

Plantar fasciitis

Extracorporeal shock wave therapy for plantar fasciitis: randomised controlled multicentre trial

J A Ogden

Technological change in general orthopaedics and its multiple specialisations is continual. These changes are regulated, to varying degrees, by delegated authorities within appropriately mandated concepts. One relatively recent technology, since approximately 1990, has been the revision of treating relatively deep seated urolithiasis, whether in the renal parenchyma or the ureter, to more superficial musculoskeletal indications. Although originally conceived to dissipate calcifications in rotator cuff tendinopathy and to alter osseous biology, the technology rapidly spread to other common disorders that affect the musculoskeletal system. Unfortunately many of these applications were not tested through appropriate randomised clinical trials or practical clinical trials, which could adequately assess clinical efficacy and significant modification of the natural history of a given musculoskeletal disorder. Such studies are obviously in demand by clinicians and healthcare provider organisations to justify the application of both a given treatment modality and the efficiency of a new drug or device to accomplish an end result that is personally satisfactory to the patient and doctor and economically justifiable to the healthcare insurer/provider.

Musculoskeletal conditions are an underrepresented major affliction of most patients, especially in the active, otherwise medically healthy patient population. Many of these conditions limit the enjoyment of participation in recreational activities. Many musculoskeletal disorders also affect productivity (overuse, a controversial concept). Efforts to restore tissue tensesgrity to alleviate pain and restore function in these situations deserve careful, well conceived evaluations.

In 1995 the Food and Drug Administration (FDA) in the United States approved the initial studies to evaluate the application of a device specifically redesigned to apply extracorporeal (transcutaneous) shock waves

to chronic plantar fasciopathy (fasciitis). This study approval process led to subsequent studies of other indications (lateral epicondylitis, fracture non-union) and other devices.

Shock waves for clinical use, whether in urology or orthopaedics, are generally generated by three methods: electrohydraulic, electromagnetic, and piezoelectric. Other technologies will undoubtedly emerge as physics merges with medicine. The different medical methods vary considerably in the total amount of shock wave energy delivered to the target issue, the size of f_2 (which is the maximal energy), the size and volume of the energy, ellipsoid, and the depth of penetration of f_2 into the tissue involved. Physician training and familiarity with the physics of the treatment is integral to the appropriate application of the technology to accomplish a satisfactory treatment outcome, as it is for a radiologist to understand the risks and benefits of diagnostic technologies.

Recent publications have both supported and questioned the applicability of extracorporeal shock waves to musculoskeletal conditions. Some studies have led to "global" interpretations that extracorporeal shock wave treatment (ESWT) is not effective. Such concepts are not appropriate. The three shock wave generation methods differ significantly in the overall size and volume of the applied shock waves. Even with a specific device, these variables may change. Speed and coworkers¹ recently stated that "efficacy may be highly dependent upon machine types and treatment protocols", and that "further research is needed to develop evidence based recommendation for the use of ESWT in musculoskeletal complaints."

The recent study by Haake *et al*² was negative about the potential efficacy of ESWT in plantar fasciitis. This study, which was obviously well conceived, applied low energy shock waves (0.08 mJ/mm^2) to the plantar fascia in a transverse direction (medial to lateral) relying on ultrasound to focus a relatively narrow ellipsoid and f_2 into the

fascia. There were no descriptions of efforts by the treater (presumably a doctor) to specifically demarcate the primary focus of pain and to relate such to the ultrasound targeting. Low energy was applied in this study three times at two week intervals. The study concluded that this specific protocol was no more effective than a placebo. The conclusion that this protocol "is ineffective" was appropriate. However, the application of "ineffectiveness of ESWT" is equally inappropriate. The FDA data from Ossatron approval and Dornier Epos approval for treatment of plantar fasciitis were statistically significant. Haake *et al*² used the Dornier device, but under completely different circumstances from their FDA study. Such differences lead to confusion for doctors and healthcare providers. The FDA studies, carried out using appropriate, well conceived treatment protocols, show that the technology with high energy (which requires anaesthesia) is usually effective. The recent studies by Buchbinder *et al*,³ Speed *et al*,¹ and Haake *et al*² strongly suggest that multiple dosed, low energy, non-anaesthetically based treatments cannot accomplish the same clinical outcomes and patient satisfaction.

Evaluations need to be continued, comparing the efficacy of different generational methods and variations in the applied energy of a specific generational method. Increasing numbers of basic science publications support positive responses in the target musculoskeletal tissues (fascia, tendon, bone). Our responsibility as doctors, in an age of increasing emphasis on minimally (or even non-) invasive surgery, is to continue to evaluate, through effective and well designed clinical trials, the potential application of a procedure that is widely accepted in urology to a variety of musculoskeletal problems.

Br J Sports Med 2004;**38**:382.
doi: 10.1136/bjsm.2004.011601

Correspondence to: Dr J A Ogden, Skeletal Educational Association, 3435 Habersham Road, Atlanta, GA 30305, USA; OrthoZap@aol.com

This editorial was inspired by an article originally published in *BMJ* 2003;**327**:75-7.

REFERENCES

- Speed CA, Nichols D, Wiles J, *et al*. Extracorporeal shock wave therapy for plantar fasciitis. A double blind randomized controlled trial. *J Orthop Res* 2003;**21**:937-40.
- Haake M, Buch M, Schoellner C, *et al*. Extracorporeal shock wave therapy for plantar fasciitis: randomized controlled multicentre trial. *BMJ* 2003;**327**:75-9.
- Buchbinder R, Ptasznik R, Gordon J, *et al*. Ultrasound-guided extracorporeal shock wave therapy (ESWT) for plantar fasciitis (painful heel): a randomized controlled trial. *JAMA* 2002;**288**:1364-72.

Osteoarthritis

Anterior cruciate ligament rupture: is osteoarthritis inevitable?

J Feller

Anterior cruciate ligament rupture, whether treated surgically or not, is associated with an increase in osteoarthritis in former soccer players

Alarming is the word Von Parat, Roos, and Roos choose to describe their findings of significant knee osteoarthritis in middle aged former soccer players who had sustained a rupture of the anterior cruciate ligament more than a decade previously.¹ Not only was there a high incidence of osteoarthritis in these former players, but reconstruction of the anterior cruciate ligament did not appear to provide protection from degenerative change in the knee.

In a 14 year follow up of subjects who had formed the basis of an earlier study,² the authors identified 238 male soccer players who were diagnosed with anterior cruciate ligament injuries in 1986. They were able to contact 205 of the players. Of these, 154 answered questionnaires and a further subgroup of 122 consented to have knee radiographs.

In just over half of the 95 subjects with radiographic changes, there was osteoarthritis equivalent to Kellgren-Lawrence grade 2 or higher. Of the subjects who answered questionnaires, 58% had undergone anterior cruciate ligament reconstruction. Interestingly, and perhaps surprisingly, there was no difference in radiographic outcome between those that had been treated with anterior cruciate ligament reconstruction and those who had not undergone reconstructive surgery. On the other hand, subjects who had sustained a meniscal tear had an increased prevalence of osteoarthritis, but the severity of radiographic changes was similar to those who did not have meniscal pathology associated with their anterior cruciate ligament rupture.

This study raises some interesting issues. The lack of benefit of anterior cruciate ligament reconstruction in terms of protection from osteoarthritis represents a challenge to knee surgeons. The authors do acknowledge that because there was no randomisation with respect to surgery, their findings are difficult to interpret. However, it is

clearly difficult to design and implement a randomised comparison of reconstructive surgery with non-operative management of anterior cruciate ligament injuries, especially in active sportspeople. We therefore have to rely on studies such as the one under consideration to determine the best advice for a young, active sportsperson who has sustained a rupture of the anterior cruciate ligament. Although successful reconstruction will theoretically provide some protection from further damage to the menisci and articular cartilage, findings such as those being reported challenge this concept.

The authors state that there has been no study to date that shows that anterior cruciate ligament reconstruction protects the knee from osteoarthritis. However, Fink *et al*³ have reported a lesser severity of osteoarthritic change, albeit with a higher prevalence, in those who had undergone anterior cruciate ligament reconstruction and returned to sport compared with those who did not have reconstructive surgery but nonetheless returned to sporting activities. It is noteworthy that, in both the current study and that of Fink *et al*, a patellar tendon graft was used for all reconstructive procedures.

Recently Pinczewski *et al*⁴ reported an increased prevalence of osteoarthritis associated with patellar tendon grafts compared with hamstring grafts seven years after anterior cruciate ligament reconstruction. We have recently used three dimensional motion analysis to compare the biomechanical function of subjects who had undergone anterior cruciate ligament reconstruction using either patellar tendon or hamstring tendon grafts.⁵ We identified differing patterns of abnormal moments about the knee in the two groups. The patellar tendon group had a reduced external knee flexion moment at mid stance, whereas the hamstring group had a reduced external extension moment at terminal stance. A reduced external knee flexion moment associated with

patellar tendon grafts has also been reported in the setting of single limb landing tasks.⁶ This may provide an explanation for the increased incidence of osteoarthritis in the patellar tendon group as reported by Pinczewski *et al*, as reduced external knee flexion moments may be associated with reduced attenuation of forces passing across the knee joint. The apparent lack of protection from osteoarthritis after anterior cruciate ligament reconstruction as reported by von Parat *et al* therefore needs to be evaluated cautiously.

Efforts have been made by various authors, including those of the current study, to determine the role that soccer participation in itself plays in the development of knee osteoarthritis. It continues to be difficult to establish the relative roles of recognised injury, unrecognised injury, and simple participation in soccer in the development of secondary osteoarthritis. Nonetheless, there is evidence to suggest that soccer participation, particularly at an elite level, does in itself contribute to development of knee osteoarthritis.⁷ The current study could have shed considerable further light on this issue by including radiographic assessment of the contralateral knee as part of the research protocol. This would have provided an excellent control cohort of knees with which to compare the anterior cruciate ligament deficient or reconstructed knees. The rate of return to soccer after the initial injury to the anterior cruciate ligament would also help to tease out the role of participation in soccer per se in the pathogenesis of osteoarthritis in this population. Unfortunately this information is not provided.

Whatever the cause of osteoarthritis in the current group of former soccer players, it did not appear to be associated with poorer function compared with no osteoarthritis. Similarly, anterior cruciate ligament reconstructive surgery and meniscal surgery did not appear to influence functional outcome. However, despite the lack of an association between these variables and functional outcome, the vast majority of subjects had reduced their level of activity after their knee injury, and most of these subjects had reduced their activity specifically because of their knee injury.

Somewhat paradoxically, subjects reported better knee function 14 years after injury than they had at seven years after injury. Given that at the more recent follow up there was a decreased rate of participation in soccer, this presumably reflects the assumption that the subjects had come to accept the limitations imposed by the knee injury.

This highlights the difficulties associated with long term follow up of patients who have undergone anterior cruciate ligament reconstruction, or indeed those who have not had their anterior cruciate ligament injury treated surgically. Sports participation may not be a useful outcome variable in the longer term as reduced sports participation may simply reflect a change in priorities on the part of the individual, rather than be regarded by the individual as a significant functional loss.

An important methodological concern pertaining to the study under review is the potential for selection bias. As the authors correctly observe, it is possible that those subjects with knee symptoms would have been more likely to participate in the current follow up than those whose knee continued to function well. This could in turn have resulted in an overall poorer outcome than if all of the original 238 had been contactable, and had responded and undergone a radiographic assessment

of their affected knee. Clearly the logistic problems of such long term follow up are considerable, and the authors should be congratulated rather than criticised for their efforts.

Whatever its shortcomings, the message from the current paper is clear. Anterior cruciate ligament rupture, whether treated surgically or not, is clearly associated with an increase in osteoarthritis in former soccer players. It remains to be seen whether improved surgical techniques of anterior cruciate ligament reconstruction and the use of grafts other than the patellar tendon can offer greater protection, while at the same time allowing resumption of sporting activities.

Br J Sports Med 2004;**38**:383–384.
doi: 10.1136/bjsm.2004.013300

Correspondence to: Associate Professor Feller, Musculoskeletal Research Centre, La Trobe University, Melbourne, Victoria 3086, Australia

This editorial was inspired by an article originally published in *Annals of the Rheumatic Diseases* 2004;**63**:269–73.

REFERENCES

- 1 von Parat A, Roos EM, Roos H. High prevalence of osteoarthritis 14 years after an anterior cruciate ligament tear in male soccer players: a study of radiographic and patient relevant outcomes. *Ann Rheum Dis* 2004;**63**:269–73.
- 2 Roos H, Ornell M, Gärdsell P, et al. Soccer after anterior cruciate ligament injury: an incompatible combination? *Acta Orthop Scand* 1995;**66**:107–12.
- 3 Fink C, Hoser C, Benedetto KP. Development of arthrosis after rupture of the anterior cruciate ligament. A comparison of surgical and conservative therapy *Unfallchirurg* 1994;**97**:357–61.
- 4 Pinczewski L, Russell V, Salmon L. Osteoarthritis after ACL reconstruction. A comparison of patellar tendon and hamstring tendon graft for ACL reconstruction over 7 years. *J Sci Med Sport* 2003;**6**:97.
- 5 Webster KE, Witwer JE, O'Brien J, et al. Gait patterns following anterior cruciate ligament reconstruction are related to graft type. *Am J Sports Med* 2004;in press.
- 6 Webster KE, Gonzalez-Adrio R, Feller JA. Dynamic joint loading following hamstring and patellar tendon anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2004;**12**:15–21.
- 7 Roos H, Lindberg H, Gärdsell P, et al. The prevalence of gonarthrosis and its relation to meniscectomy in former soccer players. *Am J Sports Med* 1994;**22**:219–22.

Frozen shoulder

Effect of arthrographic shoulder joint distension with saline and corticosteroid for adhesive capsulitis

R Buchbinder, S Green

Distension of the glenohumeral joint with saline and steroid has considerable short term benefit in adhesive capsulitis

Painful stiffening of the shoulder, first described by Duplay in 1834,¹ and aptly labelled “frozen shoulder” by Codman,² is a common cause of shoulder pain and disability. It is estimated to affect 2–5% of the general population and 10–20% of people with diabetes, with subsequent involvement of the contralateral shoulder estimated to occur in 5–40% of affected people.^{3,4} The cumulative incidence in general practice is estimated to be 2.4/1000/year (95% confidence interval 1.9 to 2.9).⁵ The condition is most common in the 5th and 6th decades and it is slightly more common among women. Based on his arthrographic findings of synovial inflammation and adhesions, the term “adhesive capsulitis” was first coined by Neviasser.⁶ These observations led to the commonly held hypothesis that inflammation of the capsule, leading to subsequent fibrosis,

is responsible for the clinical features of this condition.

Patients typically present with a history of gradual onset of severe, disabling shoulder pain accompanied by progressive limitation of both active and passive glenohumeral movement.⁷ Three phases have been described: an early painful phase, usually lasting two to nine months; an intermediate stiff phase, lasting 4–12 months, during which the stiffness predominates and pain is less pronounced; and a final recovery phase lasting 5–24 months, characterised by gradual return of movement.⁷ The pain and stiffness result in severe disability, restricting activities of daily living, work, and leisure activities. Although early studies suggested a self limiting condition lasting two to three years,⁸ other studies have found that up to 40% of patients have persistent symptoms and restriction

of movement beyond three years,⁹ and 15% have persistent disability.¹⁰ Therefore effective treatment that shortens the duration of symptoms and disability has the potential to be of considerable value in terms of reduced morbidity and costs to both the patient and the community.

Intra-articular glucocorticosteroid injections aimed at improving movement at the glenohumeral joint are commonly used to treat adhesive capsulitis, although evidence of their short term benefit has only recently been established.^{11,12} A randomised placebo controlled trial involving 93 participants, performed by Carette and colleagues,¹² showed that a single intra-articular injection of corticosteroid administered under fluoroscopic guidance combined with a simple home exercise programme was significantly better than placebo in improving pain and disability at six weeks, and this benefit was maintained at three months. The same study also showed that the addition of supervised physiotherapy, aimed at mobilisation of the glenohumeral joint, provided faster improvement in shoulder range of motion. Over time, the between group differences diminished, and by 12 months all treatment groups had improved to a similar degree.

We recently reported the positive results of a randomised, placebo controlled trial investigating the efficacy of intra-articular glucocorticosteroid injection combined with arthrographic distension of the glenohumeral joint with normal saline in this condition.¹³ We showed that shoulder joint distension

with a combination of saline and steroid for patients with a painful stiff shoulder of at least three months duration is of significant benefit over placebo in improving function, pain, and range of movement at three weeks, and this benefit appears to be maintained at six weeks. Consistent with the favourable natural history of this condition, we also found a statistically significant reduction in treatment group differences over time, and by 12 weeks, the sustained gain over placebo was only observed for function when measured by a patient preference questionnaire.

There are strong theoretical reasons to suggest that glenohumeral joint distension may be useful for shoulder stiffness. Andren and Lundberg¹⁴ first described arthrographic distension of the glenohumeral joint capsule leading to capsular rupture as a treatment for the painful stiff shoulder in 1965. They injected 20 ml contrast medium, and normal saline if a larger amount of fluid was required, into the joint, which was then allowed to flow back and forth between the syringe and joint several times or until capsular rupture. Subsequently, distension of the joint has been described using a variety of other substances such as local anaesthetic and air, with most including corticosteroid as part of the procedure.

Although numerous case series have reported favourable results of arthrographic shoulder joint distension, most have included corticosteroid; therefore it is not possible to directly attribute the benefit to the joint distension per se. Furthermore, two randomised controlled trials failed to find any benefit of distension combined with corticosteroid over corticosteroid alone,^{15 16} although a third trial did report significant improvements in range of motion and analgesic use but not pain.¹⁷ It is important to note that all three trials injected small volumes of fluid (9–20 ml), which may not have been sufficient to adequately distend the shoulder capsule. The median volume injected in our trial was 43.3 ml (range 21–80) in the distension group and 6 ml (of contrast medium) in the placebo group. Joint distension proceeded until the subscapular bursa was filled, capsular rupture occurred, a total of 90 ml was injected, or the participant requested termination of the procedure.

The timing of joint distension in treating the painful stiff shoulder may also influence outcome. In the early painful phase of the disorder, patients may be unable to tolerate distension of the capsule, resulting in the injection of insufficient volume. We postulated that distension may be more effective in the later phases and therefore only included

patients in our trial who had had at least three months of symptoms and whose resting pain was less than seven out of 10 on a visual analogue scale.

With hindsight it is easy to be critical of our choice of comparator (placebo). However, at the start of our trial, clear evidence of efficacy of any treatment interventions, including corticosteroid injections, for adhesive capsulitis was lacking.¹⁸ Although we think it unlikely, we were unable to exclude the possibility that the observed improvements in the distension group of our trial were partially or entirely due to the injection of corticosteroid rather than capsular distension. Over 25% of participants had received one or more steroid injections before the trial without benefit, although other presently unresolved issues, such as the accuracy of needle placement, may have influenced outcome.

It is also easy to be critical of our choice of active treatment arm (glenohumeral joint distension with a combination of saline and corticosteroid). This intervention is already part of the established standard of care in our setting, despite a lack of evidence of its value from appropriately conducted trials. We therefore chose to address the more relevant issue to us—namely the efficacy of glenohumeral joint distension (with both saline and steroid) as performed in our setting. The fact that this treatment is widely available in our setting most likely accounted for slow patient recruitment, with both patients and referrers reluctant to accept the 50% chance of placebo when the active treatment was readily accessible and affordable. This highlights the problems inherent in introducing new treatments that become incorporated into standard care before their proper evaluation.

On the basis of the available data, we currently know that both intra-articular steroid injection alone and a combination of glenohumeral joint distension with saline and steroid provide important short term benefits in this condition.^{12 13} The following remain to be determined: whether the combination of joint distension with saline and corticosteroid provides significantly more benefit than either distension with saline alone or corticosteroid injection alone; whether repeat distensions with or without steroid extend the benefit; whether the benefits of corticosteroid injection and glenohumeral joint distension vary depending on the phase of the disorder; and whether physiotherapy targeted to mobilisation and exercise after the procedure enhance the benefit of joint distension combined with steroid. We hope to obtain data to address some of these uncertainties

from further trials that are currently underway.

Br J Sports Med 2004;**38**:384–385.
doi: 10.1136/bjsem.2004.013532

Authors' affiliations

R Buchbinder, Monash Department of Clinical Epidemiology at Cabrini Hospital and Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

S Green, Monash Institute for Health Services Research, Monash University

Correspondence to:

Associate Professor Buchbinder, Department of Clinical Epidemiology, Suite 41, Cabrini Medical Centre, 183 Wattletree Rd, Malvern, Victoria, Australia 3144; rachel.buchbinder@med.monash.edu.au

REFERENCES

- Duplay S. De la peri-arthritis scapulo-humeral et ces raideurs de l'épaule qui en sont la consequence. *Arch Gen Med* 1872;**20**:513.
- Codman EA. *The shoulder*. Boston: Thomas Todd Co, 1934.
- Anton HA. Frozen shoulder. *Can Fam Phys* 1993;**39**:1773–7.
- Lundberg B. The frozen shoulder. *Acta Orthop Scand* 1969;**119**(suppl):1–59.
- van der Windt DA, Koes BW, de Jong BA, et al. Shoulder disorders in general practice: incidence, patient characteristics, and management. *Ann Rheum Dis* 1995;**54**:959–64.
- Neviaser JS. Adhesive capsulitis of the shoulder: a study of the pathological findings in peri-arthritis of the shoulder. *J Bone Joint Surg* 1945;**27**:211–22.
- Reeves B. The natural history of the frozen shoulder syndrome. *Scand J Rheumatol* 1975;**4**:193–6.
- Neviaser TJ. Adhesive capsulitis. *Orthop Clin North Am* 1987;**18**:439–43.
- Simmonds FA. Shoulder pain; with particular reference to the "frozen" shoulder. *J Bone Joint Surg [Br]* 1949;**31**:426–32.
- Hazleman BL. The painful stiff shoulder. *Rheumatol Phys Med* 1972;**11**:413–21.
- Buchbinder R, Green S, Youd JM. Corticosteroid injections for shoulder pain. (Cochrane Review). *Cochrane Library*. Issue 2. Chichester: John Wiley & Sons, Ltd, 2004.
- Carrette S, Moffet H, Tardiff J, et al. Intraarticular corticosteroids, supervised physiotherapy, or a combination of the two in the treatment of adhesive capsulitis of the shoulder. *Arthritis Rheum* 2003;**48**:829–38.
- Buchbinder R, Green S, Forbes A, et al. Arthrographic joint distension with saline and steroid improves function and reduces pain in patients with painful stiff shoulder: results of a randomised, double-blind, placebo-controlled trial. *Ann Rheum Dis* 2004;**63**:302–9.
- Andren I, Lundberg BJ. Treatment of rigid shoulders by joint distension during arthrography. *Acta Orthop Scand* 1965;**36**:45–53.
- Corbeil V, Dussault RG, Leduc BE, et al. Capsulite rétractile de l'épaule: étude comparative de l'arthrographie avec corticothérapie intra-articulaire avec ou sans distension capsulaire. *Can Assoc Radiol J* 1992;**43**:127–130.
- Jacobs LGH, Barton MAJ, Wallace WA, et al. Intra-articular distension and steroids in the management of capsulitis of the shoulder. *BMJ* 1991;**302**:1498–1501.
- Gam AN, Schydlowsky P, Rossel I, et al. Treatment of "frozen shoulder" with distension and glucocorticoid compared with glucocorticoid alone. *Scand J Rheumatol* 1998;**27**:425–30.
- Green S, Buchbinder R, Glazier R, et al. Systematic review of randomised controlled trials of interventions for painful shoulder: selection criteria, outcome assessment, and efficacy. *BMJ* 1998;**316**:354–60.



Anterior cruciate ligament rupture: is osteoarthritis inevitable?

J Feller

Br J Sports Med 2004 38: 383-384
doi: 10.1136/bjsm.2004.013300

Updated information and services can be found at:
<http://bjsm.bmj.com/content/38/4/383>

These include:

References

This article cites 5 articles, 1 of which you can access for free at:
<http://bjsm.bmj.com/content/38/4/383#BIBL>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections

Articles on similar topics can be found in the following collections

[Degenerative joint disease](#) (239)
[Musculoskeletal syndromes](#) (431)
[Osteoarthritis](#) (117)
[Football \(soccer\)](#) (227)
[Procedures](#) (46)
[Ligament rupture](#) (15)
[Injury](#) (957)
[Trauma](#) (845)
[Meniscal tears](#) (15)

Notes

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://group.bmj.com/subscribe/>