BRAIN ATROPHY WITH CHRONIC PAIN

A Call for Enhanced Treatment–

Recent studies clearly show that chronic pain unto itself causes brain atrophy and altered neurochemistry and sensory function of the central nervous system.

By Forest Tennant, MD, DrPH

As unpleasant as it may be, the evidence is in: chronic pain may produce a loss or atrophy of brain tissue.[1-3] All practicing physicians and their surrogates and allies must immediately begin understanding the ramifications of this finding. All parties must be educated about this fact and aggressively attempt to prevent brain atrophy in chronic pain patients. While our knowledge about this dire complication—and what tools we should employ to prevent and treat it—are admittedly meager, we have to begin a new chapter in practical pain management.

The Evidence

In 2004, Apkarian and colleagues at Northwestern University published their initial findings on patients with chronic back pain.[1] By use of brain scans they determined that chronic pain caused brain shrinkage by as much as 11%—equivalent to the amount of gray matter that is lost in 10-20 years of normal aging. The decrease in volume in the prefrontal cortex and the thalamus of the brain was related to the duration of time spent in pain. Every year of pain appeared to decrease gray matter by 1.3 cubic centimeters. The good news about this study is that the shrinkage was accompanied by only minimal neuronal loss suggesting that proper treatment might reverse this portion of the decreased brain matter.

Since this seminal report, a number of investigators—from a variety of institutions, using a variety of techniques—have documented loss of brain tissue in chronic pain patients, including those with chronic headaches, fibromyalgia, back pain, and irritable bowel syndrome.[2-6] Most of the major studies involving chronic pain and brain tissue loss are referenced here for readers who wish to explore these findings in greater detail.[2-8]

In any discussion or study of chronic pain complications, the question about drugs—particularly opioids, as a causative factor—is naturally asked. All the studies noted above had at least some subjects who did not take opioids. To determine whether brain structural changes occur independent of opioids, Buckalew and colleagues at the Universities of Pittsburgh and West Virginia carefully studied a group of older adults with chronic pain who did not take opioids and who had none of these confounding conditions: hypertension, diabetes, major depression disorder, post-traumatic stress disorder, or a previous stroke.[8] They found essentially the same altered and reduced brain matter as all of the other studies.[1-7] It is also cogent to point out that long term opioid therapy has not been found to produce significant decreases in neurocognitive abilities.[9,10] In fact, adequate pain relief may improve them.[9]

Not only have scans and magnetic imagery documented the loss of gray matter, a number of other studies complement these findings in that the brains of chronic pain patients demonstrate altered neurochemistry and central nervous system processing of input signals such as odors, taste, heat, emotions, and touch.[11-16] Studies show that chronic pain patients do not process external stimuli in a normal fashion.[11] Patients with chronic back pain have altered dopamine and opioid availability in the forebrain.[17,18] Fibromyalgia patients appear to have a reduction in the receptor availability of dopamine and opioid mu-receptors in parts of the forebrain.[19,20]

Table 1. Risks of Chronic Pain

- Brain atrophy
- Altered brain neurochemistry
- Altered brain sensory processing
- Hypertension
- Tachycardia
- Immune suppression
- Elevated adrenal corticoids
- Adrenal exhaustion
- Depression
- Physical immobility
- Deranged activities of daily living
- Insomnia
- Anorexia and malnutrition
- Suicide

In summary, it appears that brain neurochemicals important for pain modulation are not responding as they do in healthy individuals.[11-20]

Implications of These Findings

The findings in chronic pain patients of brain tissue loss and altered central nervous system physiology and neurochemistry is a profound discovery that should be known to all physicians. Implications of this discovery are clear. Recently, in an educational document published by the American Academy of Pain Management, Dr. Catherine Bushnell of McGill University in Montreal, who is a principal investigator in many of the studies referenced here stated, "The data suggest that patients should receive treatment as early and as aggressively as possible. The old adage "no pain, no gain" appears to be diametrically opposed to current findings about the impact of pain." She, and possibly some previous fence-sitters, now want to call chronic pain a disease unto itself.

It is now clear that the risk-benefit ratio of aggressive treatment versus moderate treatment—which leaves the patient with some degree of constant pain—needs to be reevaluated. Brain atrophy, along with altered brain physiology and neurochemistry, now joins the risk profile of undertreated chronic pain. To date, this risk profile has consisted of hypertension, tachycardia, altered adrenal hormone levels, suppression of the immune system, depression, and interference with physical function and activities of daily life (see Table 1). It is now abundantly clear that chronic pain, particularly the severe intractable form, is a disease unto itself whose risks, per se, appear to far outweigh those of essentially all applicable medical treatments—including high dose opioid therapy.[9,10]

Table 2. Four Clinical Cases Who Mentally Deteriorated

1. A 25-year-old female was referred with severe chronic pain due to fibromyalgia. She claimed undertreatment for at least three years which interfered with her promising career. Morning serum cortisol levels were over 30ug/dl and she had a resting heart rate over 110 beats per minute. Despite aggressive opioid and other treatment, within 10 years she became so mentally incapacitated that she could not work, was home-bound, and had to be cared for by family.
2. A 55-year-old male executive has severe back pain with radiculopathy in both legs. For about five years he experienced interrupted pain care consisting of standard interventions, opioid dosages, and a variety of neuropathic, anti-inflammatory, and anti-depression agents. By age 60, he had to retire and was unable to adequately concentrate, read, or do calculations to retain employment. He remains at home and cared for by his wife.
3. A 40-year-old male television camera technician developed a severe back injury requiring multiple back surgeries, fusion, and implanted rods. Despite an implanted intrathecal morphine pump and numerous medical treatments including opioids, he developed such memory loss and cognitive abilities that he could not work or do such activities as balance a checkbook.
4. A 40-year-old registered nurse was referred with severe pain due to fibromyalgia. Her resting morning cortisol was under 1ug/dl, and she had tachycardia over 100 beats per minute. Despite multiple treatments including opioids, she mentally deteriorated over a five-year period to the point that she could not work and had to live at home with her parents.

The above cases are examples of clinical observations of severe chronic pain patients. They are presented here with little knowledge of underlying causes of their mental deterioration or whether they have brain atrophy.

Clinical Ramifications

A review of the anatomic, physiologic, and neurochemistry studies of chronic pain on the brain clearly suggests that some chronic pain patients will develop clinical syndromes of poor attention span, cognitive abilities, and possibly dementia.[1-8,11-18] Is this happening? This author believes this to be the case based on long-term observations of chronic pain patients. Although chronic pain patients, in my experience, seldom admit to a loss of cognitive or mental abilities, they often complain of a poor memory. Is it time that chronic pain patients in treatment be sequentially monitored over time with mental scales such as the "Mini-Mental Exam?" Should we be trying to provide better diets, nutritional supplements, and dementia-preventing mental exercises such as crossword puzzles? Perhaps the pain patient who claimed her B-12 shot really helped knew what she was talking about. Can psychologists who specialize in dementia prevention help us? Shown in Table 2 are four cases from my personal practice which were undertreated for years before referral to me and who, I believe, developed mental deterioration. At this point, I have a poor understanding of how to diagnose, prevent, or treat mental deterioration in chronic pain patients, but these studies on brain atrophy provide insight into clinical observations.

Mechanism of Brain Atrophy

There should be no better subject to discuss in the hallways of medical practice than the possible causes of brain atrophy and neurochemical abnormalities that occur in chronic pain. Considering that some studies also show a loss of nerve

Table 3. Who Needs to Be Educated About Brain Atrophy

- Patients
- Psychologists
- Clergy
- Families
- Social Workers
- Insurance Carriers
- NP's/PA's
- Pharmacists
- Medical Boards

Table 4. Some Clinical Recommendations and Approaches

- Educate all parties
- Include brain atrophy risk in consent form and agreements
- Early and aggressive treatment
- Nutrition
- Electrical control measures
- Mental, intelligence, and memory screening and exercises

density of peripheral nerves and spinal cord of pain patients, an electrical phenomenon must be considered as a cause. Is electricity being retained by damaged peripheral nerves (e.g., change in electrical capacitance) and thus causing a "hot wire" affect that fundamentally inflames, dissolves, and scars tissue? Does pain cause a hormonal or immune dysfunction that can literally dissolve gray matter? Hypercortisolemia has been observed in chronic pain patients and is known to cause a demented state.[21-23] Severe pain is also well-known to cause hypertension and tachycardia, particularly during pain flares. Both are known to affect cerebral blood flow. Whatever future research points to as causation, physicians should take their best shot now at preventing the disappearance of gray matter. In addition to better pain control, it is obvious that we need better strategies to normalize electrical conduction, hormone metabolism, and restoration of tissue.

Start Education Immediately

The number one thing physicians should immediately do with this new research information is educate all concerned parties including patients, families, psychologists, pharmacists, surrogates, insurance carriers, and medical boards (see Table 3). In particular, any party—such as a family member who is critical of opioid treatment—needs to be bluntly told that withholding treatment, including opioid therapy, may subject the patient to brain atrophy and the loss of intelligence, memory, and possible development of dementia. Simply, the risks of delayed or undertreatment appear too great. On the other hand, we do not yet know whether opioids or any other treatment can prevent or restore brain atrophy or altered brain physiology and neurochemicals.

Clinical Recommendations

It must be recognized that we may not be able to either prevent or restore brain tissue in chronic pain states. Nevertheless, these new research findings suggest some intuitive and logical measures. Education of ourselves and patients is, naturally, first on our list. Second is sooner and more aggressive treatment with all methods that are currently available. For example, alcoholic as well as some other forms of dementia respond to nutritional therapies. Since excess electricity produced in chronic pain states may be a causative factor, techniques to reduce and control electrical flow may be in order. Certainly, the encouragement of mental exercise, increased physical activity, and social interaction should help keep brains active. Above all, doctors who treat severe chronic pain patients should focus on this complication and eagerly share any hints and tips they uncover. It's also my recommendation that we attempt to identify psychologists who have interest and skills in working with dementia.

Conclusion

Chronic pain, particularly the severe intractable forms, should be considered a disease unto itself. The finding that chronic pain, per se, causes brain atrophy and altered physiology and neurochemistry is a profound discovery and joins the already known risks of under-treatment, namely cardiovascular, hormone, immune, and physiologic function. At this time, there is no guarantee that we can prevent or restore brain atrophy with any known treatment or measures yet aggressive pain control clearly outweighs the risk of undertreatment. Now that we are aware that this complication may occur, it is time to experiment, observe, and develop strategies to prevent or ameliorate it. ■

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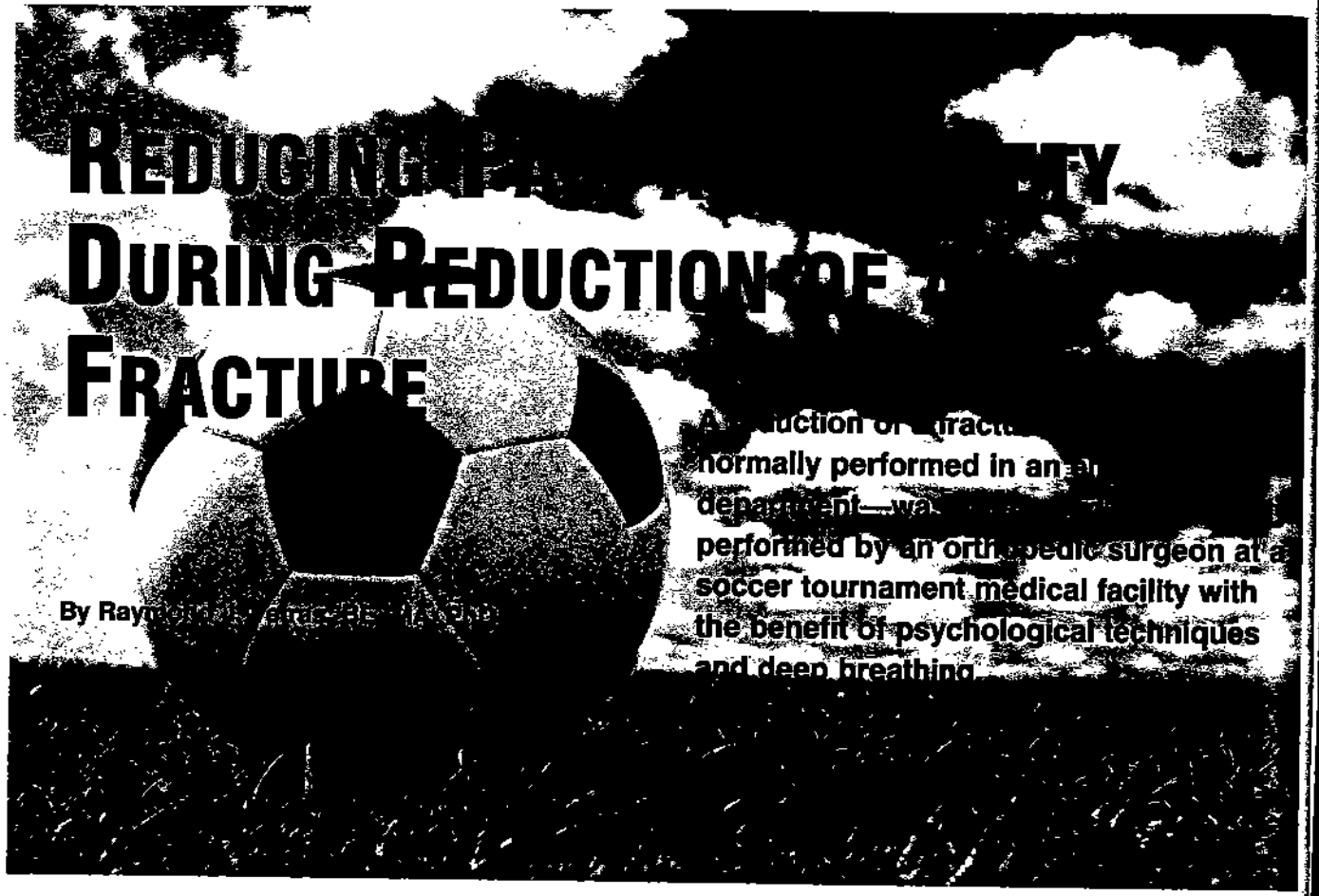

Reducing [illegible]ty During Reduction of Fracture

A[illegible]duction of [illegible]fracture normally performed in an [illegible] department—was performed by an orthopedic surgeon at a soccer tournament medical facility with the benefit of psychological techniques and deep breathing.

By Ray[illegible]

The following case utilized the psychological techniques of PsychoNeuro Pain Response™ (PNPR™)—also known as Talking Away Pain™ (TAP™)—together with deep breathing to reduce the pain and anxiety of a teenager with a fractured wrist so that it could be safely and successfully set at the tournament medical facility rather than the usual hospital emergency department. PNPR[1,2] is a combination of safe, well-known mental interventions—such as cognitive restructuring (restructuring thoughts), neurolingusitic programming (changing feeling, seeing or hearing modes of receiving information), and systematic desensitization (replaying a scene in the mind until it no longer causes stress)—that are taught to the patient.

Case Narrative

History. The patient, a 15-year old male, injured his left wrist while playing soccer at the Schwan's USA Cup Soccer Tournament in July 2002. Upon arrival in the medical facility, the patient was very anxious and experiencing significant pain. Inspection of the left wrist revealed obvious deformity with swelling localized to the distal radius. The patient demonstrated active range of motion of his fingers with intact distal neurovascular status.

Physical Exam. The patient presented with complaint of immediate onset of pain and severe deformity following a fall on his extended left wrist. Range of motion of the L-wrist was limited due to pain, without associated distal numbness or paresthesia.

Imaging. X-rays showed evidence of a displaced fracture of the left distal radius with volar angulation of the proximal aspect of the distal fragment in addition to a nondisplaced ulnar fracture.

Diagnosis. A displaced fracture of the left distal radius with volar angulation of the proximal aspect of the distal fragment in addition to a nondisplaced ulnar fracture.

Treatment. There were two options: 1) transport and treat the patient in an emergency department (hospital ER), or 2) treat the patient at the Schwan's USA Soccer Cup Tournament medical facility (MF). "This type of fracture," stated Dr. Peter Parten, an on-site orthopedic surgeon, "is typically treated in the emergency department, with reduction of the fracture under IV sedation and application of a local lidocaine hematoma block." However, Dr. Parten felt that the procedure could safely be attempted at the MF if: 1) the mother and patient agreed to have the procedure at the medical facility, and 2) a local pain management specialist (referred to as "specialist" throughout this document) was able to reduce the patient's anxiety and pain sufficiently so that he would remain calm and in control of his pain long enough to permit the local hematoma block.

Preparing the Patient

The specialist was apprised of the situation and felt that it was possible to reduce the patient's anxiety and pain using psychological techniques. He had the patient moved to the bay where the appropriate equipment and materials were located and asked him to lay on the treatment table. The bay was at the end of four other bays and consisted of sheets on the sides and front with a block wall at the back. Other than providing visual privacy, the bay was open to all surrounding sounds.

The surgeon introduced the specialist to the patient and then everyone, except

the patient and specialist, left the bay. The specialist questioned the patient about how he felt, his level of pain, and what he had been told about his injury. The patient responded that he was told that a bone in his arm was broken and that it would need to be set. He also indicated that he was scared and in a lot of pain. He asked if it was a bad break. The specialist told him that it was not bad and asked if he would he like to see the X-rays. He did, and the specialist showed him the break. The patient was relieved that it was not bad, but he was still anxious. The specialist told him that his mother was close by, the orthopedic surgeon was one of the best in the area, and the assisting staff was excellent. He told the patient that he would explain his options to him and his mother, and it would be up to them to decide what was the best option. With this information, the patient exhaled deeply and became much less anxious.[3]

The specialist proceeded to outline the options to the patient: 1) he could be transported to a local ER by ambulance, where he would be given a local and general anesthesia, or 2) he could have the bone set there at the MF. Still exhibiting anxious and scared feelings, he asked where and how far the ER was and what would they do at the ER.

The specialist explained that the ER was 15 to 20 minutes away. To transport him, an ambulance would be called. Because this was not a life-threatening situation, it might take them 15 to 20 minutes to arrive. Once there, the ambulance personnel would transfer him to a stretcher, strap him in, and secure his arm for the journey. His mother could travel with him in the ambulance, if he wished. At the ER, he would move to a waiting area where his mother would fill out the paperwork so he could be helped. Once the paperwork was complete, he would wait his turn to see a doctor, who would then contact the orthopedic surgeon and schedule the operating room to have his bone set. The specialist further explained that, at the MF, they would try to speed up this process for him by supplying the hospital (ER) with the pertinent information prior to his arrival. The patient was told that his wait in the ER could be anywhere from two to three hours or more, depending on how busy they were. After surgery, he would be in recovery then taken to his room for an overnight stay, or longer, depending on his condition. Upon release from the hospital, he would be referred to his doctor for follow-up care.

The second option, the patient was told, would be to have the bone safely set there at the MF. However, for that to occur, his anxiety and pain level would need to be lowered.

PNPR and Deep Breathing Lowers Anxiety and Pain

How, the patient asked, could he lower his anxiety and pain level? Was he going to get some pills or something else? The specialist told him that medication was not available, but he (the specialist) thought that he (the patient) could reduce or eliminate his anxiety and pain himself with the specialist's help. The patient was surprised and said, "Do you think that I can do it?" The specialist said that he was not absolutely positive he (the patient) could, but he (the specialist) would help if he (the patient) was willing to try. Cautiously the patient asked, "What do I do?" "First," said the specialist, "I want you to take a deep breath[3,4] and then let it out slowly. This will help to relax you and allow you to become calmer." After a few deep breaths, the patient started to become visibly calmer, so the specialist asked the patient if he could think of a fun or enjoyable time in his life. It could be with friends, family or by himself. It could be something very beautiful like a sunset or receiving a special gift. When asked if he had thought of a fun time, the patient said that he had.

He was then instructed to take a deep breath, close his eyes, then to go back to that fun, enjoyable time. He was told to relive it as best as he could with all the sights, smells, tastes, and sounds. "Do not view it as on a TV screen," he was told, "but relive it as if you were there now, as best you can. If it was sunny, feel the warmth of the sun. If there was a breeze, feel the breeze on your skin." The patient was instructed to use all the senses that he could to relive this fun time then let the specialist know when he was finished. After about 20 to 40 seconds, the patient indicated that he was finished and opened his eyes. The specialist asked him how he felt. He said that he felt great, and offered, "Hey, my pain is all gone." With this admission, the specialist suggested that he (the patient) close his eyes and relive that fun time again while he (the specialist) left for a few moments.

The specialist went to the waiting orthopedic surgeon and the patient's mother. He reported that the patient no longer exhibited any anxiety or pain behavior. The surgeon then turned to the mother and asked her what she would like to do. Would she like to go to the ER or have the procedure done there at the MF? When she deferred to the surgeon, the surgeon indicated that the procedure could be safely done there at the MF. "It would eliminate all the anxiety of transport, the hospital wait, general anesthesia, and still be safe," he said. The mother concurred. However, before they proceeded, the specialist said that it was very important that his young patient be informed of their recommendation, and asked his opinion. Everyone agreed and the specialist returned to the patient.

"After the reduction, the patient indicated that he experienced very little pain during the reduction and was "feeling pretty good." The patient experienced reduced anxiety and minimal pain behavior."

The patient was still calm and pain free. The specialist told the patient that he conferred with his mother and the orthopedic surgeon. They both felt that it would be best for him to have his bone set at the MF, but they wanted to know what he thought. He said it was okay to have the bone fixed there, but again indicated that he was scared.

Final Preparations for the Reduction

The specialist motioned acceptance to the patient's mother and surgeon. As the orthopedic surgeon and his team began preparations for the reduction in the bay, the specialist positioned himself at the head of the treatment table to work on the patient's new anxiety. The specialist told the patient to take a few deep breaths and then to think of another fun time to relax himself. In less than a minute, after the patient had once again relaxed himself,

the specialist told the patient that he would now go over everything that the surgeon would be doing to set his bone break. The specialist told the patient that if at any time he (the patient) got anxious, he was to tell the specialist and the specialist would wait until he had relaxed himself sufficiently, using the techniques he had just learned, before continuing. During the explanation of the steps, the patient indicated three times that he was scared: once when the needle for administering the local anesthetic was mentioned, again when the injection was described, and finally when the fracture reduction was mentioned. Each time, the explanation was stopped and the patient was instructed to breathe deeply, think of something fun, and then indicate when he was ready to proceed. This process continued until he was able to go through the whole procedure mentally without feeling scared. The whole process took less than ten minutes and was done in conjunction with the preparations being made for the reduction.

Assuring and Empowering Patient

The specialist told the patient that no one would do anything to him until he was ready. In addition, if he wanted, the specialist would remain with him throughout the entire procedure. The patient indicated that he wanted the specialist to remain with him. The specialist told the patient that he would rest his hand on his shoulder for the whole procedure, so that he would know that he was there. He (the specialist) would speak to him softly, if there was a need.[5] The patient smiled.

The MF and surgical bay were busy with considerable noise and distractions. The patient, however, remained calm throughout the preparations. When he was ready, the surgeon nodded to the specialist. The specialist spoke to the patient saying, "The doctor is ready, but he won't do anything until you tell us that you are ready to start." There was silence for three to five seconds, after which the patient said that he was ready.

At this point, the surgeon spoke to the patient about the preparation for, and administration of, the local anesthetic and the reduction procedure. After the surgeon finished speaking, the specialist moved his mouth close to the patient's ear. He spoke softly and reassured the patient that he was in good hands and he was doing very well.

The specialist's hand stayed on the patient's shoulder throughout the procedure. Whether it was the preparation, the hand contact, the periodic speaking to the patient during the procedure, or some combination of those factors, the patient remained calm and expressionless throughout the procedure. He did not exhibit any pain behavior or anxiety, even as the surgeon inserted the needle and moved it around a few times to position it to administer the medication. The patient winced only once during the whole procedure, for three to four seconds, when the surgeon used a great deal of force to reduce the fracture.

After the procedure was complete, the patient sat up and the surgeon asked how he was doing. He replied, "I feel pretty good." His mother, an RN, who was in attendance for the procedure, asked him if he had any pain. He smiled and said, "No, I do not have any pain at all."

The patient was then transported down the hall to X-ray, which verified that a satisfactory reduction was achieved. The patient was placed in a long arm splint and referred to his orthopedist for follow-up. Smiling, he walked out of the MF with his mother.

Discussion

The total psychological preparation for the patient took approximately ten minutes. Some of the time was concurrent with other preparations. The surgeon spent some time talking to the patient, mother, and specialist about the options. Once informed, the specialist focused on reducing the patient's anxiety and pain behaviors. It is important to note that the patient's pain had completely disappeared without any medication and without any suggestion to that effect, prior to administering the local lidocaine hematoma block.[1,6] Other than the time that the specialist spent alone with the patient, the reduction took place with the patient's mother (an RN) and many residents, fellows and staff physicians observing the procedure. [Note: the Schwan's USA Soccer Cup Tournament is used as a training venue for residents and fellows in conjunction with the University of Minnesota Medical School with Dr. Steven R. Elias, MD, PhD, CAQ Sports Medicine, as Medical Director of the Schwan's USA Soccer Cup Tournament since its inception.] As the reduction was taking place, normal loud emergency medical activities were occurring elsewhere within the MF. As mentioned earlier, only once, for three to four seconds, did the patient wince and his breathing change with a deep, abrupt inhalation. After the reduction, the patient indicated that he experienced very little pain during the reduction and was "feeling pretty good." The patient experienced reduced anxiety and minimal pain behavior. His parents and insurance company were spared the time and costs of ambulance transportation to an ER, the wait, costs associated with the ER, the cost of an anesthesiologist and anesthesia, a hospital stay, and other related procedures and costs.[6] The surgeon estimated that all the costs associated with this procedure would normally have been between $15,000-$25,000.[7] ■

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