Clinical evaluation of the effects of immobilization followed by remobilization and exercise on the metacarpophalangeal joint in horses

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Objectives—To evaluate clinical effects of immobilization followed by remobilization and exercise on the metacarpophalangeal joint (MPJ) in horses.

Animals—5 healthy horses.

Procedure—After lameness, radiographic, and force plate examinations to determine musculoskeletal health, 1 forelimb of each horse was immobilized in a fiberglass cast for 7 weeks, followed by cast removal and increasing amounts of exercise, beginning with hand-walking and ending with treadmill exercise. Lameness examination, arthrocentesis of both MPJ, single-emulsion radiographic examination, nuclear scintigraphic examination, ground-reaction force-plate analysis, and computed tomographic examination were done at various times during the study.

Results—All horses were lame in the immobilized MPJ after cast removal; lameness improved slightly with exercise. Force plate analysis revealed a significant difference in peak forces between immobilized and contralateral limbs 2 weeks after cast removal. Range of motion of the immobilized MPJ was significantly decreased, and joint circumference was significantly increased, compared with baseline values, during the exercise period. Osteopenia was subjectively detected in the immobilized limbs. Significant increase in the uptake of radionucleotide within bones of the immobilized MPJ after cast removal and at the end of the study were detected. Loss of mineral opacity, increased vascular channels in the subchondral bone, and thickening within the soft tissues of the immobilized MPJ were detected.

Conclusions and Clinical Relevance—Results indicate that 8 weeks of enforced exercise after 7 weeks of joint immobilization did not restore joint function or values for various joint measurements determined prior to immobilization. (*Am J Vet Res* 2002; 63:282–288)

Joint immobilization causes substantial structural and biomechanical alterations in articular and periarticular tissues in numerous species.[1-3] These alterations have been seen at the gross and microscopic level and have resulted in diminished joint function. Articular cartilage, cancellous and cortical bone, and joint capsule have been evaluated separately and in various combinations after joint immobilization of variable duration. Severity of tissue alterations is dependent on the age of the individual and the duration of immobilization.[1-4]

Prolonged joint immobilization has been studied in humans and a variety of laboratory species and may cause multiple alterations in articular cartilage. These alterations include decreased **glycosaminoglycan (GAG)** content, increased GAG synthesis, and decreased proteoglycan maturation.[4-7] This may lead to development of joint surface erosions that appear to be worse in immobilized weight-bearing limbs, compared with immobilized non–weight-bearing limbs.[7] Joint immobilization may cause generalized osteoporosis of cancellous and cortical bone tissues, which may be a result of increased bone resorption or decreased bone formation.[8-11] Alterations to the joint capsule include increased numbers of WBC, synovial cell hyperplasia, and increased collagen production. Glycosaminoglycan and water content of the periarticular connective tissues may be decreased with immobilization, which may result in loss of range of motion followed by joint capsule contracture.[1,2] Fibrofatty connective tissue formation within a joint may lead to adhesions to the underlying articular cartilage that develop after 30 to 60 days of immobilization.[7] Immobilization of 12 months or longer in humans may result in obliteration of the joint space by fibrofatty proliferation and fibrous ankylosis.[3]

Permanent loss of joint function is the usual result of prolonged immobilization; however, depending on the remobilization strategy used, some of the alterations to joint function induced by short-term immobilization may be reversed.[12-16] Self-exercise protocols and enforced-exercise protocols have been examined. In 1 study that used mature dogs, loss of normal range of motion after 8 weeks of shoulder joint immobilization responded to 8 weeks of treadmill exercise with

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little improvement; however, complete recovery of joint function was obtained at 12 weeks.[15] In another study, return to normal range of motion within 4 weeks after remobilization was reported.[16] Other conflicting data suggest that alterations to a joint induced by immobilization are permanent even after extended self-exercise, especially in immature animals.[17-19] Therefore, it appears that length of immobilization, remobilization strategy, and the age of the individual all play a role in final outcome for joint function.

Little documentation exists concerning the effects of immobilization on normal limbs of horses. Cast immobilization has been used for treatment of equine fractures, joint luxations, wounds, and tendon lacerations, as well as stress protection for internal fixation. Horses may be particularly sensitive to the effects of immobilization, because the distal portions of the limbs lack protective factors such as surrounding muscle and multiple articulating surfaces. Richardson[20] reported that there was no significant atrophy in articular cartilage of the **metacarpophalangeal joint (MPJ)** in horses after 30 days of immobilization in a weight-bearing cast. Buckingham[21] reported the presence of mild osteopenia after 8 weeks of cast immobilization in horses. Bone quality measurements made by use of single photon absorptiometry, ultrasonographic velocity, and radiographic photodensitometry were significantly different between limbs at various times during the study, especially at the time of cast removal (8 weeks). Results also indicated faster return of bone mineral mass and quality to preimmobilization values during the return-to-exercise phase of the study, compared with stall rest alone. These 2 equine studies did not evaluate the effects of immobilization or remobilization on joint function.

At present, little data obtained from clinical evaluations on the effects of remobilization of an immobilized equine joint are available. The purpose of the study reported here was to determine effects of immobilization followed by remobilization on the function of the MPJ of clinically normal horses.

Materials and Methods

Animals—Five healthy sound horses, 22 to 26 months old, were used in this study. Musculoskeletal health and soundness were determined by use of physical, lameness, radiographic, and ground-reaction force-plate examinations of both forelimbs. Each horse was vaccinated, dewormed, housed in 12 X 12-ft box stalls, and fed a diet in accordance to the National Research Council. The study protocol was approved by the Institutional Animal Care and Use Committee.

Cast application and clinical assessment—A randomly chosen forelimb of each horse was immobilized in a cast for 7 weeks, followed by an 8-week period of increasing exercise on a treadmill,[a] as described elsewhere.[22] During the exercise period, each horse was evaluated every 2 weeks for lameness and assigned a subjective score from a standardized scoring system.[23] Lameness evaluation was made at the trot before and after flexion tests of the distal limb joints. Limb circumference (cm) at each MPJ and goniometric assessment of range of motion of the MPJ were measured and recorded every 2 weeks.

Synovial fluid analysis—Synovial fluid (1 to 2 ml) was aspirated from each MPJ through the collateral sesamoidean ligament by use of a 19-gauge needle at the beginning of the study and every 2 weeks after cast removal. Total WBC count, total protein concentration, and cytologic examination were performed to evaluate effects of immobilization and remobilization in both joints.

Ground reaction forces—Ground reaction forces of each forelimb were calculated from measurements obtained with a force plate[b] prior to cast placement and 2 and 8 weeks after cast removal for objective lameness evaluation. Trials required 5 foot-strikes for each forelimb at the trot (mean speed, 3 m/s; acceptable trials, 2.92 to 3.08 m/s) with speed measured by use of 2 photocells placed a known distance apart and integrated into the computer software package. Peak vertical force normalized by body weight (kg) was determined for each forelimb.

Radiography—Radiography of both MPJ was performed prior to cast application, at the time of cast removal, and every 4 weeks until the end of the study. Radiography was performed by use of a single-screen cassette[c] and single-emulsion film[d] to provide high detail and contrast. Radiographs were subjectively evaluated for the presence of disuse osteoporosis caused by immobilization and osteochondral damage caused by remobilization and exercise.

Nuclear scintigraphic imaging—At the time of cast removal and at the end of the study, horses were given technetium Tc 99m medronate (0.05 mCi/kg of body weight, IV) for nuclear scintigraphic imaging of the distal portions of both forelimbs. Dorsal and lateral nuclear scintigraphic images of each MPJ were recorded at 2 hours after injection. Variability in distribution of the radionucleotide between paired MPJ was controlled by using dorsal-plane images that contained both MPJ to normalize distance between the MPJ and the gamma camera. In addition, by using a selected site in the proximal portion of **metacarpal bone III (MC III)** as an area of standardization, differences in regional blood flow between limbs were controlled. The ratio of radioisotope uptake between paired MPJ normalized by the area of standardization in the proximal portion of the ipsalateral MC III were compared. Use of this procedure for objective comparison of radionucleotide uptake has been reported.[24]

Computed tomography—At the end of the study, horses were euthanatized with a lethal dose of barbiturate, and in 4 horses both forelimbs were removed at the middle carpal joint for **computed tomographic (CT)** examination. In the paired MPJ regions, axial slice images (2.0 mm) were acquired by use of a high-resolution protocol and a bone algorithm with a CT unit.[e] The area examined by use of CT extended from the middle of MC III to the middle of the **proximal phalanx (PP)**. Subchondral bone margins were subjectively evaluated for evidence of osteolysis, osteonecrosis, sclerosis, and alterations in bone vascularity.

Additional tissues, including articular cartilage, subchondral bone, synovial fluid, joint capsule, and sesamoid bones were harvested and preserved in 70% ethyl alcohol or frozen after euthanasia for future analysis.

Statistical methods—Comparisons for each limb and between limbs over time were assessed by use of a general linear model statistical program[f] and used ANOVA for repeated measures; where appropriate, a least-square means procedure was used to further determine significance. Data were also evaluated with a residual plot procedure to ensure random distribution. Nuclear scintigraphy comparisons were evaluated by use of a Student *t*-test for paired data. A significance level of $P \leq 0.05$ was used for all statistical tests.

Results

No complications with general anesthesia, cast application, or recovery from anesthesia were observed for any horse. Mild partial-thickness dermal ulcerations were detected over the proximodorsal aspect of MC III and over the proximal sesamoid bones in 4 of 5 horses; these lesions healed in 1 to 2 weeks. Four of the 5 horses completed the exercise program. One horse failed to complete the exercise protocol in week 15 because of a persistent grade-3/5 lameness. The data point for this horse was excluded from statistical evaluation of the final force plate analysis, because it fell outside the residual plot procedure. Likewise, multiple data points for the WBC data for all horses fell outside the residual plot procedure. The remainder of the data obtained from the lame horse was similar to that of the other 4 horses. For all horses, body weight increased during the study (mean increase, 3.3%; range, 1.6 to 5.8%).

Lameness examination—All horses were free of lameness (grade, 0/5) in both forelimbs at the beginning of the study. At the time of cast removal (week 7), each horse was lame in the limb that had been immobilized (grade, 2/5). At week 11, 4 horses had grade-2 lameness, and 1 horse had grade-3 lameness. At week 13, 1 horse had grade-1 lameness, 3 horses had grade-2 lameness, and 1 horse had grade-3 lameness. At the end of the study period, 3 horses had improved to grade-1 lameness, 1 horse remained grade-2 lame, and lameness in 1 horse progressed to grade 3. All horses had a positive response (increase in lameness) to flexion of all distal immobilized limb joints at all times examined.

Ground-reaction forces—Results of the subjective lameness examination were supported by results of force plate analysis. There was no significant difference in peak vertical forces between forelimbs prior to casting in each horse. A significant ($P < 0.001$) decrease in peak vertical forces was recorded in the immobilized forelimb of each horse, compared with the contralateral limb, 2 weeks after cast removal (**Fig 1**). Peak vertical forces were typically 20 to 30% less in the immobilized limb after cast removal, compared with the other forelimb. Peak vertical forces of the immobilized forelimb at the end of the study were not significantly different from preimmobilization values ($P = 0.1$).

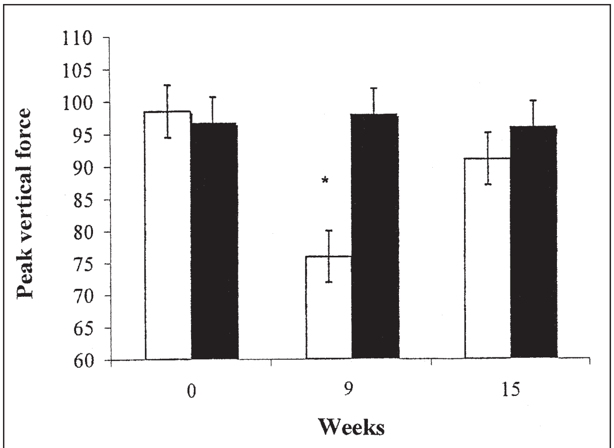

Figure 1—Mean ± SD values of peak vertical forces expressed as percentage body weight (kg) over time, evaluated at the trot (2.92 to 3.08 m/s) in 4 horses in which a cast was applied to 1 forelimb (open bars) at time 0, whereas the contralateral forelimb (solid bars) was not cast; the cast was removed after 7 weeks, and horses received increasing exercise until 15 weeks. *Significant ($P < 0.05$) difference between forelimbs and from baseline values.

Range of motion—A significant decrease in the range of motion of the immobilized MPJ, compared with the ipsilateral and contralateral baseline values,

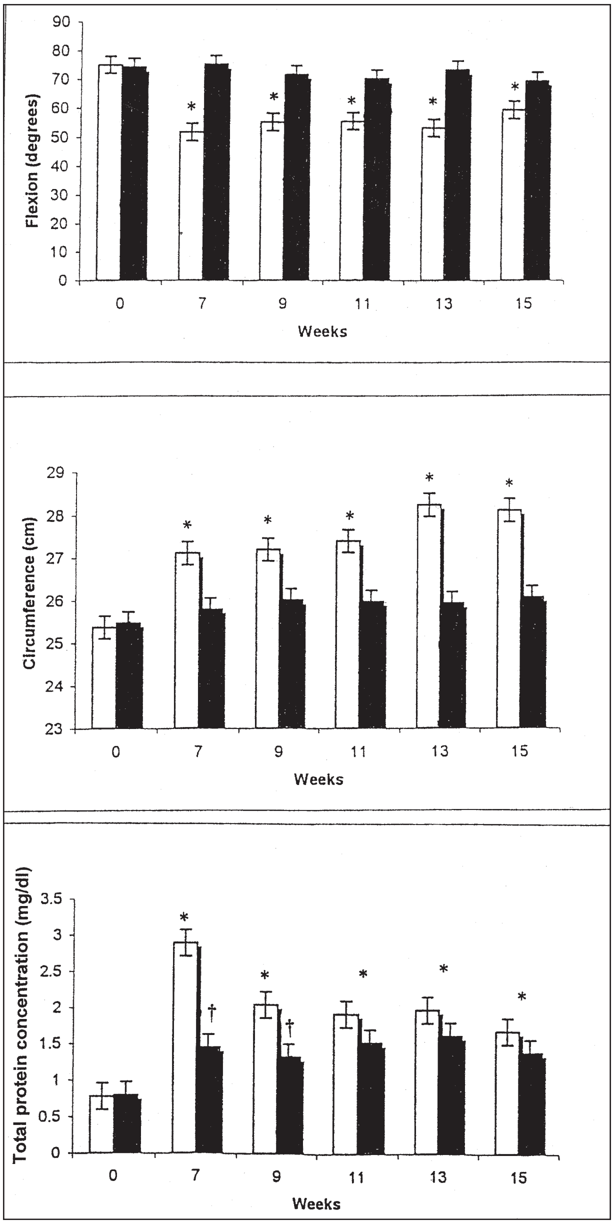

Figure 2—Measurements relating to lameness in 5 horses in which a cast was applied to 1 forelimb (open bars) at time 0, whereas the contralateral forelimb (solid bars) was not cast; the cast was removed after 7 weeks, and horses received increasing exercise until 15 weeks. Top—Mean ± SD range of motion (degrees of flexion) of the metacarpophalangeal joint. *Significantly ($P \le 0.05$) different between forelimbs and from baseline values. Middle—Mean ± SD joint circumference (cm). *Significantly ($P \le 0.05$) different between forelimbs and from baseline values. Bottom—Mean ± SD total protein concentration (mg/dl) in synovial fluid. *Significant ($P \le 0.05$) difference between ipsalateral baseline values. †Significant ($P \le 0.05$) difference between forelimbs.

was apparent for each horse after cast removal (**Fig 2**). This decrease in range of motion continued through the study period (week 15). Range of motion of the immobilized MPJ was decreased a mean of 20.5% at the end of the study (week 15), compared with baseline values (week 0). Slight increases in the range of motion detected in the immobilized limb were not significant over time. Range of motion of the contralateral limb remained unaltered throughout the study.

Circumference of the MPJ—A significant increase in MPJ circumference was observed in the immobilized limb at the time of cast removal (week 7), compared with ipsalateral and contralateral baseline values, and this finding persisted throughout the study (Fig 2). Circumference of the MPJ of the immobilized limb was increased a mean of 10.8% at the end of the study, compared with that measured at the beginning of the study. The circumference of the MPJ of the contralateral limb was slightly increased at the end of the study, but not significantly. Circumference of the MPJ of the immobilized limbs was significantly greater than that of the contralateral limbs at cast removal and at the end of the 15-week study period.

Synovial fluid analysis—Total protein concentrations of the synovial fluid from immobilized and contralateral limbs were significantly increased, compared with ipsilateral and contralateral baseline values, from the time of cast removal until the end of the study (Fig 2). The increase within immobilized joints was significantly greater than that of contralateral joints following cast removal. At weeks 7 and 9 of the study, there was a significant difference in total protein concentration in synovial fluid between immobilized and contralateral MPJ. Statistically, WBC count was similar before and after immobilization and remobilization within and between immobilized and contralateral joints and among horses (time 0, immobilized mean 1,002 ± 935 cells/µl, contralateral mean 784 ± 587 cells/µl; time 1, immobilized mean 497 ± 807 cells/µl, contralateral mean 793 ± 584; time 2, immobilized mean 795 ± 753 cells/µl, contralateral mean 422 ± 726 cells/µl; time 3, immobilized mean 1,057 ± 811 cells/µl, contralateral mean 957 ± 1,098 cells/µl; time 4, immobilized mean 459 ± 535 cells/µl, contralateral mean 207 ± 61 cells/µl; and time 5, immobilized mean 464 ± 463 cells/µl, contralateral mean 282 ± 457 cells/µl).

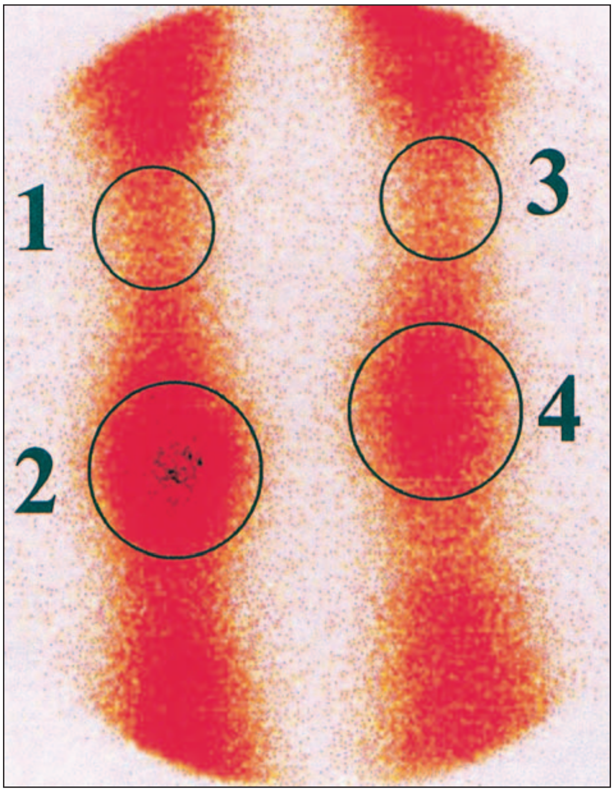

Figure 3—Nuclear scintigraphic image of distal portions of the forelimbs of a horse 7 weeks after a cast had been applied to the forelimb on the left side of the figure. Notice areas of standardization (1,3) and areas of interest (2,4) on the third metacarpal bones and increased radiopharmaceutical uptake in the forelimb that had been immobilized.

Radiography—Osteopenia, defined as decreased mineral opacity and content of the cortical bone of MC III, the PP, and the proximal sesamoid bones, was apparent in all immobilized limbs at the time of cast removal. Osteopenia remained until the end of the study, although bone density appeared to improve in each horse. The observed osteopenia was most evident in the proximal sesamoid bones and articular margins of MC III and the PP. Radiographic changes were not identified in the contralateral limb of any horse during the study.

Nuclear scintigraphy—Nuclear scintigraphy detected a significant increase in radioisotope uptake in MC III and the PP of the immobilized forelimbs, compared with the contralateral forelimbs, after cast removal (**Fig 3**). The ratio of values obtained from the immobilized MPJ and the standardized site in the proximal portion of the ipsalateral MC III was compared with the ratio for the contralateral MPJ and its area of standardization. Mean ratio ± SD for the immobilized limb was 2.722 ± 0.13, whereas mean ratio for the contralateral limb was 1.938 ± 0.08 (P = 0.007). Difference in radioisotope uptake between the immobilized MPJ (1.936 ± 0.11) and the

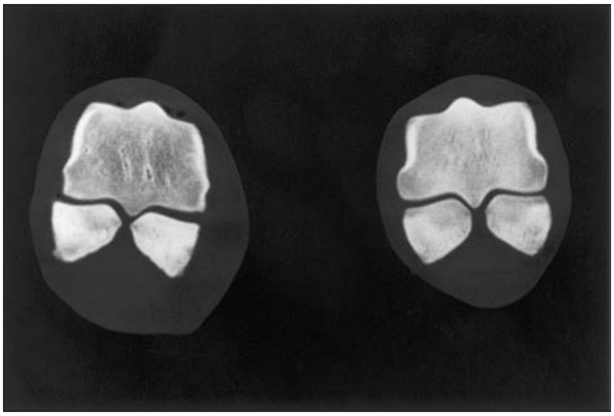

Figure 4—Transverse computed tomographic images of the distal portion of the third metacarpal bones and proximal sesamoid bones of a horse in which a cast was applied to 1 forelimb (left side of figure), whereas the contralateral forelimb was not cast; the cast was removed after 7 weeks, and the horse received increasing exercise until 15 weeks. Notice the decrease in bone opacity, prominent bone vascularity, and diffuse soft-tissue thickening of the bones in the forelimb that had been immobilized, compared with the other forelimb.

contralateral forelimb (1.756 ± 0.07) was still significant ($P = 0.01$) at the end of the study. There was no significant difference ($P = 0.2$) in radioisotope uptake in the contralateral limb between values obtained after cast removal and those obtained at the end of the study.

Computed tomography—Results of the CT examinations were subjectively evaluated for 4 horses. Regions of interest from the distal portion of MC III to the PP were examined. Consistent findings for all horses included prominent subchondral bone vessels, decreased mineral density, and soft-tissue thickening in the immobilized forelimb (**Fig 4**).

Discussion

Horses in this study had consistent lameness after 7 weeks of MPJ immobilization and 8 weeks of remobilization. Site of the source of the lameness was localized to the MPJ by use of physical, lameness, and nuclear scintigraphic examinations, and this finding was supported by results of ground-reaction force-plate analysis. Lameness may have had many possible origins; pain is the most common cause. Local anesthesia is 1 method used to determine the location of pain; diagnostic nerve blocks were not performed in this study because of potential interference with nuclear scintigraphy.[25] It is possible that abnormalities in other locations in the distal portion of the forelimb may have contributed to the observed lameness. Results of ground-reaction force-plate analysis were consistent with results of the subjective lameness scoring system 2 weeks after cast removal. At the end of the study, however, mechanical lameness (joint stiffness) may have been responsible for a portion of the lameness score, because ground-reaction force-plate analysis did not detect a significant difference between the forelimbs that had been immobilized and the contralateral forelimbs. However, results of force plate analysis at the end of the study for 1 horse were eliminated from statistical evaluation, because that horse had a grade-3/5 lameness, which was different from the other 4 horses and would have skewed the data. At the end of the study, stiffness of the MPJ, as detected via reduction of range of motion and increase in circumference, may have altered the biomechanical loading of the joint, thus creating the clinical impression of lameness.

The severity of lameness in 4 of 5 horses decreased with time and as horses were introduced to treadmill exercise. The lameness may be have been the result of immobilization, remobilization, or both; however, on the basis of results of studies[14-17] in other species, immobilization may have a greater influence on lameness, compared with remobilization. The goal of this study was to examine the combined effects of immobilization and exercise. Additional studies would have to be conducted to examine the individual effect of immobilization versus immobilization and exercise; however, it would be difficult to justify sacrificing a group of horses to look at this effect alone.

A 7-week period of immobilization was selected for this study to mimic application of casts to the distal portions of the limbs of horses. In clinical practice, the period of immobilization is dictated by the primary disease and may range from a few weeks for simple lacerations to several weeks for tendon lacerations or fractures. The exercise protocol was similar to rehabilitation protocols for musculoskeletal injures (4 weeks of light exercise), while providing enough stress to identify possible induced alterations to joint function (4 weeks of heavy exercise). A similar protocol for simulating the heavy exercise of race training by use of a high-speed treadmill has been reported recently.[25] For horses with injuries that necessitate immobilization of the distal portion of the limb for 7 weeks, enforced exercise would not be prescribed 4 weeks after cast removal in clinical practice. Results of our study support this conservative clinical approach, in that reduced range of motion, increased joint circumference, and mild lameness are generally seen as undesirable when rehabilitating a joint injury.

The persistent decrease in range of motion and the increase in joint circumference were unexpected findings. Range of motion often decreases with increasing severity of disease that affects the MPJ.[26] Changes in joint circumference and range of motion may not be permanent; however, neither range of motion nor joint circumference improved during 8 weeks of remobilization in our study. Some improvement has been documented in other species.[16] In 1 study, immobilization of the canine shoulder joint for 12 weeks resulted in a significant decrease in range of motion.[15] Range of motion remained unaltered after 4 weeks of remobilization. The same author reported in a later study,[16] using a similar protocol, that 12 weeks of remobilization of the canine shoulder joint allowed return to normal function. Similar results may have been obtained in our study if a longer or different exercise protocol had been used, compared with the protocol we used. Interruption of the immobilization period with intermittent exercise may, however, have a detrimental effect on rehabilitation with regard to range of motion.[27] The protocol established in our study may provide a useful model for future work in a focused-exercise approach to joint rehabilitation.

Total protein concentrations in synovial fluid from the horses in this study indicated that mild to moderate synovitis may be caused by joint immobilization; values obtained were greater than reported reference ranges.[28,29] The increased total protein concentration may have been attributable to inflammation or induced alterations in synovial membrane permeability. Even without a significant increase in WBC within the immobilized joints, inflammation alone may be the primary cause for the observed increase in total protein concentration. In a recent study, an increase in total protein concentration and prostaglandin E_2 concentration in the synovial fluid of horses with osteochondral fragmentation, without an increase in WBC count, was detected.[30] Results of our study may also indicate that immobilization alters the ability of the synovial membrane to produce normal joint fluid.

Radiographic examination in this study appeared to reveal osteopenia in the immobilized forelimbs. However, results were consistent with previous work, indicating that radiography yields variable results in identification of joint and bone lesions.[31] A 30 to 50%

reduction in bone mineral density is necessary before distinct changes can be identified by single-emulsion radiographic examination.[31] It cannot be concluded from our study that osteopenia induced by immobilization contributed to lameness in the horses.

Nuclear scintigraphic examination revealed increased metabolic bone activity in the immobilized bones of the MCP joint after cast removal and at the end of the study. This could be a normal adaptive finding or a pathologic response to immobilization, remobilization, or both. A group of horses subjected to immobilization alone would be required to detect the effect of immobilization alone. Analysis of the uptake of the radionucleotide was done in the dorsal plane on paired forelimbs to eliminate variation in image acquisition time and distance. Using an area of standardization within the same limb to evaluate differences in radionucleotide uptake in regions of interest between limbs has been used to quantify results of nuclear scintigraphic data.[24] Results of our study reaffirmed the ability of nuclear scintigraphy to identify minute increases in bone metabolism, as reported in a variety of conditions that cause lameness in horses.[32-34] The results of this study may provide some insight into clinical use of nuclear scintigraphy to monitor immobilized patients.

Computed tomography identified changes in bone induced by immobilization and remobilization that were not fully detected by use of other imaging modalities used in this study, especially in defining alternations in bone mineral opacity and vascularity. The prominent appearance of the bone vascular structures was a consistent finding. Because CT was done only at the end of the study, it is difficult to make any conclusion regarding possible differences between effects of immobilization versus remobilization on the CT results. Comparatively, 1 study[35] of rat tibiae and femora found an increase in subchondral bone vascularity with exercise; therefore, the increase in vascularity within the immobilized MPJ in our study may have been a result of increased bone resorption during immobilization, increased bone formation during remobilization, or both. Computed tomography provided superior imaging of anatomic alterations in bone, as found in other studies.[36,37]

In horses that require cast application for treatment of various conditions, lameness after cast removal may be related to the original condition, effects of immobilization on local tissues, or effects of remobilization. Increasing athletic activity has been encouraged during rehabilitation soon after joint injuries in humans in order to increase range of motion and reduce pain. If the goals of joint rehabilitation in horses are the same, then clinical rehabilitation of the MPJ after cast removal in horses may be best accomplished by a different exercise protocol than that used in this study.

[a]Sato 1, Equine Dynamics, Uppsala, Sweden.
[b]Multicomponent measuring force plate, Kistler Instruments Corp, Amherst, NY.
[c]Lanes Fine, Eastman Kodak Corp, Rochester, NY.
[d]EM 1, Eastman Kodak Corp, Rochester, NY.
[e]Pace computed tomographic unit, General Electric Corp, Milwaukee, Wis.
[f]SAS, version 7.0, SAS Systems Inc, Cary, NC.

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