Evaluation of the diffusion of corticosteroids between the distal interphalangeal joint and navicular bursa in horses

Frederik E. Pauwels, DVM; James Schumacher, DVM; Fernando A. Castro, DVM; Troy E. Holder, DVM; Roger C. Carroll, PhD; Gary A. Sega, PhD; Chris W. Rogers, PhD

Objective—To determine whether clinically effective concentrations of methylprednisolone or triamcinolone can be achieved in the navicular bursa after injection of methylprednisolone acetate (MPA) or triamcinolone acetonide (TA) into the distal interphalangeal joint (DIPJ) and whether clinically effective concentrations of these drugs can be achieved in the DIPJ after injecting the navicular bursa with the same doses of MPA or TA.

Animals—32 healthy horses.

Procedures—Horses in groups 1 through 4 received 40 mg of MPA in the DIPJ, 10 mg of TA in the DIPJ, 40 mg of MPA in the navicular bursa, and 10 mg of TA in the navicular bursa, respectively. Concentrations of corticosteroids that diffused into the adjacent synovial structure were determined.

Results—For group 1, injection of MPA into the DIPJ yielded a mean ± SD concentration of 0.24 ± 0.072 µg of methylprednisolone/mL in the navicular bursa. For group 2, injection of TA into the DIPJ yielded 0.124 ± 0.075 µg of triamcinolone/mL in the navicular bursa. For group 3, injection of MPA into the navicular bursa yielded 0.05 ± 0.012 µg of methylprednisolone/mL in the DIPJ. For group 4, injection of TA into the navicular bursa yielded 0.091 ± 0.026 µg of triamcinolone/mL in the DIPJ.

Conclusions and Clinical Relevance—A clinically effective concentration of methylprednisolone or triamcinolone diffused between the DIPJ and navicular bursa after intra-articular or intrabursal injection, which would justify injection of the DIPJ with MPA or TA to ameliorate inflammation of the navicular bursa. (Am J Vet Res 2008;69:611–616)

A corticosteroid, usually MPA or TA, is commonly administered in the DIPJ to resolve lameness associated with navicular disease; resolution of lameness depends on diffusion of the corticosteroid from the DIPJ into the navicular bursa. Alternately, the corticosteroid can be administered directly into the navicular bursa, but centesis of this bursa is technically more difficult. The speed at which MPA or TA diffuses between the navicular bursa and DIPJ and the maximum concentration of the corticosteroid capable of diffusing between these synovial structures are not known.

Determining the magnitude of diffusion of commonly used corticosteroids from the DIPJ to the navicular bursa as a treatment for horses that are lame because of disease of the navicular apparatus would be useful because centesis of the navicular bursa is technically more difficult than centesis of the DIPJ. To select the most appropriate site of injection of a corticosteroid to treat horses with disease involving both the navicular bursa and the DIPJ, clinicians should be aware of the volume and direction of diffusion of the corticosteroid between these 2 synovial structures. Studies undertaken to determine whether the DIPJ and navicular bursa communicate have revealed no consistent evidence of anatomic communication. No communication was found in a latex injection dissection study, and no communication was found in several contrast arthrography

Received July 23, 2007. Accepted September 13, 2007.

From the Department of Large Animal Surgery, College of Veterinary Medicine (Pauwels, Schumacher, Castro, Holder) and the Department of Anesthesia Research, College of Medicine (Carroll, Sega), University of Tennessee, Knoxville, TN 37996; and Massey Equine Research, Institute of Veterinary, Animal, and Biomedical Sciences, Massey University, Private Bag 11 222, Palmerston North, New Zealand (Rogers). Dr. Pauwels’ present address is Department of Equine Surgery, Institute of Veterinary, Animal, and Biomedical Sciences, Massey University, Private Bag 11 222, Palmerston North, New Zealand.

Supported by a grant from the Houston Equine Research Foundation.

Presented as an abstract at the 2nd World Veterinary Orthopedic Congress, Keystone, Colo, February 2006. The authors thank Carolyn Snider for assistance with high-performance liquid chromatography and ELISA testing and Dawnya Breeding for assistance with the animals.

Address correspondence to Dr. Pauwels.

ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPA</td>
<td>Methylprednisolone acetate</td>
</tr>
<tr>
<td>TA</td>
<td>Triamcinolone acetonide</td>
</tr>
<tr>
<td>DIPJ</td>
<td>Distal interphalangeal joint</td>
</tr>
<tr>
<td>HPLC</td>
<td>High-performance liquid chromatography</td>
</tr>
</tbody>
</table>

Unauthenticated | Downloaded 01/08/24 04:41 PM UTC
between the navicular bursa and DIPJ is not clear. We are caused by incomplete diffusion of the corticosteroid (ie, DIPJ or navicular bursa) are dose-related events or and duration of clinical effect between sites of injection drolysis. Whether the differences detected in degree on many variables, including total dose and rate of hy

diffusion of mepivacaine hydrochloride from the DIPJ to the navicular bursa and with the proximal sesamoid bones with the proximal sesamoid bones with mepivacaine hydrochloride released previous to prevention of mepivacaine hydrochloride alleviated lameness associated with amphotericin B–induced navicular bursitis in all 6 horses within 5 minutes. Postmortem examination revealed that amphotericin B failed to diffuse from the navicular bursa into the DIPJ. These studies confirm that physical characteristics, including the molecular weight, of the drug injected and time play important roles in diffusion of compounds between the DIPJ and navicular bursa.

Radiographic contrast agents have a high molecular weight and high water solubility, and both of these factors reduce the rate of diffusion across a synovial membrane. Although the molecular weights of luxol fast blue dye and Evans blue dye are comparable to that of mepivacaine, mepivacaine diffuses more readily across the synovial membranes of the navicular bursa and DIPJ than do those 2 dyes, possibly because the hydrophilic and lipophilic ends of the mepivacaine molecule increase its ability to diffuse across synovial membranes. Mepivacaine is partially lipid soluble and has a molecular weight of 246.34 daltons. The similarly low molecular weights of triamcinolone (394.45 daltons) and methylprednisolone (374.46 daltons) may also enable those agents to diffuse across synovial membranes.

The degree to which a corticosteroid can diffuse from the navicular bursa into the DIPJ was examined in a clinical report in which the results of treating horses with lameness attributable to navicular disease by administration of MPA or TA into the navicular bursa were compared with the results of treating similarly affected horses by administration of the same drugs into the DIPJ. Of the horses that had resolution of lameness for 2 or more months, 60% had received the corticosteroid in the navicular bursa, whereas only 34% had received the corticosteroid in the DIPJ.

The duration of action of corticosteroids depends on many variables, including total dose and rate of hydrolysis. Whether the differences detected in degree and duration of clinical effect between sites of injection (ie, DIPJ or navicular bursa) are dose-related events or are caused by incomplete diffusion of the corticosteroid between the navicular bursa and DIPJ is not clear. We hypothesized that routinely used doses of MPA and TA instilled into the DIPJ would diffuse into the navicular bursa and achieve clinically effective minimum concentrations in the bursa and that these same doses of corticosteroids instilled into the navicular bursa would diffuse into the DIPJ and achieve clinically effective minimum concentrations in the joint.

Materials and Methods

Animals—Horses used in the study (n = 32) were adult mares from the University of Tennessee teaching herd. Most mares were American Quarter Horses or Tennessee Walking Horses. All horses were free from lameness in the distal portions of the forelimbs as determined by a lameness examination. The project was approved by the University of Tennessee Institutional Animal Care and Use Committee.

Procedures and collection of samples—Horses were allocated to 4 treatment groups on the basis of the drug injected and site of administration. Horses in group 1 received 40 mg of MPA in the DIPJ, horses in group 2 received 10 mg of TA in the DIPJ, horses in group 3 received 40 mg of MPA in the navicular bursa, and horses in group 4 received 10 mg of TA in the navicular bursa. One forelimb of each horse in each group was injected.

The trial was performed in 2 phases. Phase 1 was designed to establish the time of maximal diffusion of MPA and its active metabolite, methylprednisolone, or TA and its active metabolite, triamcinolone, from the DIPJ to the navicular bursa or from the navicular bursa to the DIPJ. Time of maximal diffusion for each treatment group was established by determining the concentration of the corticosteroid and its active metabolite in synovial fluid obtained from 6 pairs of horses (total, 12 horses/group) when samples of synovial fluid were collected 1, 2, 3, 6, 9, or 12 hours after injection. In phase 2, synovial fluid was obtained at the time of maximal diffusion from 6 additional horses for each treatment group so that, in total, 8 samples of synovial fluid/treatment group were obtained at the time of maximal diffusion. During both phases, when a synovial structure (DIPJ or navicular bursa) was injected with MPA or TA, only the synovial structure into which the drug diffused was sampled (navicular bursa or DIPJ, respectively). Because of the large number of synovial fluid samples, some horses were members of 2 treatment groups in phase 1. The contralateral limb was used in those horses, and at least 3 weeks were allowed to elapse before the contralateral forelimb was used. The allocation of the forelimb that was used first was randomized. Some horses from phase 1 were used again in phase 2. A period of 4 months elapsed prior to reuse of horses in phase 2, and the horses were allocated to a different treatment group.

For each injection, the horse was sedated with detomudine hydrochloride (5 to 10 µg/kg, IV), and a twitch was applied to the nose for restraint. The foot of 1 forelimb was desensitized by anesthetizing the palmar digital nerves at the level of the proximal sesamoid bones with mepivacaine hydrochloride; this was intended to prevent the horse from moving during centesis of the navicular
bursa. The site of centesis of the DIPJ or navicular bursa was scrubbed with chlorhexidine soap and rinsed with 70% isopropyl alcohol. A disposable, 20-gauge, 1.5-inch hypodermic needle was used for centesis of the DIPJ, and a disposable, 20-gauge, 3.5-inch spinal needle was used for centesis of the navicular bursa.

Centesis of the navicular bursa and dorsal pouch of the DIPJ was performed by use of techniques described elsewhere. To verify centesis of the navicular bursa, 1 mL of radiographic contrast solution and 1 mL of physiologic saline (0.9% NaCl) solution was combined with the MPA or TA to achieve a total of 3 mL, and a lateromedial radiographic view of the foot obtained immediately after injection of the navicular bursa was examined to verify that only the navicular bursa had been injected. Detection of contrast solution in only the navicular bursa was interpreted as evidence of successful bursal injection. Inadvertent injection into the DIPJ caused the horse to be eliminated from the trial and replaced by another.

To obtain synovial fluid from the navicular bursa, 3 mL of physiologic saline solution was injected into the navicular bursa and immediately aspirated. After aspiration of the physiologic saline solution, 3 mL of a radiocontrast solution was administered through the needle, and a lateromedial radiographic projection of the foot obtained immediately after sample collection was examined to verify that the navicular bursa was the synovial structure from which the sample was collected. Detection of contrast solution in only the navicular bursa was interpreted as evidence of successful bursal centesis. Inadvertent centesis of the DIPJ, as determined by radiographic examination, caused the horse to be eliminated from the trial and replaced by another and that synovial fluid sample to be eliminated from analysis. To obtain synovial fluid from the DIPJ, 3 to 5 mL of physiologic saline solution was injected into the DIPJ and aspirated immediately after infusion through the same needle used to administer it. To inject the DIPJ, 2 mL of physiologic saline solution was combined with the MPA or TA to achieve a total of 3 mL. It was determined that needles were within the dorsal pouch of the DIPJ when synovial fluid was observed in the needle hub, low resistance to injection was confirmed, and back pressure in the syringe was detected. A blood sample was obtained from every horse for analysis of serum urea concentration at the time the physiologic saline solution was collected by synoviocentesis.

Each synovial sample was divided into 2 aliquots, which were stored at −80°C for later analysis. Serum obtained from the blood samples was also stored at −80°C.

**HPLC analysis**—Concentration of the parent corticosteroid (MPA or TA) and its active metabolite (methylprednisolone or triamcinolone) in synovial fluid was determined via HPLC. The column temperature was maintained at 45°C. The HPLC solvent was 16% isopropanol in HPLC-grade water, to which 0.1% trifluoroacetic acid solution had been added. Analytic separations were performed under isocratic conditions with the HPLC solvent flow rate fixed at 1 mL/min.

Solid-phase extraction cartridges were used to extract corticosteroids from synovial fluid samples. To extract a corticosteroid, cartridges were washed with 1 mL of methanol followed by washing with 1 mL of water. One milliliter of synovial fluid was applied and drained through the cartridge; the cartridge was again washed with 1 mL of 5% methanol in water, and corticosteroids were eluted with 1 mL of methanol. The methanol was evaporated in a heating block at 45°C by use of a stream of nitrogen gas. The extracted corticosteroids were redissolved in 0.1 mL of isopropanol-water solution (1:1 ratio) and placed in injection vials. Vials were placed in the autosampler and maintained at 4°C, and injections (20 µL) were performed automatically. Duration of each HPLC assay was 80 minutes, with this long duration ensuring that all analytes of interest were eluted from the column.

**Data analysis**—Dilution error, caused by injecting physiologic saline solution into the DIPJ or navicular bursa prior to aspiration, was corrected by use of a correction factor for urea/synovial fluid dilution. This factor was the ratio of the urea concentration in the serum to the urea concentration in the synovial fluid. The ratio of serum urea to synovial urea is a validated correction factor for dilution of synovial fluid caused by the sampling technique. Urea concentration of serum and synovial fluid was obtained with a urea ELISA. To determine urea concentration in the serum samples, 5 µL of serum was assayed in accordance with the manufacturer’s instructions, but for the diluted synovial fluid samples, 20 µL was assayed to ensure that a measurable amount of urea was detected. To correct for that increase in dose, the concentration of urea in diluted synovial fluid was divided by 4. Results of the HPLC analysis were multiplied by the dilution correction factor to obtain the true concentration of the corticosteroid in the synovial fluid.

Diffusion quantity and diffusion quantity standard deviation to a milligram-per-milligram basis of corticosteroid injected were analyzed via commercially available software with values of P ≤ 0.05 considered significant. Within the linear model, both product (methylprednisolone vs triamcinolone) and site of injection (navicular bursa vs DIPJ) were treated as fixed factors.

**Results**

**Phase 1**—A peak diffusion time of 3 hours after injection for all groups was determined on the basis of visual assessment of diffusion curves (Figure 1).

**Phase 2**—The concentration of methylprednisolone and triamcinolone that had diffused from the DIPJ to the navicular bursa or from the navicular bursa to the DIPJ at 3 hours varied among horses. For group 1, injection of 40 mg of MPA into the DIPJ resulted in a mean ± SD concentration of 0.240 ± 0.026 µg of methylprednisolone/mL in the navicular bursa (Figure 2). For group 2, injection of 10 mg of TA into the DIPJ resulted in 0.124 ± 0.075 µg of triamcinolone/mL in the navicular bursa. For group 3, injection of 40 mg of MPA into the navicular bursa resulted in 0.091 ± 0.026 µg of methylprednisolone/mL in the DIPJ. For group 4, injection of 10 mg of TA into the navicular bursa resulted in 0.091 ± 0.026 µg of methylprednisolone/mL in the DIPJ. Methylprednisolone acetate and TA did not diffuse readily and were excluded from further analysis. Prod-
uct injected (MPA vs TA) had no significant effect on mean rate of diffusion of the corticosteroid metabolite from one synovial structure to the other. However, a site effect was detected, with significantly \( P = 0.05 \) greater diffusion of corticosteroid metabolite when the DIPJ was injected. Within the model, there was an interaction effect of site and product injected, which was primarily caused by the difference in diffusion of MPA from the DIPJ into the navicular bursa, compared with diffusion of MPA from the navicular bursa into the DIPJ, respectively \( 0.050 \pm 0.012 \, \mu g/mL \) vs \( 0.246 \pm 0.074 \, \mu g/mL \); \( P = 0.017 \); Figure 2).

To compare approximate diffusion of methylprednisolone and triamcinolone on a milligram-per-milligram basis, results of methylprednisolone diffusion were standardized by dividing the raw methylprednisolone diffusion by 4 (Figure 3). When not taking the site of injection into consideration, triamcinolone diffusion values were greater than those for methylprednisolone on a milligram-per-milligram basis, although the difference was not significant \( 0.11 \pm 0.039 \, \mu g/mL \) vs \( 0.037 \pm 0.009 \, \mu g/mL \); \( P = 0.09 \).

Comparison of the interaction between direction of diffusion and product injected revealed that the difference in diffusion of triamcinolone and methylprednisolone from the DIPJ was not significantly different, but that triamcinolone diffused 9 times as readily from the navicular bursa as did methylprednisolone on a milligram-per-milligram basis \( \text{mean} \pm 5D \text{ concentrations, } 0.0918 \pm 0.026 \, \mu g/mL \), and \( 0.0124 \pm 0.07 \, \mu g/mL \) for triamcinolone and methylprednisolone, respectively; \( P = 0.007 \); Figure 3).

**Discussion**

Measurable quantities of methylprednisolone and triamcinolone diffused from the DIPJ to the navicular bursa and from the navicular bursa to the DIPJ. On the basis of data indicating that clinically effective mini-
The rate of hydrolysis by synovial tissue enzymes may vary because of variability in the volume of synovial fluid. Therefore, the established minimum effective intra-articular concentration of methylprednisolone or triamcinolone is only an estimate. Further study may reveal that a higher dose of corticosteroids injected in the DIPJ or navicular bursa could attain a higher concentration in the navicular bursa than the DIPJ. Consequently, increasing the volume injected into the DIPJ may increase the rate of diffusion into the navicular bursa.

The rate of hydrolysis by synovial tissue enzymes and binding affinity of a corticosteroid to receptors in the cytoplasm of target cells largely determine the duration of action for a corticosteroid. Duration of action is not determined wholly by the continued presence of the drug within the circulation or within the joint, but by the changes the drug causes. A corticosteroid may continue to occupy the cellular receptor and exert an effect even after concentrations of the drug in the synovial fluid can no longer be detected. From a clinical perspective, duration of action is difficult to assess and highly variable among horses. Nevertheless, results of the present study support the hypothesis that a clinically effective concentration of methylprednisolone or triamcinolone can be achieved by diffusion of drug between the DIPJ and navicular bursa.

Methylprednisolone acetate and TA diffused erratically. The rate at which a drug diffuses is dependent on the direction of diffusion and physical characteristics of the drug, such as molecular weight. Both MPA and TA are hydrolyzed into an active ester form. The rate of hydrolysis and onset of action depend on the site of administration. Methylprednisolone acetate, which is slowly hydrolyzed into an ester when administered IM, is rapidly hydrolyzed in synovial fluid. The inconsistent diffusion of MPA and TA may be attributable to interindividual differences in hydrolysis.

In 1 study, administration of 40 mg of MPA into the tarsocrural joint of horses resulted in an undetectable concentration of methylprednisolone in the joint by 4 to 39 days. In a similar study, administration of 6 mg of TA into clinically normal tarsocrural and intercarpal joints of horses resulted in a high concentration of triamcinolone in the joints for 4 days, but the concentration was low by 14 days. The high variability of concentration of the metabolite of MPA or TA in the tarsocrural and intercarpal joints of horses in these studies is consistent with the high variability of the concentration of these metabolites in the navicular bursa and DIPJs of horses in the study reported here.

The doses of MPA and TA injected were chosen on the basis of doses that are injected into synovial structures in clinical settings. Because the volume of synovial fluid varies among joints, injecting a predetermined dose is more practical than trying to achieve a given concentration in the synovial structure. The sample size of 8 horses/sample group was chosen on the basis of use of that number of horses in another study in which investigators measured methylprednisolone concentration in the centrodigital joint after injecting 80 mg of MPA into the tarsometatarsal joint of 8 horses. The confidence intervals of our results are wide, which we believe reflects biological variability and a small sample size.

The sampling times used in phase 1 were chosen to cover the pharmacologic effect or potency of that corticosteroid, which is assessed as an indicator of its anti-inflammatory action. The potency of various corticosteroids is determined on the extent of hypothalamic-pituitary-adrenal axis suppression after parenteral administration of the corticosteroid, but transposing this suppression to the anti-inflammatory properties of intrasynovially administered drugs is difficult. Production of prostaglandin E₂ by rheumatoid synovia can be suppressed by exposure to 10⁻⁴ to 10⁻⁶ M concentrations of dexamethasone and 10⁻⁸ M concentrations of hydrocortisone. Because the potency of methylprednisolone is between those of dexamethasone and hydrocortisone, a 10⁻³ M (37 ng/mL) concentration of methylprednisolone has tentatively been considered capable of suppressing prostaglandin synthesis.

The concentration of a drug in the synovial fluid may vary because of variability in the volume of synovial fluid. Therefore, the established minimum effective intra-articular concentration of methylprednisolone or triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the DIPJ and a clinically effective concentration of methylprednisolone and triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the navicular bursa.

The definition of what constitutes a minimum therapeutic concentration of a corticosteroid depends on the pharmacologic effect or potency of that corticosteroid, which is assessed as an indicator of its anti-inflammatory action. The potency of various corticosteroids is determined on the extent of hypothalamic-pituitary-adrenal axis suppression after parenteral administration of the corticosteroid, but transposing this suppression to the anti-inflammatory properties of intrasynovially administered drugs is difficult. Production of prostaglandin E₂ by rheumatoid synovia can be suppressed by exposure to 10⁻⁴ to 10⁻⁶ M concentrations of dexamethasone and 10⁻⁸ M concentrations of hydrocortisone. Because the potency of methylprednisolone is between those of dexamethasone and hydrocortisone, a 10⁻³ M (37 ng/mL) concentration of methylprednisolone has tentatively been considered capable of suppressing prostaglandin synthesis.

The concentration of a drug in the synovial fluid may vary because of variability in the volume of synovial fluid. Therefore, the established minimum effective intra-articular concentration of methylprednisolone or triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the DIPJ and a clinically effective concentration of methylprednisolone and triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the navicular bursa.

The definition of what constitutes a minimum therapeutic concentration of a corticosteroid depends on the pharmacologic effect or potency of that corticosteroid, which is assessed as an indicator of its anti-inflammatory action. The potency of various corticosteroids is determined on the extent of hypothalamic-pituitary-adrenal axis suppression after parenteral administration of the corticosteroid, but transposing this suppression to the anti-inflammatory properties of intrasynovially administered drugs is difficult. Production of prostaglandin E₂ by rheumatoid synovia can be suppressed by exposure to 10⁻⁴ to 10⁻⁶ M concentrations of dexamethasone and 10⁻⁸ M concentrations of hydrocortisone. Because the potency of methylprednisolone is between those of dexamethasone and hydrocortisone, a 10⁻³ M (37 ng/mL) concentration of methylprednisolone has tentatively been considered capable of suppressing prostaglandin synthesis.

The concentration of a drug in the synovial fluid may vary because of variability in the volume of synovial fluid. Therefore, the established minimum effective intra-articular concentration of methylprednisolone or triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the DIPJ and a clinically effective concentration of methylprednisolone and triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the navicular bursa.

The definition of what constitutes a minimum therapeutic concentration of a corticosteroid depends on the pharmacologic effect or potency of that corticosteroid, which is assessed as an indicator of its anti-inflammatory action. The potency of various corticosteroids is determined on the extent of hypothalamic-pituitary-adrenal axis suppression after parenteral administration of the corticosteroid, but transposing this suppression to the anti-inflammatory properties of intrasynovially administered drugs is difficult. Production of prostaglandin E₂ by rheumatoid synovia can be suppressed by exposure to 10⁻⁴ to 10⁻⁶ M concentrations of dexamethasone and 10⁻⁸ M concentrations of hydrocortisone. Because the potency of methylprednisolone is between those of dexamethasone and hydrocortisone, a 10⁻³ M (37 ng/mL) concentration of methylprednisolone has tentatively been considered capable of suppressing prostaglandin synthesis.

The concentration of a drug in the synovial fluid may vary because of variability in the volume of synovial fluid. Therefore, the established minimum effective intra-articular concentration of methylprednisolone or triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the DIPJ and a clinically effective concentration of methylprednisolone and triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the navicular bursa.

The definition of what constitutes a minimum therapeutic concentration of a corticosteroid depends on the pharmacologic effect or potency of that corticosteroid, which is assessed as an indicator of its anti-inflammatory action. The potency of various corticosteroids is determined on the extent of hypothalamic-pituitary-adrenal axis suppression after parenteral administration of the corticosteroid, but transposing this suppression to the anti-inflammatory properties of intrasynovially administered drugs is difficult. Production of prostaglandin E₂ by rheumatoid synovia can be suppressed by exposure to 10⁻⁴ to 10⁻⁶ M concentrations of dexamethasone and 10⁻⁸ M concentrations of hydrocortisone. Because the potency of methylprednisolone is between those of dexamethasone and hydrocortisone, a 10⁻³ M (37 ng/mL) concentration of methylprednisolone has tentatively been considered capable of suppressing prostaglandin synthesis.

The concentration of a drug in the synovial fluid may vary because of variability in the volume of synovial fluid. Therefore, the established minimum effective intra-articular concentration of methylprednisolone or triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the DIPJ and a clinically effective concentration of methylprednisolone and triamcinolone was achieved (in most instances) in the DIPJ after MPA and TA were injected into the navicular bursa.
innocuous, and collection of multiple samples of this
synovial structure was inadvisable from an animal wel-
fare perspective. However, this precluded statistical
comparison of the sampling times, and the choice of 3
hours was selected on the basis of visual analysis of the
diffusion curves.

In a study18 in which 1 intercarpal joint received
MPA, MPA and methylprednisolone were not found in
the synovial fluid at any time in the contralateral (nonin-
jected) joint, although low (< 10 ng/mL) concentrations
of MPA and methylprednisolone were found in plasma.
Those results led our group to believe that use of the DIPJ
and navicular bursa of both forelimbs of the same horse
in our protocol was justified. Allowing a period of at least
3 weeks to elapse before use of the contralateral joint or
bursa ensured that administration of a corticosteroid into
a synovial structure on 1 limb would not affect the con-
centration of a corticosteroid administered into the con-
tralateral synovial structure. We cannot explain the reason
that there was a 9-fold difference in magnitude of diffusion
between triamcinolone and methylprednisolone from the
navicular bursa but no difference in the diffusion of these
2 products from the DIPJ.

Results of the study reported here suggested that
administration of MPA or TA into the DIPJ for treatment
of horses with inflammation of the navicular apparatus
can be effective. Results also suggested that the clinical
experience of longer-acting effects of intrabursal injec-
tion, compared with the duration of effects after DIPJ
injections, for treatment of horses with navicular dis-
ease1,12 may be more attributable to the high concentra-
tion of corticosteroid achieved in the navicular bursa
than to a difference in direction of diffusion.

References
the horse—the effect of controlled intrabursal cortical injec-
2. Verschooten F, Zaman K, Peremans K. Clinical navicular disease
syndrome in the horse: effect of corticosteroid injection into the
distal interphalangeal joint. Vlaams Diergeneeskundig Tijdschrift
3. Calislar T, St Clair LE. Observations on the navicular bursa and
the distal interphalangeal joint cavity of the horse. J Am Vet Med
4. Gibson KT, McIlwraith CW, Park RD. A radiographic study of the
distal interphalangeal joint and navicular bursa of the horse.
equine distal interphalangeal joint (articulationes interpha-
langeae distalis manus) and navicular bursa (bursa podotroch-
ic and dye distribution studies of nerves potentially desensiti-
tized by injections into the distal interphalangeal joint or the
1714.
7. Bowker RM, Van Wilfen KK, Grenitz DJ. Nonselectivity of local
anesthetics injected into the distal interphalangeal joint and the
8. Gough MR, Mayhew G, Munroe GA. Diffusion of mepivacaine
between adjacent synovial structures in the horse. Part 1: fore-
the distal interphalangeal joint alleviates lameness associated
10. Keegan KG, Wilson DA, Creeger JM, et al. Local distribution of
mepivacaine after distal interphalangeal joint injection in horses.
13. Gough MR, Munroe GA, Mayhew I. Urea as a measure of dilu-
kinetics of methylprednisolone and methylprednisolone acetate
in horses following intra-articular administration of methyl-
15. Trotter GW. Intra-articular corticosteroids. In: McIlwraith CW,
Trotter GW, eds. Joint disease in the horse. Philadelphia: WB
Saunders, 1996;237–256.
16. Kanitrowitz E, Robinson DR, McGuire MB. Corticosteroids in-
hibit prostaglandin production by rheumatoid synovia. Nature
1975;258:737–739.
17. Todhunter RJ, Fubini SL, Wootton JA, et al. Effect of methyl-
prednisolone acetate on proteoglycan and collagen metabolism
18. Lillich JD, Bertone AL, Schmall LM, et al. Plasma, urine, and syn-
ovial fluid disposition of methylprednisolone acetate and iso-
flupredone acetate after intra-articular administration in horses.
19. Axellrod L. Glucocorticoids. In: Harris ED, Kelley WN, Ruddy
Saunders, 1996;237–256.
of triamcinolone following intraarticular administration of
triamcinolone acetonide in the horse. J Vet Pharmacol Ther
21. Goodrich LR, Nixon AJ. Medical treatment of osteoarthritis in
methylprednisolone in the distal intertarsal joint after admin-
istration of methylprednisolone acetate in the tarsometatarsal