Neuropathic pain, a potentially disabling chronic pain disorder, may develop after nerve injury or as part of diseases. Therapy-resistant pain and severely impaired function of the affected extremity may develop. At present, a consensus concerning the etiology of neuropathic pain is still lacking. Search for the pathophysiologic mechanism of neuropathic pain has been an area of extensive investigation since the description of a rat model of neuropathic pain by chronic constriction injury (CCI) of the sciatic nerve. Findings from clinical observations and systematic experimentation on human patients and animal models suggest that both peripheral and central nervous system mechanisms may be involved in the development of neuropathic pain. Several studies suggest that proinflammatory cytokines may have an important role in the injury-induced peripheral nerve alterations, and they seem to contribute to the development of neuropathic pain. Tumor necrosis factor-alpha (TNF-α) is involved in the pathogenesis of neuropathic pain in peripheral nerve alterations, and it seems to contribute to the development of neuropathic pain. Therefore, TNF-α production is a potential target for the treatment of chronic pain.

**Hyperbaric Oxygenation Therapy Alleviates Chronic Constrictive Injury–Induced Neuropathic Pain and Reduces Tumor Necrosis Factor-Alpha Production**

Fenghua Li, MD,* Lili Fang, MD,* Shiwei Huang, MD,* Zhongjin Yang, MD,* Jyotirmoy Nandi, PhD,* Sebastian Thomas, MD,† Chung Chen, PhD,‡ and Enrico Camporesi, MD§

**BACKGROUND:** The development of hyperalgesia and allodynia after chronic constriction injury (CCI) is associated with significantly increased tumor necrosis factor (TNF-α) and interleukin (IL-1β). Theoretically, if the production of TNF-α and/or IL-1β could be reduced, neuropathic pain syndrome may be alleviated. Recently, a beneficial effect of hyperbaric oxygenation therapy (HBOT) in the treatment of pain disorders has been suggested. Our present study was designed to examine the hypotheses that (1) CCI-induced neuropathic pain may be associated with increased production of TNF-α and IL-1β, (2) HBOT may alleviate CCI-induced neuropathic pain, and (3) the alleviated neuropathic pain may be associated with reduced production of TNF-α and/or IL-1β.

**METHODS:** Male rats (weighing 250–300 g) were anesthetized with ketamine and xylazine. The common sciatic nerve was exposed through the biceps femoris. Proximal to the sciatic’s trifurcation, 4 ligatures were loosely tied around the nerve. In the sham group, an identical dissection was performed without ligation of the sciatic nerve. Mechanical allodynia and cold allodynia were tested by von Frey filament stimulation and the spread of acetone, respectively. HBO rats (n = 18) were exposed to pure oxygen for 1 hour at 2.4 atm once a day. Non-HBO (n = 18) and sham rats (n = 6) were placed in the HBO chamber breathing air. TNF-α and IL-1β in the sciatic nerve were assayed with ELISA. The presence of TNF-α protein in homogenates was verified by Western blot analysis.

**RESULTS:** CCI induced significant cold and mechanical allodynia as measured after CCI on days 4 and 7. The cold allodynia response frequency was significantly lower in HBO rats than in non-HBO rats. The values were 20% ± 1.6% vs 50% ± 4.5% on day 4 and 40% ± 4.6% vs 70% ± 4.5% on day 7 (F = 87.42, confidence interval [for the difference between HBO and non-HBO] = 29.612 ± 8.781, P < 0.05 for day 4 and day 7). The threshold of mechanical allodynia significantly increased in HBO rats compared with non-HBO rats. The values were 6.20 ± 0.9 vs 4.1 ± 1.0 g on day 4 and 3.8 ± 0.5 vs 2.3 ± 0.4 g on day 7 (F = 18.8, confidence interval [for the difference between HBO and non-HBO] = 1.806 ± 1.171, P < 0.05 for day 4 and day 7). TNF-α content was significantly higher in non-HBO rats than in sham rats on day 4 (17.89 ± 0.83 vs 10.66 ± 1.1 pg/mg protein, P < 0.05) and day 7 (18.97 ± 1.57 vs 9.09 ± 1.5 pg/mg protein, P < 0.05). HBOT significantly reduced TNF-α content to near the level in sham rats, which was 10.94 ± 2.78 and 11.32 ± 2.98 pg/mg protein on day 4 (P < 0.05 versus non-HBO) and 7 (P < 0.05 versus non-HBO), respectively. Western blot analysis confirmed the presence of proteins with molecular weights of 51 kDa in the rat sciatic nerve homogenates. IL-1β content was also significantly higher in non-HBO rats than in sham rats on day 4 (636 ± 74 vs 256 ± 51 pg/mg protein, P < 0.05) and on day 7 (687 ± 89 vs 288 ± 35 pg/mg protein, P < 0.05). HBOT had no effect on IL-1β content, which was 671 ± 85 pg/mg protein on day 4 and 672 ± 75 pg/mg protein on day 7 in HBO rats (P = not significant versus non-HBO rats).

**CONCLUSION:** These data show that HBO therapy alleviates CCI-induced neuropathic pain and inhibits endoneuronal TNF-α production, but not IL-1β in CCI-induced neuropathic pain. Reduced TNF-α production may, at least in part, contribute to the beneficial effect of HBOT. (Anesth Analg 2011;113:626–33)
factor (TNF-α) has been identified as a key pain mediator. In animal models, the endoneurial or IM injection of TNF-α induces pain-associated behaviors whereas blocking TNF-α attenuates pain in animal models of CCI-induced neuropathic pain. Interleukin (IL)-1 is another proinflammatory cytokine, which has been implicated in the induction and maintenance of neuropathic pain. Mice lacking the 2 isoforms IL-1α and IL-1β display reduced time to onset, duration, and magnitude of mechanical allodynia after CCI. Similar to TNF-α, the application of IL-1β also induces pain and blocking of IL-1β has analgesic effects. Theoretically, if the production of TNF-α and/or IL-1β could be reduced, neuropathic pain syndrome may be alleviated.

Hyperbaric oxygen therapy (HBOT) has been documented by the Undersea and Hyperbaric Medical Society to be beneficial for 13 different diseases. Recently, the beneficial effect of HBOT has been suggested in the treatment of pain disorders, including delayed onset muscle soreness, fibromyalgia, inflammatory pain, and complex regional pain syndrome. The mechanisms underlying the beneficial effect of HBOT are unknown, but some beneficial effects of HBOT may be attributable to an altered inflammatory process. HBOT has been shown to enhance some aspects of host defense and its overall effect seems to be immunosuppressive. More specifically, HBOT inhibits macrophage function and in ischemia-reperfusion intestinal injury. The beneficial effect may be attributable to reduced TNF-α and IL-1β production in the blood and peripheral tissues. The CCI model of neuropathic pain results in the development of hyperalgesia and allodynia after ligation. The development of CCI-induced neuropathic pain is associated with significantly increased production of TNF-α and IL-1β in the sciatic nerve. Behavioral tests indicate that CCI-induced behavioral changes are similar to those seen in clinic neuropathic pain patients. This animal model provides a powerful tool for us to investigate the pathophysiology of neuropathic pain. A recent study suggested that HBOT may be successful in relieving CCI-induced neuropathic pain for an extended period of time.

The present study was designed to examine our hypotheses that (1) CCI-induced neuropathic pain may be associated with increased production of TNF-α and IL-1β in the sciatic nerve, (2) HBOT may alleviate CCI-induced neuropathic pain, and (3) the alleviated CCI-induced neuropathic pain may be associated with reduced production of TNF-α and/or IL-1β in the sciatic nerve.

**METHODS**

**Experimental Animals**

The proposed study was approved by the Institutional Committee for the Humane Use of Animals and was in accordance with the guidelines established by the National Institutes of Health. Pathogen-free, male, Sprague-Dawley rats (Taconic, Hudson, NY) weighing 250 to 300 g were chosen. They were acclimated for 10 days in standard solid-bottom “shoebox”-type caging with free access to water and coarsely ground Purina Chow (Diet #5008; Ralston Purina, St. Louis, MO). Forty-two rats that appeared healthy and that gained weight were randomly divided into an HBO-treated group (HBO, n = 18), a non–HBO-treated group (non-HBO, n = 18), and a sham group (n = 6).

**Induction of Mononeuropathic Pain**

Sciatic neuropathy was induced in the right hindlimbs in HBO and non-HBO rats. The surgical procedure was performed under general anesthesia with the injection of ketamine and xylazine (150:30 mg/mL) at 0.7 mL/kg IM on the left buttck. The common sciatic nerve was exposed at the middle of the right thigh by blunt dissection through the biceps femoris. Approximately 7 mm of nerves was freed and 4 ligatures (4.0 chromic gut) were loosely tied around the nerves with 1 mm of spacing. The incision was then closed in layers with 3-0 monofilament nylon sutures. In the sham group, an identical dissection was performed; however, the sciatic nerves were not ligated.

**Behavioral Tests**

As described by Choi et al., foot withdrawals after applications of von Frey filaments (Stoelting, Wood Dale, IL) and acetone were considered signs of mechanical allodynia and cold allodynia, respectively. Behavioral assessment was performed in a quiet room between 9:00 AM and 12:00 PM by a person blinded to the experimental design.

**Assessment of Mechanical Allodynia**

Rats were placed individually in clear Plexiglas boxes (10 × 12 × 30 cm) on elevated wire mesh platforms to allow access to the ventral surface of the right hindpaw. In brief, von Frey filaments were applied to the paw over 4 seconds perpendicularly in ascending order of stiffness. An up-down method was used to assess mechanical sensitivity by using a set of von Frey filaments with logarithmically incremental stiffness from 0.16 to 26.0 g (0.16, 0.40, 0.6, 1.0, 1.4, 2.0, 4.0, 8.0, 10.0, 15.9, and 26.0 g). The 2.0-g stimulus, in the middle of the series, was applied first. In the event of paw withdrawal absence, the next-stronger stimulus was selected. On the contrary, a weaker stimulus was selected. The withdrawal threshold of mechanical allodynia was determined as the lowest force that provoked paw withdrawal at least twice in a single trial of 5 applications. Baseline testing was performed 3 days before the start of the experiment.

**Assessment of Cold Allodynia**

Briefly, a drop of 100% acetone was gently applied to the heel of the rat with a syringe connected to a thin polyethylene tube. Applications were made 5 times (once every 5 minutes) to each rat. The response frequency to acetone was expressed as a percent ([number of paw withdrawals/number of trials] × 100).

**Hyperbaric Oxygen Treatment**

HBOT has been described in our previous studies. The HBO group rats were exposed to 100% oxygen for 1 hour at the pressure of 2.4 atm in a cylindrical pressure chamber (Sechrist Model 1300B, Sechrist Industries, Inc., Anaheim, CA). A tray of calcium carbonate crystals was used to reduce the accumulation of CO2 in the chamber.
environment. Oxygen content was maintained at ≥98% and CO₂ at ≤0.03%. HBOT proceeded for 1 hour once a day post-CCI for 7 days. The sensory testing was performed 60 minutes after the completion of HBOT. The choice of the time interval between HBOT and the sensory testing allowed the rats to fully recover from HBOT-induced stress. The non-HBO and sham rats were placed in the same chamber breathing room air.

### TNF-α and IL-1β Assay

Sciotic nerves were harvested by cutting slightly above the site of the constrictive ligatures and 1.5 cm distally. The nerve from the sham rats was identically removed. The nerves were immediately frozen on dry ice and stored at −80°C until assay. Sciotic nerves were pooled and homogenized in ice-cold phosphate-buffered saline, pH 7.4, containing protease inhibitors (aprotinin, leupeptin, pepstatin, 1.0 mM each) and phenylmethanesulfonyl fluoride (1.0 mM) in a total volume of 0.9 mL for 2 minutes at a revolution of 12,000 rpm using an Ultra-Turrax homogenizer (Model No. SDT-1810; Tekmar Co., Cincinnati, OH). After centrifugation at 10,000g for 10 minutes, supernatant (S) was removed. The remaining pellet (P) was resuspended in the original volume of homogenization buffer. Triton X-100 (Amersham, Arlington Heights, IL) was added to S and P at a final concentration of 0.01%. The samples were mixed thoroughly. P was rehomogenized, and recentrifuged at 10,000g for 10 minutes. Supernatants from S and P were aliquoted and assayed in duplicate using the quantitative sandwich enzyme immunoassay technique from R&D systems specific for Rat TNF-α and IL-1β/IL-1F2 Kits (Quantikine M; R&D Systems, Minneapolis, MN). Protein was determined by bicinchoninic acid protein assay (BCA Protein Assay Kit; Pierce, Rockford, IL). A concentration of TNF-α and IL-1β was expressed as pg/mg protein.

### Western Blot Analysis

Western blot analysis was performed to confirm the presence of proteins of TNF-α in the sciatic nerve. Tissue homogenates of sciatic nerves (days 4 and 7 post-CCI) were separated on a 15% sodium dodecyl sulfate–polyacrylamide gel and transferred to a nitrocellulose membrane (Bio-Rad Laboratories, Hercules, CA). The Western blots were blocked for 2 hours at 4°C and then incubated overnight with polyclonal sheep antiserum to mouse TNF. Goat antsheep immunoglobulin G horseradish peroxidase conjugate (KPL, Inc., Washington, DC) was used as the second antibody. The blots were developed with a 3,3’-diaminobenzidine/H₂O₂ solution.

### Statistical Analysis

Behavioral data are expressed as mean values ± SE. Two-way (time and treatment) analysis of variance, followed by the Tukey post hoc test, was used to determine the statistical significance in changes of values pre- and post-CCI procedure between HBO and non-HBO groups. *P < 0.05 was considered statistically significant. TNF-α and IL-1β data are expressed as means ± SE. One-way analysis of variance was used to test for statistical difference among groups. *P < 0.05 was considered statistically significant.

### RESULTS

#### Behavioral Test

Studies have shown that CCI on the sciatic nerve induces spontaneous pain behaviors and long-lasting allodynia and hyperalgesia in the affected paw. The behavioral testing data in the present study were in agreement with previous reports. All the CCI rats showed shaking and licking, and often held the affected hindpaws off the floor, which are behaviors suggestive of spontaneous pain. The results of the behavioral test for mechanical allodynia of the hindpaw are shown in Figure 1. The time course of post-CCI painful behaviors in this study was identical to those reported previously. The threshold of mechanical allodynia of the hindpaw was significantly lower in HBO rats compared with non-HBO rats. The withdrawal threshold of non–HBO-treated rats was significantly increased in HBO rats compared with non-HBO rats. *P < 0.05 was considered statistically significant.
static throughout the test period. No significant mechanical hypersensitivity was observed on the left side (contralateral, nonoperated).

The results of the behavioral test for cold allodynia of the hindpaw are shown in Figure 2. Before surgery, the rats rarely responded to acetone application. After CCI, the ipsilateral hindpaw became much more sensitive to acetone application. When the acetone was applied to the plantar surface of the foot on the operated side, rats briskly withdrew the paw after some delay (approximately 0.2–0.3 seconds) and subsequently shook, tapped, or licked it. Cold allodynia response frequency was significantly lower in HBO rats than in non-HBO rats (20% vs 70% on day 7, \( P < 0.05 \)). Cold hypersensitivity in sham group rats remained stable throughout the test period.

**TNF-\( \alpha \) Content in Sciatic Nerve After CCI**

As shown in Figure 3, the endoneurial TNF-\( \alpha \) content was significantly higher in non-HBO rats than in sham rats on day 4 (17.89 \( \pm \) 0.83 pg/mg protein, \( P < 0.05 \)) and on day 7 (18.97 \( \pm \) 1.57 pg/mg protein, \( P < 0.05 \)). The endoneurial TNF-\( \alpha \) content was significantly lower in HBO rats than in non-HBO rats on day 4 (10.94 \( \pm \) 2.78 vs 17.89 \( \pm \) 0.83 pg/mg protein, \( P < 0.05 \)) and on day 7 (11.32 \( \pm \) 2.98 vs 18.97 \( \pm \) 1.57 pg/mg protein, \( P < 0.05 \)).

**IL-1\( \beta \) Content in Sciatic Nerve After CCI**

As shown in Figure 4, the endoneurial IL-1\( \beta \) content was significantly higher in non-HBO rats than in sham rats on day 4 (636 \( \pm \) 74 vs 256 \( \pm \) 31 pg/mg protein, \( P < 0.05 \)) and on day 7 (687 \( \pm \) 89 vs 288 \( \pm \) 35 pg/mg protein, \( P < 0.05 \)). The endoneuronal IL-1\( \beta \) content was 671 \( \pm \) 85 pg/mg protein on day 4 and 672 \( \pm \) 75 pg/mg protein on day 7 in HBO rats (\( P = \) not significant versus non-HBO rats).

**Western Blot Analysis**

As shown in Figure 5, Western blot analysis confirmed the presence of proteins with molecular weights of 51 kDa in the rat sciatic nerve homogenates.

**DISCUSSION**

The effect of HBOT in animal models of painful neuropathy has been evaluated. HBOT decreased inflammation and mechanical hypersensitivity in an animal model of acute inflammatory pain.\(^{18}\) HBOT may be comparable to acetylsalicylic acid treatment in alleviating joint inflammation and reducing mechanical hyperalgesia in an animal model of arthritis.\(^ {30}\) These studies show that HBOT produced a prolonged antinociceptive effect in animals that persisted after cessation of treatment. Thompson et al.\(^ {26}\) recently evaluated the effect of HBOT on 2 common models of neuropathic pain, L5 ligation and CCI of the sciatic nerve. In their study, HBOT was administered for 90 minutes at 2.4 ata after surgical manipulations daily for 2 weeks. They observed that both models demonstrated significant improvement in response to treatment over the course of the 2-week period, with CCI animals recovering more quickly and maintaining this recovery throughout the posttreatment period. They suggested that HBOT seems to be successful in relieving neuropathic pain for an extended period of time, and future research should be aimed at investigating the precise mechanisms underlying this positive effect. Our present study confirms their observations that HBO treatment reduced CCI-induced neuropathic pain, and
further shows that the alleviated neuropathic pain was associated with significantly reduced TNF-/\alpha/ production in the affected sciatic nerve. Both peripheral and central nervous system mechanisms are proposed to be involved in the development of neuropathic pain.3–5,31 TNF-/\alpha/ is the prototypic proinflammatory cytokine produced by macrophages/monocytes and is responsible for a diverse range of signaling events within cells. The correlations between the tissue levels of TNF-/\alpha/ and pain have been well known in a number of painful diseases.32,33 Several studies suggest that TNF-/\alpha/ may have an important role in the injury-induced peripheral nerve alterations, and seems to contribute substantially to the development of neuropathic pain6,7,34 and inflammation-induced hyperalgesia.8 Sacerdote et al.25 investigated the temporal pattern of TNF mRNA expression in the sciatic nerve in a mouse CCI model of neuropathy. Their results indicate that a transient early TNF upregulation takes place in the peripheral nervous system after CCI that may activate a cascade of proinflammatory/pronociceptive mediators contributing to the development of neuropathic pain. George et al.35 evaluated temporal changes of TNF-/\alpha/ production in the sciatic nerve after CCI. The significantly increased production of endoneuronal TNF-/\alpha/ was detected 12 hours after CCI. Thereafter, TNF-/\alpha/ production was gradually decreased and reached the control level 14 days after CCI. We noted the same findings as George et al.35 that endoneuronal TNF-/\alpha/ production significantly increased at days 4 and 7 after CCI. The increased TNF-/\alpha/ was associated with increased mechanical and cold sensitivity. These data suggest that increased endoneuronal TNF-/\alpha/ content may be involved in the initiation and early development of CCI-induced neuropathic pain.

In animal models, the endoneurial or IM injection of TNF-/\alpha/ induces pain-associated behavior9,10 whereas blocking TNF-/\alpha/ attenuates pain in animal models of neuropathy.36 Thalidomide inhibits TNF-/\alpha/ synthesis in stimulated monocytes. In the study by George et al.,34 thalidomide significantly reduced the endoneurial TNF-/\alpha/ contents during the first week and alleviated thermal hyperalgesia and mechanical alldynia in CCI-induced neuropathic pain. Clinical and experimental evidence suggests that glucocorticoids may be effective in the treatment of neuropathic pain.37 One study suggests that inhibition of CCI-induced endoneurial TNF-/\alpha/ production may be one of the mechanisms of HBOT in...
neuropathic pain, and is at least partly responsible for the beneficial effect of HBOT.

There are several possible explanations for the ability of HBOT to influence the production of TNF-α in the present study. HBOT increases the physically dissolved oxygen content of circulation, thus increasing the oxygen supply to damaged tissue and resulting in an increase of oxygen in the tissue. Many of the axons in the CCI model undergo Wallerian degeneration, which seems to be linked to the development of neuropathic pain in the CCI neuropathy model.\(^{39,40}\) CCI-induced neuronal injury, similar to other acute peripheral nerve lesions, has an important inflammatory component and is considered an ischemia-reperfusion injury.\(^{41}\) The beneficial effect of HBOT in ischemia-reperfusion injury has been demonstrated.\(^{42}\) The present study suggests that HBOT may alleviate CCI-induced nerve injury, therefore alleviating CCI-induced neuropathic pain.

Another possible explanation is that HBOT alleviates inflammation. Inflammation is a protective response to injury or infection and is the most common cause of pain.\(^{43}\) A previous study indicates that HBOT decreases paw edema in an acute inflammatory condition.\(^{44}\) Wilson et al.\(^{18}\) first reported that HBOT decreased mechanical hyperalgesia associated with an acute inflammatory pain condition. However, the antinociceptive effects of HBOT were apparent immediately after treatment and continued to 5 hours posttreatment. This dissociation suggests that there might be distinct mechanisms involved in the antiinflammatory and antinociceptive properties of HBOT. TNF-α has been identified as a key regulator of the inflammatory response. Our results suggest that the antiinflammatory property of HBOT may partly result from its inhibitory effect on TNF-α production.

Increased endoneurial IL-1β content in the sciatic nerve has been reported in CCI-induced neuropathic pain\(^{34}\) and in complete Freund adjuvant–induced painful perineural inflammatory neuritis.\(^{45}\) The present study confirms these findings showing that CCI induced significantly increased IL-1β in the sciatic endoneurial on 4 and 7 days after surgery. George et al.\(^{38}\) observed that thalidomide treatment alleviated CCI-induced neuropathic pain, which was associated with reduced sciatic endoneurial TNF-α content, but no change in IL-1β. In a recent study, Orhan et al.\(^{46}\) reported that the administration of sirolimus, an immunosuppressive antibiotic, significantly alleviated CCI-induced neuropathic pain associated with a reduced TNF-α protein level in the spinal cord. However, the spinal cord IL-β and IL-6 protein levels were not affected. In the present study, HBOT also alleviated CCI-induced neuropathic pain in association with reduced endoneurial TNF-α content. However, HBOT did not change IL-1β content. These studies suggest that TNF-α and IL-1β may have independent roles in the development of CCI-induced neuropathic pain. It seems that the beneficial effect of HBOT may partially result from the prevention of TNF-α production in the sciatic nerve after CCI injury. The action of HBOT on other mediators cannot be excluded by our study, which must therefore be considered preliminary.

A limitation in our study is that the administration of HBOT reduced CCI-induced endoneuronal TNF-α production; the cause and effect in relationship to alleviated neuropathic pain was not tested. Exposure to HBO at higher than atmospheric pressure leads to increased reactive oxygen species (ROS) formation, which is in direct proportion to the increased oxygen tension.\(^{47}\) ROS have been recently suggested to regulate expression of some apoptotic genes in the spinal cord, and therefore may be responsible for the onset of CCI-induced neuropathic pain.\(^{48}\) TNF-α has been suggested to be the most potent inducer of several intracellular signals, including apoptosis, cell differentiation, and gene transcription. TNF-α mediates its intracellular signaling by adjusting the redox potential of the cell, specifically through ROS.\(^{49}\) Our previous studies suggested that HBOT may produce its protective action partially by inhibiting the production of hydroxyl free radicals in ischemia-reperfusion brain injury,\(^{50}\) and enhancing antioxidant enzyme activity in postischemic skeletal muscle injury.\(^{29}\) The use of an antioxidant, such as N-acetylcysteine, has been reported to alleviate CCI-induced neuropathic pain.\(^{51}\) The effect of HBO on ROS activity in CCI-induced neuropathic pain warrants further investigation.

This study demonstrated that administering HBOT mitigated CCI-induced cold and mechanical allodynia and reduced the endoneurial production of TNF-α. However, the cause-and-effect relationship to neuropathic pain needs to be tested in the future.

DISCLOSURES

Name: Fenghua Li, MD.
Contribution: This author helped conduct the study and write the manuscript.
Attestation: Fenghua Li has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.

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Hyperbaric Oxygenation Therapy Reduces CCI Pain and Endoneuronal TNF-Alpha Content

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Activated Charcoal Effectively Removes Inhaled Anesthetics from Modern Anesthesia Machines: Erratum

In the article that appeared on page 1363 in the June 2011 issue of volume 112 of Anesthesia & Analgesia, the authors omitted the disclosure that they are cofounders of Dynasthetics LLC, the device manufacturer. The authors regret the omission.

Reference: