly higher when cats were active compared to when they were sleeping or at rest ($p<0.05$). The average 24-hr BP in 20 healthy cats was 118.4 ± 11.0 (systolic), 78.0 ± 8.7 (diastolic) and 94.8 ± 9.5 mmHg (mean) by the telemetry system.

KEY WORDS: blood pressure, feline, diurnal variation.

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Currently blood pressure (BP) is commonly measured in cats by noninvasive methods such as oscillometry and Doppler ultrasonography in the clinical setting [3, 12, 13, 15]. Accurate and stable BP measurements, however, have been difficult with these indirect techniques, because cuff placement and restraint can be very stressful to animals and may interfere with BP readouts. The results may also be variable among methods and operators. In addition, because BP is constantly affected by various factors, it is difficult to reliably evaluate BP of an animal based on a single measurement. To solve these problems, it is necessary to understand the diurnal pressure pattern in cats.

Circadian rhythmic or diurnal variations of BP have been known in humans and mice [1, 22, 23]. We have previously shown that dogs also have diurnal BP variations using a telemetry system that continuously monitors BP for 24 hr without anesthetizing or restraining the animals [16]. On the other hand, only a handful of studies have documented circadian BP patterns in healthy, unrestrained cats. Brown *et al.* have reported changes in diurnal BP patterns in six healthy cats after administration of certain vasoactive agents [7]. The study by Sei *et al.* has focused on BP changes during paradoxical sleep and slow-wave sleep in cats [19]. In this study, we monitored BP in 20 healthy cats continuously for a long term by using the stress-free telemetry system. Obtained data were analyzed for diurnal and nocturnal circadian rhythmic patterns and for influences by daily activities. We also addressed whether the 24-hr BP obtained in this study represented the baseline BP in healthy cats.

MATERIALS AND METHODS

Animals: Twenty adult mixed-breed cats (four males and 16 females) weighing 2.0 to 4.0 kg were used. No abnormalities were found in these animals by general physical examination and blood, serology and urinary tests. They were individually housed in cages for several months prior to the study (for acclimatization) and during the study period under a 12L/12D cycle (light on at 8:00 and off at 20:00). They were given water *ad libitum* and fed twice daily between 8:00 and 9:00 and between 19:00 and 20:00. The animals finished the meals as soon as provided. The access to the animal room was restricted, and the cages were cleaned during the feeding hours.

BP measurement by the telemetry system: The femoral artery was exposed under anesthesia, and the transmitter catheter was placed intra-arterially. The BP transmitter body (model TA11PA-C40, Data Science Co., Ltd., Minnesota, U.S.A.) was secured in the subcutaneous pocket that was created during the operation. BP was measured as previously described [17]. Briefly, measured BP is relayed as a digital signal from the transmitter to a receiver (RLA1020) and sequentially transmitted via a multiplexer (RMX10), a consolidation matrix (BCM100) and a universal adapter (UA10) (Fig. 1). The universal adapter converts the signal from digital to analog for computer-assisted analysis (Softron ECG Processor SBP4.8, Softron Co., Tokyo, Japan). Systolic, diastolic and mean BP measurements were obtained every 5 min as a 10-sec mean of continuous BP input. Hourly averages of systolic, diastolic and mean BPs were calculated as the averages of these BP measurements within the corresponding hour. BP was continuously measured for 24 hr over several weeks.

Examination of the BP changes after transmitter implantation: To examine the influence of the surgical invasion required for transmitter implantation, BP was monitored in six cats used in this study for 14 days postsurgery. Systolic, diastolic and mean BPs obtained every 5 min were averaged every 24 hr (24-hr BP) and used for analysis.

Examination of the diurnal BP variations: BP was taken for seven days after an interval of at least a month postsurgery to examine diurnal BP variations in healthy cats. The average systolic, diastolic and mean BPs were obtained every hour in 16 cats as described above and analyzed. To

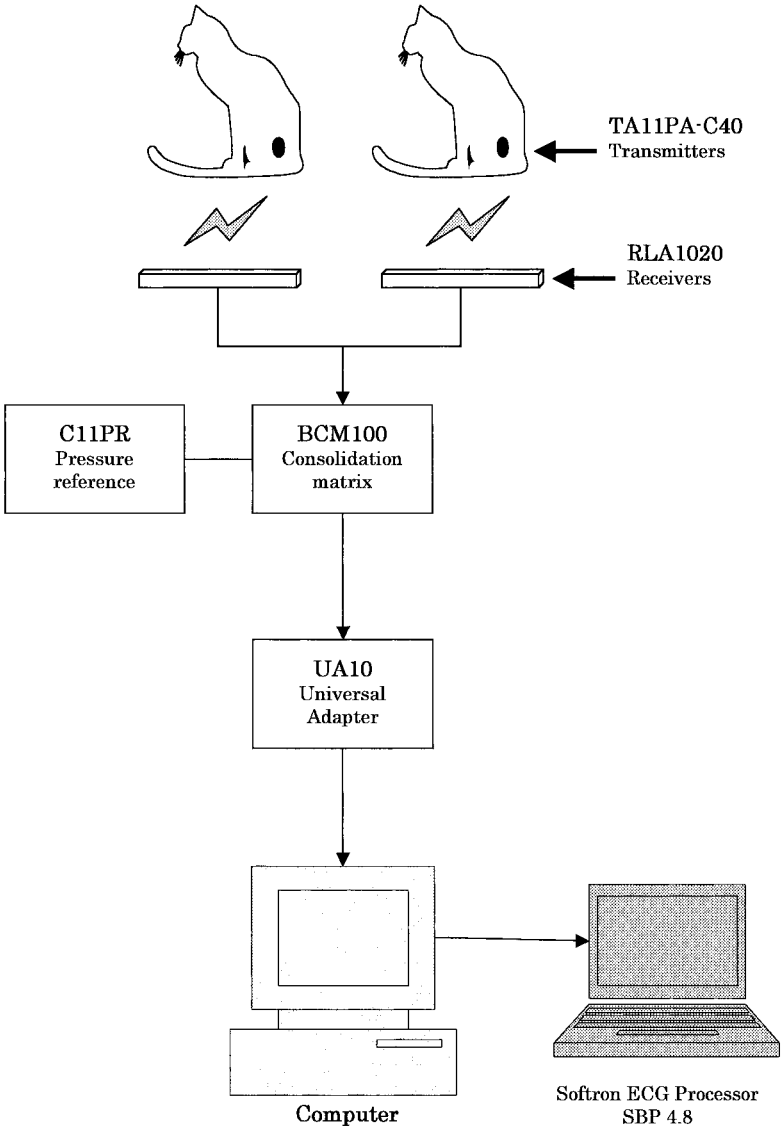

Fig. 1. A schematic representation of blood pressure measurement using a telemetry system.

examine the correlation between BP and activity, the day was divided into five periods based on cats' activities observed during acclimatization: nighttime sleep hours (0:00–6:00); daytime sleep hours (9:00–15:00); the rest period when cats were awake but relatively calm (15:00–18:00) and the two active periods (6:00–9:00, 18:00–21:00). The average BP was compared among these time periods. BP during each time period was also compared with 24-hr BP obtained from the same 16 cats. Average 24-hr BP was obtained also from all 20 cats used in the study.

For statistical analysis, the Kruskal-Wallis test was used after analysis of variance (ANOVA) by the Bartlett's method. The Scheffe method was used if a significant difference was identified. The significance level less than 5% was considered indicative of a statistically significant difference.

RESULTS

BP changes after transmitter implantation: When the effect of surgical implantation of the transmitter on 24-hr BP was examined in 6 cats, systolic, diastolic and mean BPs were all elevated on the day of implantation. The 24-hr BP gradually decreased from the following day until ten days postsurgery and stabilized thereafter (Fig. 2).

Diurnal BP variation: When systolic, diastolic and mean BPs taken at 5-min intervals were plotted on a graph, they showed constant fluctuations throughout the day (Fig. 3).

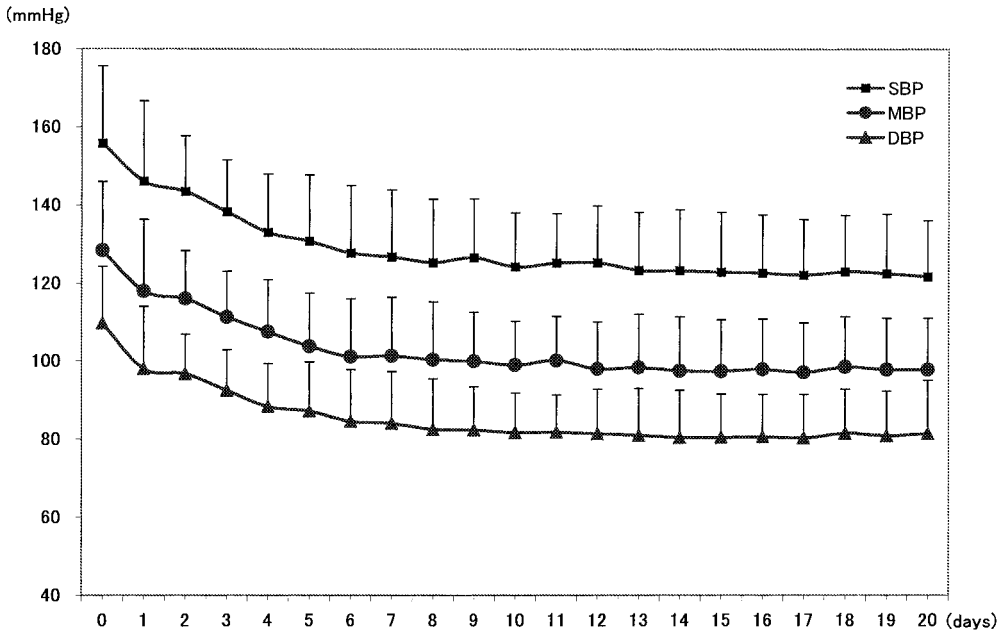

Fig. 2. Time-course of changes in systolic, diastolic and mean blood pressures (24-hr BP) in 6 cats after transmitter transplantation. Elevated BPs immediately after surgical invasion gradually decreased and stabilized after 10 days postsurgery (Surgical transmitter implantation was performed on Day 0). Values are means + standard deviation (S.D.). SBP: Systolic blood pressure; MBP: Mean blood pressure; DBP: Diastolic blood pressure.

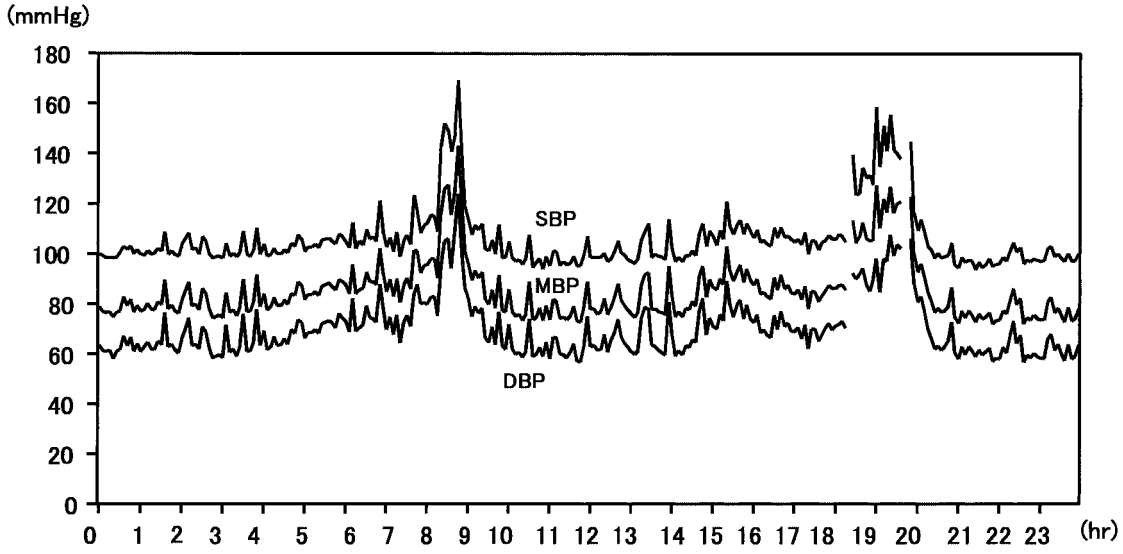

Fig. 3. Systolic, diastolic and mean BP measurements obtained at 5-min intervals in a cat. BPs were elevated and showed larger fluctuations between 6:00 and 9:00 and between 16:00 and 20:00 compared to the other time periods.

Remarkably elevated BPs were observed at 6:00–9:00 and 16:00–20:00 compared to the other time points (Fig. 3). The hourly averages of these 5-min BPs also revealed two diurnal peaks at 8:00 and 19:00 in all of systolic, diastolic and mean BPs (Fig. 4). When these two peaks were compared, there was a sharp increase in BP at 8:00, whereas the increase at 19:00 occurred gradually. After both peaks, BP rapidly decreased within an hour and remained within the normal ranges. At other time points during the day (10:00–14:00) and night (21:00– 4:00), BP changes were relatively stable.

We also found that systolic, diastolic and mean BPs dur-

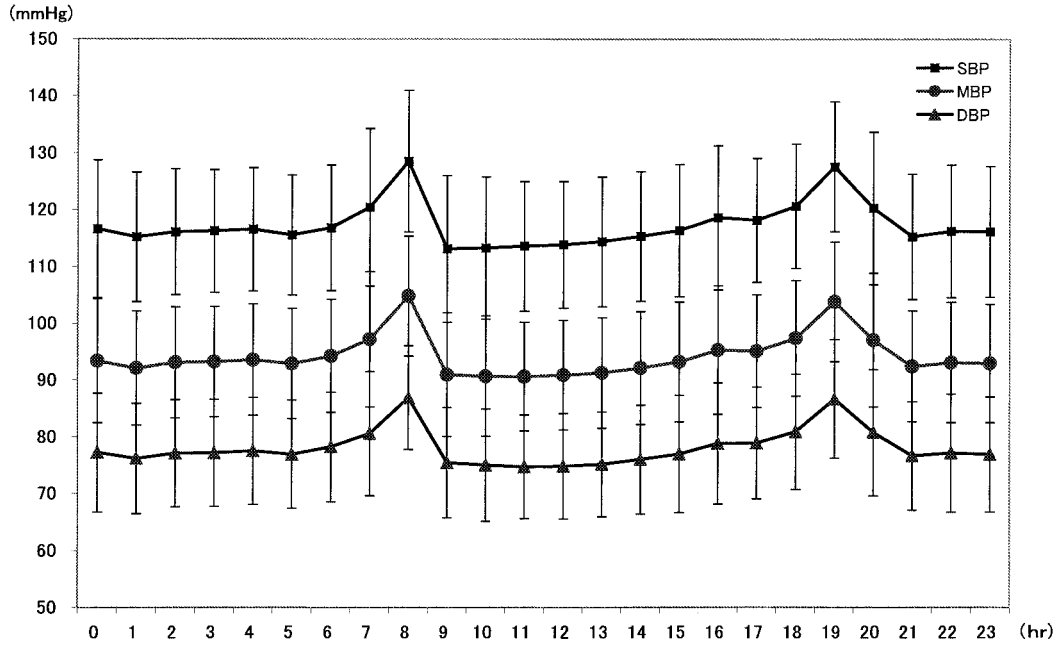

Fig. 4. Hourly averages of systolic, diastolic and mean BPs taken for 10 days in 16 cats. Systolic, diastolic and mean BPs showed diurnal, biphasic elevations at 8:00 and 19:00. These peaks rapidly returned to the standard ranges and stabilized within an hour. Values are means ± standard deviation (S.D.). SBP: Systolic blood pressure; MBP: Mean blood pressure; DBP: Diastolic blood pressure.

ing the active period were significantly higher than those during the nighttime and daytime sleep periods and the rest period ($p<0.05$). When BP at each time period was compared to 24-hr BP, only the active-period BP showed a significant difference ($p<0.05$), while no significant difference was observed at the other time periods (Table 1). The average BPs at the rest period were similar to 24-hr BPs.

The average 24-hr BPs obtained from all 20 cats were 118.4 ± 11.0 (systolic), 78.0 ± 8.7 (diastolic) and 94.8 ± 9.5 mmHg (mean), and the average heart rate was 141.3 ± 31.1 beats/min.

Table 1. Average blood pressures during four different time periods and average 24-hr blood pressures by continuous telemetry monitoring in 16 cats (means ± S.D., mmHg)

	SBP	MBP	DBP
Night-time-Sleep	116.0 ± 10.8	93.1 ± 9.7	77.0 ± 9.4
Day-time-Sleep	113.9 ± 11.5	91.1 ± 9.8	75.2 ± 9.2
Rest	117.7 ± 11.4	94.5 ± 10.3	78.3 ± 10.0
Active	122.4 ± 12.6	99.1 ± 11.2	82.3 ± 10.5
24-hour	117.0 ± 12.0	94.2 ± 10.9	78.0 ± 10.1

SBP: Systolic blood pressure, MBP: Mean blood pressure, DBP: Diastolic blood pressure * $p<0.05$.

DISCUSSIONS

Although there has been an increasing concern over hypertension in dogs and cats, testing and treatment of hypertension are not actively initiated in current practice. One reason for this is that diagnosis of hypertension is difficult, because hypertension may progress without manifesting any clinical symptoms. Further, a reliable BP measurement method in conscious animals, which constitutes the basis of diagnosis of hypertension, has not been established for animals, and even when BPs of freely moving animals are obtained, these results must be interpreted with caution. Also, criteria of hypertension in small animals have not yet clearly defined. All together, these factors are hindering the progress of veterinary research in hypertension.

Noninvasive techniques that are used for BP measurement in humans, such as oscillometry and Doppler ultrasonography, are also theoretically feasible in cats. However, when used in cats, these methods give variable ranges of normal and high BPs [12–15, 21]. Not only do these variations arise from the technical differences among operators, but also the procedure itself is stressful for cats and may induce artifactual influence on BP. A similar effect has been recognized also in humans; BP may rise only in the hospital setting (known as "white-coat hypertension"), although the same patient shows a normal BP at home [17, 18]. For this reason, BP is often taken both at the hospital (casual BP) and home (home BP) for reliable evaluation. In addition, ambulatory blood pressure monitoring (ABPM) has been clinically tested for over 10 years and proven for its effectiveness [1, 10, 11, 18, 23]. Given these situations, we aimed to establish the standard BP range and variations in unanesthetized and unrestrained cats by using the telemetry

system, an invasive but direct BP measurement method. Newly developed for animal studies, the telemetry system allows accurate BP measurements in unanesthetized, freely moving animals [2, 4–7, 16, 19, 22] .

In this study, the systolic, diastolic and mean BPs were all elevated on the first day after telemetry transmitter implantation in healthy cats. These BPs were then gradually decreased and stabilized seven to 10 days postsurgery, indicating that the influence of surgical invasion on BP remained at least a week in cats. Sei *et al.* have also reported that the BP pattern during sleep is different when BP is measured 2–5 days postsurgery or when it is measured 10 days or later after surgery [19]. Thus, for telemetry BP measurements, BP should be taken after at least two weeks postsurgery for reliable evaluation.

BP taken at 5-min intervals showed constant fluctuations throughout 24 hr in cats. The amplitude of fluctuation was significantly large within the day. However, when hourly averages were calculated from these 5-min BPs, the systolic, diastolic and mean BPs all showed biphasic, diurnal elevations at 8:00 and 19:00. BP was relatively stable throughout the other time periods. This diurnal BP pattern was similar to that observed in dogs [16]. In humans BP rises during the day and decreases at night, while in rats it increases during the dark cycle and falls during the light cycle. This is because humans are diurnal, sleeping at night and active during the day, whereas rats are nocturnal, active when it is dark and sleeping during the light cycle [1, 22]. Broten *et al.* has also examined canine BP by the telemetry system and reported that the mean BP remains low through the night and early morning but increases during the daytime [5]. Brown *et al.* has carried out an experiment similar to our study in six cats, but they saw only a single peak in BP around 10:00–11:00, probably because cats were fed and their cages were cleaned at these hours [6]. A similar effect was observed in our experiments; systolic, diastolic and mean BPs were all highest during the feeding and cleaning hours. However, cats showed a gradual rise in BP few hours ahead of these hours along with increased activeness. This concurrent BP and activity pattern was thought to reflect the daily schedule to which they were subjected. After each meal, cats' activities subsided and entered the sleeping period, which was accompanied by a decrease in BP, regardless of day or night.

It has been known that human nighttime workers show higher BPs at night [1, 20]. This indicates that not only the endogenous circadian rhythm but also acquired activity cycles, *i.e.* work at night and sleep during the daytime, determine diurnal BP changes. That is, BP is more likely influenced by individual's status, such as sleeping, awakening or actively working. Also in this study, the association between BP and activities was observed in cats; BP was highest when the cats were active and lowest during sleep. These results were consistent with those in dogs. Because cats are crepuscular, sleeping at both day and night, feline BP seemed to correlate more strongly with their environment than with the light-dark cycle. The circadian BP variation in cats observed in this study may have been determined by the acquired biological rhythm, which was learned through their experiences such as timing of feeding and changes in the rearing environment, in addition to the endogenous circadian rhythm.

Feline BP clearly has diurnal variations with significantly large amplitudes. Therefore, a single BP measurement is unreliable and may give a false diagnosis. Because our study also showed that 24-hr BP was approximately equal to the resting BP, 24-hr BP should be also evaluated as a definitive BP of the individual, when examining long-term variations in BP. In our study, the average 24-hr BPs obtained from 20 cats were not largely different from those obtained by other telemetry experiments in cats (systolic 122.5 ± 2.1, diastolic 85.5 ± 1.8 and mean 101.8 ± 1.9 mmHg by Brown *et al.* [7] and systolic 107.5 ± 1.2 and diastolic 76.1 ± 1.4 mmHg by Sei *et al.* [19]) and from those in dogs [16]. Further, these values were not distinctively higher when compared to human 24-hr BP [1, 8, 9, 18, 20]. Although telemetric BP monitoring can not be used as a routine clinical procedure, the data obtained through this system is highly reliable. We believe that this technique will greatly contribute to clinical advances, *e.g.* understanding pathophysiology of hypertension, by providing long-term or transient BP variations in various hypertension models and animals treated with vasoactive agents.

REFERENCES

1. Baumgart, P. 1991. Circadian rhythm of blood pressure: internal and external time triggers. *Chronobiol. Int.* **8**: 444–450.
2. Bidani, A. K., Griffin, K. A., Picken, M. and Lansky, D. M. 1993. Continuous telemetric blood pressure monitoring and glomerular injury in the rat remnant kidney model. *Am. J. Physiol.* **265**: F391–398.
3. Binns, S. H., Sisson, D. D., Buoscio, D. A. and Schaeffer, D.J. 1995. Doppler ultrasonographic, oscillometric sphygmomanometric, and photoplethysmographic techniques for noninvasive blood pressure measurement in anesthetized cats. *J. Vet. Intern. Med.* **9**: 405–414.
4. Brockway, B. P., Mills, P. A. and Azar, S. H. 1991. A new method for continuous chronic measurement and recording of blood pressure, heart rate and activity in the rat via radiotelemetry. *Clin. Exp. Hypertens.* **13**: 885–895.
5. Broten, T. P., Zehr, J. E. and Livnat, A. 1988. Statistical criteria for using short-term measurements as an index of 24-hour mean arterial pressure in unanesthetized unrestrained dogs. *Life Sci.* **42**: 1625–1633.
6. Brown, S. A., Langford, K. and Tarver, S. 1997. Effects of certain vasoactive agents on the long-term pattern of blood pressure, heart rate, and motor activity in cats. *Am. J. Vet. Res.* **58**: 647–652.
7. Brown, S. A., Brown, C. A., Jacobs, G., Stiles, J., Hendi, R. S. and Wilson, S. 2001. Effects of the angiotensin converting enzyme inhibitor benazepril in cats with induced renal insufficiency. *Am. J. Vet. Res.* **62**: 375–383.
8. Guidelines Subcommittee. 1999 World Health Organization-International Society of Hypertension Guidelines for the Management of Hypertension. *J. Hypertens.* **17**: 151–183.
9. Joint National Committee on Detection 1997. Evaluation ,and

Treatment of High Blood Pressure. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC VI). *Arch. Intern. Med.* **157**: 2413–2446.
10. Imai, Y., Abe, K., Munakata, M., Sakuma, H., Hashimoto, J., Imai, K., Sekino, H. and Yoshinaga, K. 1990. Does ambulatory blood pressure monitoring improve the diagnosis of secondary hypertension? *J. Hypertens* **8**: S71–S75.
11. Kawano, Y., Tochikubo, O., Minamisawa, K., Miyajima, E. and Ishii, M. 1994. Circadian variation of haemodynamics in patients with essential hypertension: comparison between early morning and evening. *J. Hypertens.* **12**: 1405–1412.
12. Kobayashi, D. L., Peterson, M. E., Graves, T.K., Lesser, M. and Nichols, C.E. 1990. Hypertension in cats with chronic renal failure or hyperthyroidism. *J. Vet. Intern. Med.* **4**: 58–62.
13. Littman, M. P. 1994. Spontaneous systemic hypertension in 24 cats. *J. Vet. Intern. Med.* **8**: 79–86.
14. Maggio, F., DeFrancesco, T. C., Atkins, C. E., Pizzirani, S., Gilger, B. C. and Davidson, M. G. 2000. Ocular lesions associated with systemic hypertension in cats: 69 cases (1985–1998). *J. Am. Vet. Med. Assoc.* **217**: 695–702.
15. Mishina, M., Watanabe, T., Fujii, K., Maeda, H., Wakao, Y. and Takahashi, M. 1998. Non-invasive blood pressure measurements in cats: clinical significance of hypertension associated with chronic renal failure. *J. Vet. Med. Sci.* **60**: 805–808.
16. Mishina, M., Watanabe, T., Matsuoka, S., Shibata, K., Fujii, K., Maeda, H. and Wakao, Y. 1999. Diurnal variations of blood pressure in dogs. *J. Vet. Med. Sci.* **61**: 643–647.
17. Pickering, T. G., James, G. D., Boddie, C., Harshfield, G. A., Blank, S. and Laragh, J. H. 1988. How common is white coat hypertension? *JAMA.* **259**: 225–228.
18. Prasad, N., MacFadyen, R. J., Ogston, S. A. and MacDonald, T. M. 1995. Elevated blood pressure during the first two hours of ambulatory blood pressure monitoring: a study comparing consecutive twenty-four-hour monitoring periods. *J. Hypertens.* **13**: 291–295.
19. Sei. H., Sakai, K., Kanamori, N., Salvert, D., Vanni-Mercier, G. and Jouvet, M. 1994. Long-term variations of arterial blood pressure during sleep in freely moving cats. *Physiol. Behav.* **55**: 673–679.
20. Sundberg, S., Kohvakka, A. and Gordin, A. 1988. Rapid reversal of circadian blood pressure rhythm in shift workers. *J. Hypertens.* **6**: 393–396.
21. Syme, H. M., Barber, P. J., Markwell, P. J. and Elliott, J. 2002. Prevalence of systolic hypertension in cats with chronic renal failure at initial evaluation. *J. Am. Vet. Med. Assoc.* **220**: 1799–1804.
22. Van den Buuse, M. 1994. Circadian Rhythms of blood pressure, heart rate, and locomotor activity in spontaneously hypertensive rats as measured with radio-telemetry. *Physiol. Behav.* **55**: 783–787.
23. Van Ittersum, F. J., Ijzerman, R. G., Stehouwer, C. D. and Donker, A. J. 1995. Analysis of twenty-four-hour ambulatory blood pressure monitoring: what time period to assess blood pressures during waking and sleeping? *J. Hypertens.* **13**: 1053–1058.