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Intraocular pressure and tear production in five herbivorous wildlife species

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The intraocular pressure and rate of tear production were measured in 18 addax antelopes (*Addax nasomaculatus*), four impalas (*Aepyceros melampus*), 11 wide-lipped rhinoceroses (*Ceratotherium simum*), 10 white-tailed wildebeests (*Connochaetes gnou*) and seven scimitar-horned oryxes (*Oryx dammah*). The animals were anaesthetised with an intramuscular injection of etorphine hydrochloride and acepromazine maleate, and the Schirmer tear test I was used to evaluate tear production, and applanation tonometry was used to evaluate the intraocular pressure. The mean (sd) rate of tear production ranged from 17·6 (3·1) mm/minute in the rhinoceros to 28·8 (8·3) mm/minute in the addax. The intraocular pressure ranged from 8·0 (1·2) mmHg in the impala to 32·1 (10·4) mmHg in the rhinoceros. The rate of tear production in the addax and the intraocular pressure in the rhinoceros appear to be the highest values of these variables to have been reported in any species.

Veterinary Record (2002) **151,** 265-268

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TEARS play an important role in maintaining the health and normal function of the cornea and conjunctiva. Tears form an important refractive surface on the eye, provide essential nutrients to the cornea, help remove foreign matter, and contain immunoglobulins, lysozymes and other components of the ocular defence mechanisms. Deficiency in tear production results in keratoconjunctivitis sicca (KCS) and inflammation of the cornea and conjunctiva. In its acute form, the disease may cause corneal ulceration and perforation, and in chronic cases vision may be lost owing to progressive corneal pigmentation (Moore 1999).

Glaucoma is another ocular disease that may lead to a loss of vision. The disease is defined as a progressive loss of retinal sensitivity and function, stemming from the death of ganglion cells and their axons, which results in an incremental reduction in the visual field and eventual blindness. An increase in intraocular pressure is considered to be the most important risk factor in the pathogenesis of the disease (Brooks and Gelatt 1999).

Unfortunately, many of the clinical signs associated with these two potentially blinding diseases are non-specific. An ocular discharge, corneal pigmentation and vascularisation may be observed in most cases of chronic corneal inflammation and infection. The diagnosis of KCS is therefore based on the Schirmer tear test I, which measures the rate of production of the aqueous portion of the tear film (in mm/minute), rather than on clinical signs (Moore 1999). Similarly, ocular pain, ciliary injection and corneal oedema are associated with both uveitis and glaucoma. In veterinary medicine the diagnosis of glaucoma is therefore based on tonometry, or the measurement of intraocular pressure (Brooks and Gelatt 1999).

However, in order for the Schirmer tear test and tonometry to be diagnostic, the practitioner must be able to refer to normal baseline values for the species being investigated. There are large interspecies variations in intraocular pressure and the results of the Schirmer tear test, even between members of the same family. For example, the intraocular pressure of the Burchell's zebra (*Equus burchelli*), 29·5 mmHg, is four times that of the Thomson gazelle (*Gazella thomsoni*), 7·6 mmHg (Ofri and others 1998, 2000). In the Felidae family, the normal rate of tear production in the African lion (*Panthera leo*) is 44 per cent higher than in the domestic cat (24·4 and 16·9 mm/minute, respectively) (Veith and others 1970, Ofri and others 1997). It is therefore not possible to extrapolate values of intraocular pressure and tear production, even between closely related species, and it is important to establish reference values for each species, to facilitate the diagnosis and monitoring of the two vision-threatening diseases. Furthermore, the large range of values raises questions concerning the anatomical and physiological differences between species, and the answers to these questions may contribute to the understanding of the pathophysiology of the diseases. The aim of this study was to establish reference values for the Schirmer tear test and intraocular pressure in five herbivorous wildlife species that had not previously been studied.

MATERIALS AND METHODS

Animals

The measurements were made in 18 addax antelopes (*Addax nasomaculatus*), four impalas (*Aepyceros melampus*), 11 wide-lipped rhinoceroses (*Ceratotherium simum*), 10 white-tailed

wildebeests (*Connochaetes gnou*) and seven scimitar-horned oryxes (*Oryx dammah*). The animals' sex, age (derived from zoo records) and estimated weight are given in Table 1. The animals roamed freely in a 1000-acre park with members of other herbivorous and avian wildlife species, some of which have been investigated in the same way (Ofri and others 1998, 1999, 2000, 2001). All the animals were born in captivity and had uneventful medical histories. No abnormalities were observed during their physical examination which, in some cases, included complete blood counts and a serum biochemistry profile, or during ophthalmic evaluation.

TABLE 1: Species and mean (sd) ages and estimated bodyweights of the animals investigated

Species	Number	Age (years) Range	Age (years) Mean (sd)	Estimated weight (kg) Range	Estimated weight (kg) Mean (sd)
Addax	11 F, 7 M	0·3-8·5	3·3 (3·6)	30-140	85·6 (35·6)
Impala	3 F, 1 M	0·3-8·0	4·1 (3·9)	20-90	52·5 (28·7)
Rhinoceros	6 F, 5 M	7·0-30·0	20·3 (9·1)	1850-2300	2055·0 (235·0)
Wildebeest	3 F, 7 M	0·5-19·0	3·9 (6·0)	40-180	121·0 (68·2)
Oryx	4 F, 3 M	0·3-2·0	0·9 (0·7)	40-200	111·4 (63·1)

F Female, M Male

Anaesthesia

Data were collected from the animals when they were anaesthetised for other purposes. The rhinoceroses were anaesthetised for fertility examinations, and the other four species were anaesthetised before they were transported. The animals were anaesthetised with an intramuscular injection delivered by dart. The anaesthetic agent was a commercial mixture (Large Animal Immobilon; C-Vet) containing etorphine hydrochloride (2·45 mg/ml) and acepromazine maleate (10 mg/ml). The doses were adjusted to estimates of the animals' bodyweights (Table 2). In the rhinoceroses, 5 to 15 mg butorphenol (Torbugesic; Fort Dodge Animal Health) and 10 to 15 mg of detomidine (Domosedan; Pfizer), depending on the estimate of bodyweight, were added to the mixture.

Data collection

The rate of tear production and the intraocular pressure were estimated, in that order, as soon as the animal could be approached safely, approximately 12 minutes after it had been darted. Owing to time constraints, the rate of tear production was not evaluated in the oryxes. Bilateral measurements were made, except in the rhinoceroses, in which bilateral measurements could be made only in the three animals that became sternally recumbent; as a result, only 14 rhinoceros eyes were examined, and the single eye evaluated in the other eight animals was dictated by the side on which it had fallen. In the other species, the order in which the eyes were evaluated was determined randomly.

Tear production was estimated by using a commercial paper test strip of a single lot number (Schering-Plough Animal Health). The sterile test strips contain a small amount of dye that is carried by the tears which the paper absorbs. A strip was inserted for one minute in the lower conjunctival fornix of the eye, and the distance in mm that the dye covered was determined from the scale imprinted on the strip. The intraocular pressure was measured with an applanation tonometer (Tono-Pen XL; Mentor Ophthalmics). This digital tonometer takes several readings through the topically anaesthetised cornea, and then displays the average pressure and its variance. Four such averaged readings, with a variance of up to 10 per cent, were taken from each eye. The instrument had recently been calibrated by the manufacturer, and its calibration was rechecked at the beginning of each recording day. The fertility examinations in seven of the rhinoceroses required a longer period of anaesthesia, and in these animals it was possible to repeat the tonometry measurements after 10 minutes and evaluate the effect of the period of anaesthesia on the intraocular pressure.

Statistical analysis

Repeated measures analysis of variance was used initially to evaluate the main effects of age, weight, sex, eye (left or right) and replicate (systematic changes in intraocular pressure over the four recordings), and their respective higher order interactions. For the impalas, the effects of sex, age and weight were not analysed because there were only four of them. No systematic changes in the results of the tonometry measurements were observed across the replicate measurements, and the average results for each animal were calculated and used to obtain the mean (sd) values for each of the species.

Repeated measures analysis of variance was also used to compare the results with data collected in previous studies, to determine whether they differed significantly between closely related species, for example, the scimitar-horned oryx studied here and the Arabian oryx (*Oryx leucoryx*) studied by Ofri and others (1998). Repeated measures analysis of variance was also used to evaluate the effect of the duration of anaesthesia on the intraocular pressure of the rhinoceroses. All the analyses were made by using a computer statistics program (PC 90; BMDP Statistical Software). Values of $P<0·05$ were considered statistically significant.

RESULTS

The mean (sd) results are shown in Table 2. No significant effects of age, weight, sex, eye side or replicate readings of intraocular pressure were recorded in any of the species, and there were no significant higher order interactions. In the seven rhinoceroses in which tonometry was repeated after 10 minutes, no significant differences in the intraocular pressure were observed as a result of the prolonged period of anaesthesia ($P=0·24$). The mean intraocular pressure in the rhinoceroses was higher than in any other species the authors have studied to date ($P=0·02$), and the mean value of the Schirmer tear test in the addaxes was also significantly higher ($P<0·0001$) than in any of the species evaluated previously.

DISCUSSION

These results increase the range of intraocular pressures recorded in the animal kingdom. To the best of the authors' knowledge, the value of 32·1 mmHg recorded in the rhinoceroses is the highest normal intraocular pressure measured in any terrestrial species, surpassing the values of 29·5 mmHg

TABLE 2: Range of anaesthetic doses given, and mean (sd) intraocular pressure (IOP) and Schirmer tear test (STT) values for the five wildlife species

Species	Range of anaesthetic* dose (ml)	IOP (mmHg)	STT (mm/minute)
Addax	0·7-2·0	11·2 (3·2)	28·8 (8·3)
Impala	0·15-0·3	8·0 (1·2)	18·8 (1·8)
Rhinoceros	0·8-1·4†	32·1 (10·4)	17·6 (3·1)
Wildebeest	0·6-1·4	15·5 (3·7)	19·3 (4·6)
Oryx	0·7-2·0	15·8 (1·5)	Not measured

* Large Animal Immobilon (C-Vet), a commercial preparation containing a mixture of etorphine hydrochloride (2·45 mg/ml) and acepromazine maleate (10 mg/ml)
† In the rhinoceroses, butorphenol (Torbugesic; Fort Dodge Animal Health) and detomidine (Domosedan; Pfizer) were added to the mixture

in the zebra (P=0·02) (Ofri and others 1998) and 29·6 mmHg in the horse (Kotani and others 1993). In contrast, the intraocular pressure in the Thomson gazelle is only 7·6 mmHg. Such a large range of normal values in wildlife species raises questions about the understanding of the dynamics of aqueous humour and the pathophysiology of glaucoma. What, for instance, are the physiological and anatomical differences in the anterior uvea and iridocorneal angle of the gazelle and the rhinoceros that are responsible for this large difference? Also, what are the differences in the retinas and optic nerves of the two species that enable the rhinoceros to maintain vision in the face of such high pressures? It is possible, for example, that the rhinoceros possesses highly developed vascular autoregulatory mechanisms that enable it to maintain a normal blood supply to the retina despite the high intraocular pressure. It is also possible that the lamina cribrosa of the rhinoceros eye has unique attributes that prevent the optic nerve axons from kinking as they exit the eye.

The intraocular pressure may be determined phylogenetically. For example, both the impala (Table 2) and Thomson gazelle (Ofri and others 2000), two species belonging to the Antilopinae subfamily, have an intraocular pressure less than 8 mmHg. Similarly, there are no significant differences (P=0·14) between the scimitar-horned oryx and the wildebeest (Table 2), two members of the Hioppotraginae subfamily, and virtually identical values of 29·5 and 29·6 mmHg have been recorded, respectively, in the zebra (Ofri and others 1998) and horse (Kotani and others 1993), two members of the Equidae family. However, there are exceptions. Significant differences in intraocular pressure between non-anaesthetised llamas and alpacas, both of which belong to the Camelidae family, were reported by Willis and others (2000), and there were significant differences (P=0·04) between the closely related scimitar-horned oryx (Table 2) and the Arabian oryx (Ofri and others 1998).

Differences between the anatomy and physiology of the ciliary body and the drainage pathways for aqueous humour probably contribute to some of the differences recorded between species. Systemic physiological differences between species may also account for some of the interspecies variation, because factors as diverse as serum osmolarity (Ashkenazi and others 1992), haematocrit (Klein and others 1992), and the levels of adrenocorticotrophic hormone and growth hormone (Kass and Sears 1977) have all been shown to affect the intraocular pressure in human beings. Another potential source of variation may be the anatomy of the cornea. The applanation tonometer used in this investigation was designed for use in human beings. Its readings may be affected by factors such as the rigidity, curvature and thickness of the cornea, and the measurements in animals should therefore be regarded as estimates. True intraocular pressures can only be measured by direct anterior chamber manometry. Such methods have shown that the applanation tonometer used consistently underestimates or overestimates the pressure in cats, horses and dogs (Miller and others 1991, Dziezyc and Millichamp 1992). Thus, it is possible that the greater rigidity or thickness of the cornea of the rhinoceros may have contributed to the high readings in this species. Comparative measurements of the thickness and curvature of the cornea may help to elucidate the effect of corneal anatomy on tonometry in the animal kingdom.

The accuracy of the specific applanation tonometer for use in the species described here is unknown. However, owing to its portability, ease of use, reliability and cost, it has become the most popular tonometer in veterinary practice, and is used routinely to obtain clinical readings of intraocular pressure and to diagnose glaucoma in many mammalian, avian and reptilian species. Clinicians wishing to diagnose glaucoma in any of the species in this report are most likely to use a similar applanation tonometer, and they will be interested in baseline readings obtained with such an instrument, rather than in absolute values determined by manometry.

There are also differences in the rate of tear production between species. These are not as large as the differences in intraocular pressure but they are significant. In herbivorous wildlife, the results of the Schirmer tear test range from 10·5 mm/minute in the Asian fallow deer (*Dama mesopotomica*) (Ofri and others 2001) to 28·8 mm/minute in the addax (Table 2) (P<0·0001). Before this study, Ofri and others (1999, 2001) speculated that differences in tear production might be the result of different habitats. For example, in desert-dwelling species, including the Arabian oryx, Nubian ibex (*Capra ibex nubiana*) and Asian fallow deer, Schirmer tear test values were significantly lower than in herbivorous species living in more moderate climates, including the Thomson gazelle, the zebra and the eland (*Taurotragus oryx*) (P<0·0001). However, it is very unlikely that a lower rate of tear production would have evolved as a fluid conservation method in species living in arid habitats, because of the small volumes involved (Lemp and Wolfley 1992). The present sudy indeed refutes this hypothesis, as in the addax, a desert-dwelling species, the Schirmer tear test value was significantly higher than in any other species studied to date (P<0·0001). Nor is it possible to assume that the rate of tear production is phylogenetically determined; in the addax it was significantly higher (P<0·0001) than in either the wildebeest (Table 2) or the Arabian oryx (Ofri and others 1999), even though all three species belong to the Hioppotraginae subfamily. Similarly, in the Felidae family, the value in lions (24·4 mm/minute) is higher than in the domestic cat (16·9 mm/minute) (Veith and others 1970, Ofri and others 1997). It is possible that some of these variations may be due to differences between species in the size of the conjunctival sac or the available tear reservoir on the surface of the eye.

The animals were anaesthetised for their examination, and the measurements should therefore be regarded as estimates, rather than true measurements of pressure and tear production. In general, it is assumed that both variables will be lower in anaesthetised animals. Preanaesthetics and anaesthetics usually depress tear production, and may even predispose dogs to KCS (Moore 1999). Anaesthesia also causes relaxation of the extraocular muscles and decreases the episcleral blood pressure, thus potentially reducing the intraocular pressure. However, the effects of general anaesthesia are not always predictable. For example, in cats, ketamine increases the intraocular pressure (Hahnenberger 1976), whereas xylazine reduces it (Burke and Potter 1986). Tear production may not always be affected by anaesthesia: ketamine has no effect on Schirmer tear test results in the rhesus monkey (*Macaca mulatta*) (Jaax and others 1984). To the best of the authors' knowledge, there have been no studies of the effects of etorphine hydrochloride, the primary anaesthetic agent used in this study, on tear production or intraocular pressure in any species.

It is clearly impossible to make these measurements in unanaesthetised wildlife, except in tamed animals. However, wildlife practitioners will conduct these tests in anaesthetised animals, and will therefore be interested in baseline values determined under similar conditions

Glaucoma is a disease that is rarely diagnosed in exotic and wildlife species. It has been reported in wildlife primates, avian and camelid species, and in lions (Ofri 2002), but not, so far as the authors are aware, in the species evaluated here. The scarcity of these reports is almost certainly not due to the fact that wildlife species are not susceptible to glaucoma, but rather to the problems associated with veterinary care for wildlife animals – the need for chemical restraint, the relatively small number of animals that are kept in zoos and receive daily supervision, and the lack of normal reference values of intraocular pressure for most species. However, the

number of cases of glaucoma reported in camelids has risen rapidly during the last few years, as they are being raised for commercial purposes in North America, and are subject to more frequent veterinary inspections (Willis and others 2000, Ofri 2002).

While there are no reports of KCS in wildlife, there have been many reports of infective keratoconjunctivitis in wildlife, mostly in ruminant species. The disease has been reported in bighorn sheep, wild mule deer, common waterbuck, red deer, reindeer, alpine ibex, Grant's gazelle and black-tailed deer (Kern 1999). The agents most commonly associated with it have been *Moraxella* and *Chlamydia* species. However, since there are no reports of the Schirmer tear test having been performed on any of these animals, it is impossible to know whether the bacterial infection was the primary disease, or whether it was an opportunistic infection, secondary to tear deficiencies and KCS. For example, Mayer and others (1997), reporting on infectious keratoconjunctivitis in alpine ibex, stated that the *Mycoplasma conjunctivae* and *Chlamydia psittaci* that they isolated did not appear capable of producing the severe form of the disease. This observation was made in the ibex, a species with a mean Schirmer tear test value of 13·2 mm/minute (Ofri and others 1999), one of the lowest baseline values recorded in any mammalian species. This low value may increase the susceptibility of the ibex to infectious corneal and conjunctival pathogens, and may exacerbate the signs associated with the infection. Support for this suggestion comes from the Cervidae (deer) family, several of which appear in the list of wildlife species in which keratoconjunctivitis has been reported. Furthermore, the lowest normal baseline Schirmer tear test value reported in any mammalian species (except the rabbit) was 10·5 mm/minute in fallow deer, another member of the Cervidae family (Ofri and others 2001). Since the aqueous layer measured in the Schirmer tear test is the layer that contains immunoglobulins, lysozymes, lactoferrin and other defensive proteins, it is possible that the low values in the Cervidae family make these species more susceptible to corneal and conjunctival infections. Furthermore, a decrease in tear production of only 1 to 2 mm/minute, which may have little clinical significance in species with higher baseline values, could have serious implications in species with low rates of tear production. Measurements of baseline Schirmer tear test values may therefore be relevant not only for the diagnosis of KCS, but also for assessing an animal's susceptibility to infectious keratoconjunctivitis.

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ABSTRACT

Disseminated intravascular coagulation in horses with acute colitis

TWELVE of 37 horses (32 per cent) with acute colitis admitted to a veterinary teaching hospital met the criteria for a clinicopathological diagnosis of subclinical disseminated intravascular coagulation (DIC) based on six tests (platelet count, plasma fibrinogen concentration, prothrombin time, activated partial thromboplastin time, antithrombin activity and serum fibrin degradation concentration). Five of 12 horses with subclinical DIC and two of 25 without DIC did not survive. Treatment of subclinical DIC may improve the outcome in horses with acute colitis.

DOLENTE, B. A., WILKINS, P. A. & BOSTON, R. C. (2002) Clinicopathologic evidence of disseminated intravascular coagulation in horses with acute colitis. *Journal of the American Veterinary Medical Association* **220,** 1034-1038