

# Special Report

## Results of a survey of equine practitioners on the use and perceived efficacy of polysulfated glycosaminoglycan

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**Objective**—To determine the patterns of use and perceived efficacy of polysulfated glycosaminoglycan (PSGAG) for the treatment of degenerative joint disease in horses.

**Design**—Cross-sectional mail survey.

**Sample Population**—1,522 equine practitioners.

**Procedure**—Information was obtained on frequency and route of administration of PSGAG for the treatment of each of 4 forms of degenerative joint disease, the efficacy of PSGAG, and its efficacy compared with that of sodium hyaluronate. Data were analyzed by nonparametric and multivariate regression methods.

**Results**—Response rate was 40.5%. Of practitioners responding, 26% were classified as having a special interest in lameness and 74% as general practitioners. Use of PSGAG was reported by 90.5% of all practitioners, but lameness practitioners used PSGAG more frequently than general practitioners. Use of PSGAG also was significantly more common among practitioners involved predominately with racing Thoroughbreds, Standardbreds, or show horses. Use of PSGAG was reported to be moderately effective in the treatment of the 4 joint disease conditions. Practitioners treating Thoroughbred racehorses gave highest efficacy scores, and pleasure horse practitioners gave lowest efficacy scores. Use of PSGAG was considered more effective than sodium hyaluronate for the treatment of subacute degenerative joint disease and less effective for idiopathic joint effusion and acute synovitis.

**Clinical Implications**—Use of PSGAG is regarded as moderately effective overall and is considered most useful in the treatment of subacute degenerative joint disease. The efficacy of PSGAG for incipient and chronic forms of degenerative disease is considered comparable to that of sodium hyaluronate. (*J Am Vet Med Assoc* 1996;209:1564–1568)

**D**egenerative joint disease is an important problem for human beings and domestic animals. It is characterized by signs of pain and degeneration of articular tissues, particularly articular cartilage. For decades, pharmaceutical companies have been developing substances

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to ameliorate clinical signs as well as the progression of the disease. Polysulfated glycosaminoglycan (PSGAG), a mixture of highly sulfated glycosaminoglycans of bovine origin, has been used in the treatment of degenerative joint disease. It has been hypothesized that the main beneficial effects of PSGAG are to protect articular cartilage by inhibiting matrix-degrading enzymes and to augment and normalize the synthetic activities of articular tissues, including articular cartilage and synovial membranes.<sup>1-4</sup> Results of studies that used animals in models of osteoarthritis would suggest that PSGAG has beneficial effects,<sup>5-9</sup> because treated animals developed fewer and less-severe lesions than did control animals; however, the ameliorative effects of PSGAG were less dramatic for treatment of horses with experimentally induced joint disease.<sup>10-11</sup>

It is generally believed that the optimal method to determine the therapeutic efficacy of any antiarthritis medication is the use of adequately controlled, double-blind, long-term clinical evaluations.<sup>12,13</sup> Unfortunately, there have been few such adequately controlled clinical trials on horses, so that objective data on the efficacy of antiarthritis drugs in naturally developing degenerative joint disease in horses are lacking. Without such studies, practitioners have had to rely on results of the limited studies available, their own experiences, and the experiences of other practitioners on which to base their decisions on the efficacy and usage of PSGAG and other antiarthritis drugs. Use of PSGAG by equine practitioners suggests that practitioners perceive that PSGAG has clinical efficacy. The purposes of the study reported here were to characterize the extent and manner in which equine practitioners use PSGAG, to determine the perceived efficacy of PSGAG for the treatment of joint conditions in horses; and to compare the perceived efficacy of PSGAG with that of sodium hyaluronate for the treatment of these joint conditions.

### Materials and Methods

A cross-sectional survey of members of the American Association of Equine Practitioners (AAEP) was conducted. A questionnaire was sent to all 3,754 members of the AAEP. After 3 weeks, a reminder was mailed to AAEP members who had not yet responded, which was followed by a similar, final reminder that was mailed 1 month after the first reminder.

The survey was designed to provide information on respondent demographics, including year of graduation from

veterinary school, geographic location of practice, proportion of the practitioners' efforts devoted to horses, relative proportions of various breeds or types of horses seen, and proportion of the time veterinarians spent working on lameness problems in horses. The geographic location of each respondent's practice was classified according to 9 districts defined by the AAEP, but included a 10th district for respondents residing outside the United States and Canada.

In addition, practitioners were asked whether they used PSGAG and, when applicable, their reasons for electing not to use it. Specific information was requested regarding the use of PSGAG in the treatment of each of 4 joint disease conditions, including idiopathic joint effusion without lameness, acute synovitis with lameness (radiographic changes not evident), subacute degenerative joint disease (mild radiographic changes), and chronic degenerative joint disease (moderate-to-severe radiographic changes). For each condition, practitioners were asked whether they used PSGAG for treatment, frequency of use, route of administration (intramuscular or intra-articular), and whether other drugs were used concomitantly with PSGAG. Practitioners also were asked to score the perceived efficacy of PSGAG for treatment of each condition, using the following 3-point scale: 1, minimally effective; 2, moderately effective; and 3, very effective. For the aforementioned joint disease conditions, practitioners were asked to compare the perceived efficacy of PSGAG with that of sodium hyaluronate for use in treating each condition, using the following 3-point scale: 1, less effective than sodium hyaluronate; 2, equally effective; and 3, more effective than sodium hyaluronate.

On the basis of results of the descriptive statistics, respondents were divided into 2 groups to determine whether the opinions of practitioners with a special interest in lameness of horses differed from those of other equine practitioners. One group (lameness practitioners) was defined as veterinarians who spent at least three fourths of their time working on horses and who spent at least half of their time working on lameness in horses. General equine practitioners (general practitioners) were veterinarians who spent less than three fourths of their time working on horses or who spent less than half of their time working on lameness in horses. Also, the opinions of respondents were further evaluated by subgroups of lameness practitioners whose practice activities involved mainly Standardbred racehorses, Thoroughbred racehorses, show horses (horses used for hunting, jumping, eventing, dressage, and other shows), or pleasure horses. Practitioners were assigned to one of these categories when at least four fifths of their practice effort involved one of these particular horse types.

Basic descriptive statistics of respondents were generated for all demographic and usage variables reported in the survey. After respondents were classified, nonparametric statistical tests (Wilcoxon's rank sum, Mantel-Haensel  $\chi^2$ , and Mantel-Haensel odds ratio estimates with 95% confidence intervals) were used to determine whether there were significant ( $P \leq 0.05$ ) differences between groups of practitioners for demographic variables, usage of PSGAG, and usage of other agents concomitantly with PSGAG, and for attitudes regarding PSGAG efficacy and perceived efficacy of PSGAG compared with that of sodium hyaluronate. Variables determined to be significant by use of these nonparametric tests were included in the multivariate analyses.

Multivariate logistic regression models were developed to determine factors that significantly influenced PSGAG use. Models for overall PSGAG use and PSGAG use for each of the 4 specific joint disease conditions were developed, using a backward model development approach ( $P \leq 0.05$  for inclusion of variables), with PSGAG use as the dependent variable and all demographic variables as independent

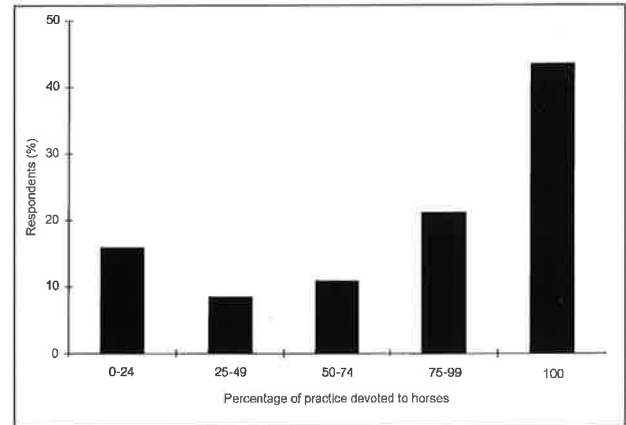


Figure 1—Distribution of respondents to a survey on use of polysulfated glycosaminoglycan (PSGAG), analyzed by the proportion of their practice devoted to horses.

variables. Odds ratios were computed for independent variables in each model. An odds ratio of  $< 1.0$  indicated that an increasing value for an independent variable was associated with a decreased likelihood of the use of PSGAG, whereas an odds ratio of  $> 1.0$  indicated that an increasing value for an independent variable resulted in an increased likelihood of PSGAG use. In addition, multivariate linear regression models were developed to determine those factors that affected perceptions of PSGAG efficacy and PSGAG efficacy compared with sodium hyaluronate efficacy, using PSGAG efficacy scores as the dependent variable and all demographic variables as independent variables. Saturated models with all demographic variables were developed for each joint disease condition, and backward model development, using an exit criterion of  $P \leq 0.10$ , was used to create the final version of the efficacy models.

## Results

Of 3,754 questionnaires mailed, 1,604 (42.7%) were returned. Of those returned, 1,522 were suitable for use in the study (usable response rate of 40.5%). A substantial proportion of respondents (664/1,522, 43.6%) were full-time equine practitioners (Fig 1).

Three hundred ninety-six (26.0%) of the respondents were classified as lameness practitioners, whereas the remainder were classified as general practitioners. Among the lameness practitioners, there were 251 veterinarians whose practices involved working at least four fifths of the time on a specific breed or type of horse (Standardbred racehorses, 55 respondents [13.9%]; Thoroughbred racehorses, 78 [19.7%]; show horses, 42 [10.6%]; pleasure horses, 76 [19.2%]).

Use of PSGAG was common among all respondents, with 370 of 396 (93.4%) lameness practitioners and 1,007 of 1,126 (89.4%) general practitioners reporting use of PSGAG for at least 1 of the 4 joint disease conditions. As anticipated, the proportion of lameness practitioners who used PSGAG was significantly ( $P \leq 0.01$ ) higher than that of general practitioners for overall use and for use in treating each of the 4 specific joint disease conditions (Fig 2). Analysis of patterns of overall PSGAG use for all respondents whose practice activities involved working at least four fifths of the time with a specific breed/use category revealed that PSGAG use was significantly ( $P \leq 0.05$ ) more common

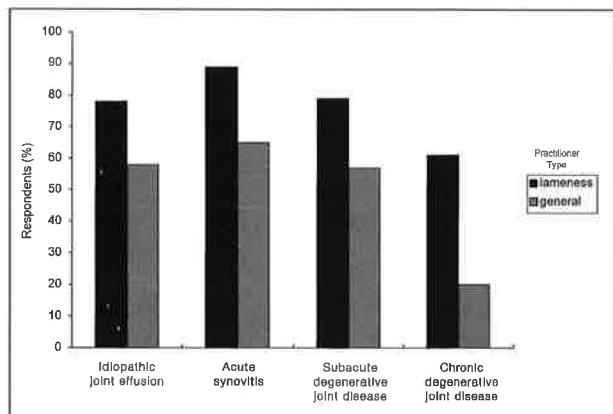


Figure 2—Practitioners use of PSGAG for treating each of 4 forms of degenerative joint disease in horses. Lameness practitioners were veterinarians whose practices were devoted to working at least three fourths of the time with horses and involved at least half of their time devoted to working with lameness in horses. General practitioners were veterinarians whose practices were devoted to less than three fourths of their time working with horses or involved less than half of their time working with lameness in horses.

for practitioners treating Standardbred racehorses, Thoroughbred racehorses, and show horses than for practitioners whose efforts involved mainly pleasure horses. When practitioners in these categories were classified into lameness and general groups, significant differences were not detected in PSGAG use.

Only 26 of 396 (6.6%) lameness practitioners and 119 of 1,126 (10.6%) general practitioners identified their reasons for not using PSGAG. For lameness practitioners, lack of efficacy was the most frequent reason for not using PSGAG, whereas cost was the most common reason among general practitioners. Both practitioner groups used the product more frequently as joint disease increased in severity. Lameness practitioners administered more doses of PSGAG for all joint disease conditions than did general practitioners, but the number of doses administered was not significantly different, and analysis of scores suggested that extended periods of treatment with PSGAG was uncommon among all respondents.

Respondents were asked to indicate the route of administration (intramuscular, intra-articular, or both) of PSGAG for each of the 4 disease conditions. Intramuscular administration of PSGAG was reported by 754 of 1,126 (67.0%) general practitioners and 329 of 396 (83.1%) breed/use specific practitioners, whereas 360 of 1,126 (32.0%) general practitioners and 174 of 396 (43.9%) lameness practitioners administered PSGAG intra-articularly. When classified by breed-use criteria, there were significant differences in the proportions of practitioners who administered PSGAG intramuscularly versus intra-articularly. Intra-articular administration was reported by 42 of 55 (76.4%) respondents treating racing Standardbreds, which was significantly ( $P < 0.0001$ ) different, compared with 23 of 78 (29.5%) for practitioners treating racing Thoroughbreds, 12 of 42 (28.6%) for practitioners treating show horses, and 20 of 76 (26.3%) for practitioners treating pleasure horses. This proportionately higher

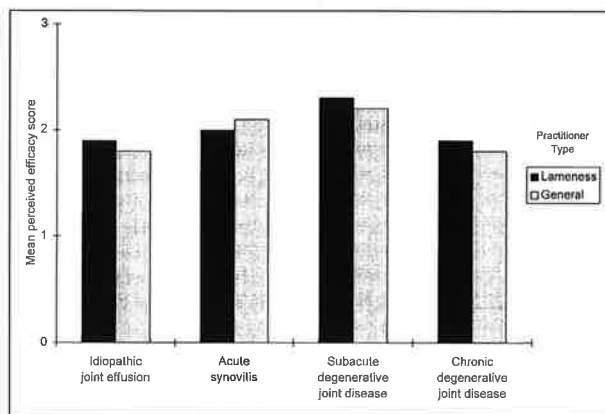


Figure 3—Perceived efficacy of PSGAG for use in treatment of each of 4 forms of degenerative joint disease in horses. Perceived efficacy was scored as follows: 1, minimally effective; 2, moderately effective; and 3, very effective. See Figure 2 for key.

intra-articular use by practitioners who worked mainly on racing Standardbreds was detected for 3 of the joint disease conditions, with the exception being idiopathic joint effusion.

On the basis of multivariate analysis, factors that increased the overall likelihood of PSGAG use were whether a practitioner was one who worked mainly on lameness in horses (odds ratio, 3.75) and whether the practitioners did at least four fifths of their work on racing Thoroughbreds (odds ratio, 1.79). Use of PSGAG was significantly less likely among practitioners who did at least four fifths of their work on pleasure horses (odds ratio, 0.56). These results were paralleled by results of practitioners for each of the joint conditions. Lameness practitioners and practitioners who worked mainly on racing Thoroughbreds were most likely to use PSGAG for the treatment of idiopathic joint effusion and acute synovitis. In addition, practitioners who spent at least four fifths of their time working on pleasure horses were less likely to use PSGAG for treatment of acute synovitis and subacute or chronic degenerative joint diseases.

Overall, PSGAG was reported to be perceived as moderately effective in the treatment of the 4 joint disease conditions (Fig 3). Multivariate linear regression analysis for the perceived efficacy of PSGAG for use in the treatment of idiopathic joint effusion revealed that practitioners who spent at least four fifths of their time working on racing Standardbreds had a lower perception of PSGAG efficacy, whereas practitioners who worked predominately on Thoroughbred racehorses had higher perception scores ( $R^2 = 5.4$ ,  $P = 0.0001$ ). Analysis of perceived efficacy scores for PSGAG in the treatment of chronic degenerative joint disease revealed that practitioners who worked mainly on show horses had higher ( $R^2 = 1.8$ ,  $P = 0.001$ ) scores for perceived PSGAG efficacy than did other respondents.

Overall, respondents considered the perceived efficacy of PSGAG and sodium hyaluronate to be similar (Fig 4). Results of multivariate linear regression analyses comparing the efficacy of PSGAG to sodium hyaluronate were analyzed for each of the 4 joint disease conditions. For acute synovitis, practitioners who

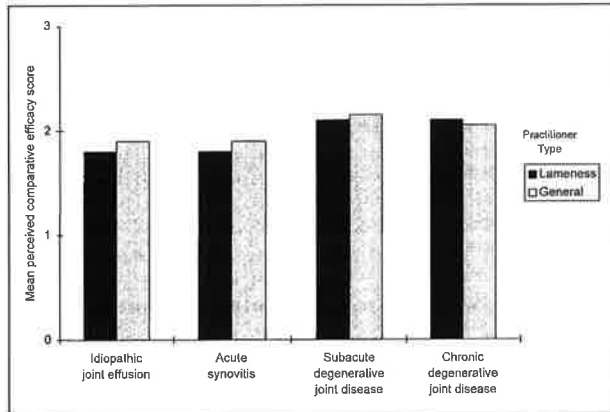


Figure 4—Perceived efficacy of PSGAG, compared with the perceived efficacy of sodium hyaluronate, when used to treat each of 4 forms of degenerative joint disease in horses. Perceived comparative efficacy was scored as follows: 1, less effective than sodium hyaluronate, 2, equally effective, and 3, more effective than sodium hyaluronate). See Fig 2 for key.

worked mainly on pleasure horses had lower perceived efficacy scores ( $R^2 = 1.3$ ,  $P = 0.001$ ) compared with other respondents. In the case of subacute degenerative joint disease, lameness practitioners had higher perceived efficacy scores ( $R^2 = 1.8$ ,  $P = 0.09$ ), whereas practitioners who worked mainly on pleasure horses provided lower perceived efficacy scores ( $R^2 = 1.8$ ,  $P = 0.0002$ ). For chronic degenerative joint disease, practitioners who worked mainly on pleasure horses had lower perceived efficacy scores, whereas lameness practitioners had higher perceived efficacy scores ( $R^2 = 4.5$ ,  $P = 0.0001$ ).

In general, there were low values for  $R^2$  in the study reported here, indicating that factors other than those included in the study contributed to practitioners' perceptions of PSGAG efficacy. Nonetheless, the fact that reported  $R^2$  values were significantly correlated suggested that these factors played an important role in practitioners' perceptions of the product and should be considered in future studies.

Although efforts were made to optimize the response to the survey, the response rate (40.5%) was low. It may be argued that the conclusions of the study may not be representative of the entire AAEP membership. Nonetheless, it did comprise the largest survey of this nature conducted to date, and these data were representative of a broad cross-section of equine practitioners in North America.

The decision to categorize respondents into the lameness and general practitioner categories was prompted by the observation that the majority of respondents were engaged in predominately equine practices, but the proportion of practitioners who spent more than half of their time doing lameness work included only one fourth of the respondents. We hypothesized that patterns of PSGAG use for practitioners whose practice activities involved a substantial amount of lameness work would differ from those of general practitioners. Multivariate logistic regression analysis revealed several patterns in PSGAG use that reflected these differences. Analysis of these differences suggested that lameness practitioners were approximately 3 times more likely to use PSGAG

than general practitioners were. In addition to increased overall usage, lameness practitioners also tended to use PSGAG more often for joint conditions other than established degenerative joint disease (eg, idiopathic joint effusion and acute synovitis). This may have represented a greater familiarity of this group of practitioners with the expected responses to PSGAG when treating these conditions or, at least, a willingness of this group of practitioners to investigate the use of PSGAG for treatment of less-advanced joint diseases.

The use of PSGAG was extremely common among the group of equine veterinarians who responded to our survey, with approximately nine tenths of the respondents reporting the use of PSGAG. Although this may misrepresent the overall use of PSGAG by practitioners in North America, it does illustrate that the product is widely used. Firm conclusions regarding the efficacy of PSGAG and its efficacy compared to sodium hyaluronate cannot be made on the basis of the results of the survey reported here, because concurrent use of PSGAG and other anti-inflammatory drugs was reported by a number of respondents, which also may be true of practitioners who used sodium hyaluronate. Nevertheless, respondents regarded PSGAG as being moderately effective in the treatment of degenerative joint disease in horses, and they perceived that the efficacy of PSGAG was comparable with that of sodium hyaluronate for the treatment of various forms of degenerative joint disease. It is generally believed that sodium hyaluronate is best suited for the treatment of incipient degenerative joint disease, namely mild-to-moderate synovitis and capsulitis.<sup>18,19</sup> Moreover, anecdotal reports suggest that horses with subacute or chronic degenerative joint disease often have a more favorable response to PSGAG treatment than that associated with sodium hyaluronate treatment. As such, it was of interest to learn that respondents considered PSGAG and sodium hyaluronate equally effective in the treatment of chronic degenerative joint disease.

Although there were a number of reasons provided by practitioners who did not use PSGAG, lack of efficacy was the most common reason among lameness practitioners, and cost was the major reason for general practitioners. It was possible that economic concerns precluded the use of PSGAG on a greater proportion of horses treated by general practitioners. Conversely, lameness practitioners were probably more likely to treat horses engaged in athletic activities in which economic considerations are of lesser concern. In that situation, evaluations of efficacy may be more stringently defined by lameness practitioners, potentially augmenting the likelihood of observing results considered suboptimal. Obviously, in some instances, treatment with PSGAG or other antiarthritis drugs may be attempted in horses that have lesions of sufficient severity or that are engaged in athletic activities of sufficient rigor that none of the treatments will provide satisfactory results, which was another possible reason for perceived lack of efficacy of PSGAG by lameness practitioners who have discontinued their use of the product.

The types of horses seen by practitioners appeared to influence the use of PSGAG. Overall PSGAG use and use of PSGAG for treatment of idiopathic joint effusion, acute synovitis, and subacute degenerative joint disease

was significantly more common among respondents whose practices involved working predominately on Thoroughbred racehorses. Specifically, lameness practitioners who worked mainly on racing Thoroughbreds were 2 to 3 times more likely to use PSGAG for treatment of acute synovitis and subacute degenerative joint disease than other practitioner groups, but lameness practitioners who worked mainly on Thoroughbreds were not more likely to use PSGAG as a treatment for chronic degenerative joint disease than other practitioner groups. The reason for the latter observation was not known, but may have been the result of concerns regarding the perceived efficacy of PSGAG for more-chronic and more-serious joint disorders for which other drugs may be used most frequently. On the basis of multivariate analyses, respondents who treated mainly pleasure horses were only half as likely as other practitioners to use PSGAG. This was expected, given the nature of the athletic activities of the horses typically associated with practitioners in each of the breed/use groups.

Classification of responses on the basis of breed/use groups of horses was of interest, because it was hypothesized that there may have been differences in the perceived efficacy of PSGAG depending on the particular athletic activities of treated horses. Regression analyses led to the conclusions that PSGAG was most highly regarded by practitioners working with racing Thoroughbreds for treatment of idiopathic joint effusion and by practitioners working with show horses for treatment of chronic degenerative joint disease. Conversely, practitioners working with racing Standardbreds believed the product was less useful for the treatment of idiopathic joint effusion than did other respondents. The finding of higher perceived efficacy scores for chronic degenerative joint disease among practitioners working with show horses suggested that this form of joint disease in horses may have been more amenable to PSGAG treatment in show horses than in racehorses. It may be argued that the musculoskeletal demands of a racehorse are often greater than those of many show horses and that an equal biologic response to treatment may have been perceived as an apparently unequal clinical result by practitioners in the 2 groups.

Another consistent trend when examining perceived efficacy scores and horse type was that practitioners who worked mainly with pleasure horses had lower scores for perceived PSGAG efficacy and comparative efficacy of PSGAG and sodium hyaluronate, compared with scores for other practitioner groups. When considering the potential response of pleasure horses to PSGAG treatment, it might be predicted that this group of horses would have a dramatic response to treatment, because the population of horses treated by this group of practitioners often participate in less-demanding athletic activities than the other groups. Reasons for the lack of a trend for increased perceived efficacy scores among practitioners who worked mainly with pleasure horses were unclear. It was possible that scores were influenced by suboptimal results observed by pleasure horse practitioners who were treating horses that had retired from more-rigorous athletic activities because of degenerative joint disease of sufficient severity that none of the medications would prove ameliorative. Moreover, many plea-

sure horses are not as highly valued as performance horses, and owners may be less inclined to pay for expensive forms of treatment. As such, financial constraints may have prevented treatment at an optimal dose, frequency, or duration that could have provided more-satisfactory results.

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