SPINE Volume 29, Number 8, pp 833–837

The Use of Intradiscal Steroid Therapy for Lumbar Spinal Discogenic Pain

A Randomized Controlled Trial

Abhay Khot, MS (Orth), DNB (Orth), FRCS (Orth), Mark Bowditch, FRCS (Orth), John Powell, FRCS, and David Sharp, MD, FRCS

Study Design. A prospective randomized study of the therapeutic effect of intradiscal steroid injection compared to a saline placebo.

Objectives. To determine whether intradiscal steroid injection influences the clinical outcome at 1 year in patients with chronic low back pain of discogenic origin.

Summary of Background Data. Steroids have been used empirically in the treatment of back pain. They have been used in the epidural space and around nerve roots and have been used as an alternative to chymopapain within the disc. Previous studies have, however, shown variable results.

Methods. A total of 120 patients with chronic low back pain of discogenic origin were enrolled in the study. At discography, if they had concordant pain, they were randomized to injection of normal saline or methylprednisolone into the disc space. These patients were prospectively followed up for 12 months, and they were asked to report pain according to a visual analogue score and their Oswestry Disability Index was recorded. The primary outcome measure was determined as a percentage change in disability, and the results were analyzed using independent samples *t* test. The secondary outcome measure was a change in the pain score, and this was analyzed using the Mann-Whitney U test.

Results. There was no significant difference in the primary outcome between the two groups ($P = 0.71$). The steroid group had a mean change of 2.28 (SE 2.49) in percentage disability, while the saline group had a mean change of 3.42 (SE 1.79). With respect to the change in pain score, there was no significant difference between the two groups ($P = 0.72$). Those patients who had saline injection had a median change in pain score of 0 (interquartile range −1 to 1), whereas those given steroid treatment had a median change in pain score of 0 (interquartile range −0.25 to 1).

Conclusions. This study demonstrates that intradiscal steroid injections do not improve the clinical outcome in patients with discogenic back pain compared with placebo. [Key words: intradiscal steroids, intervertebral disc, discogenic low back pain, randomized controlled trial] **Spine 2004;29:833–837**

From the Department of Trauma and Orthopaedics, Ipswich Hospital, Ipswich, U.K.
Acknowledgment date: December 5, 2002. First revision date: June 12, 2003. Acceptance date: June 25, 2003.
The manuscript submitted does not contain information about medical device(s)/drug(s). The legal regulatory status of the device(s)/drug(s) that is/are the subject of this manuscript is not applicable in my country.
No funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.
Address correspondence to David Sharp, MD, Trauma and Orthopaedics, Ipswich Hospital, Heath Road, Ipswich IP4 5PD, United Kingdom; E-mail sharp.sec@ipsh-tr.anglox.nhs.uk

Discography has developed over the last five decades since the first reports by Lindblom[1] and Hirsch.[2] Lindblom[1] speculated on the use of a contrast material to outline the inner anatomy of the intervertebral disc, and Hirsch[2] used saline in an attempt to localize lesions in the disc. As a procedure, discography has been able to demonstrate the presence of anular tears and degenerative change and also allows clinical correlation with symptoms of low back pain.[3,4] Pressure studies that cause pain, which may be similar to the patients' symptoms,[5] have been explained by stimulation of nociceptive fibers within the innervated part of the anulus, or the endplate or body, and by chemical stimulation.[6–8]

Although there have been reports questioning the effectiveness of discography as a diagnostic tool,[9] techniques have improved over the years and discography is now well established.[10] There have been attempts to extend the indications of discography to use it as a therapeutic measure.[11] Steroids and chymopapain have been used within the disc space for many years.[12–14] These indications have been in patients with back pain and sciatica, and the reported results have not been consistent.

There has been only one randomized trial[15] to test the therapeutic effect of intradiscal steroids in patients with low back pain, and this study reported no significant change at an average follow-up of only 2 weeks, in a small number of patients. Our unit had previously reported a retrospective survey,[16] which suggested some improvement in 24.5% of patients at 6 weeks following injection. This prospective study was therefore set up to test the hypothesis that steroids are therapeutic as intradiscal injections in discogenic pain over a period of 1 year.

Methods

To investigate the efficacy of intradiscal steroids, a prospective randomized study was set up at the authors' institution. Local Ethics Committee approval was obtained. Patients were those presenting with symptoms and signs of discogenic low back pain without radicular leg pain, together with MRI findings demonstrating degenerative disc disease, and had failure of at least 6 weeks of conservative treatment and without any medical conditions requiring systemic steroid therapy. We defined discogenic back pain as being typically chronic low back pain of a deep, aching, nagging, or throbbing character, not completely relieved by rest, and sometimes with referred pain to one or both lower limbs. These patients were listed for investigation

Table 1. Flow Chart of Patient Progress Through the Trial

Patients eligible for the trial (n = 274)
Not randomized (n = 154)
Reasons for not being randomized:
1. Patient refusal to be in the trial (n = 32)
2. Nonconcordant pain or having radiating leg pain(sciatica) (n = 75)
3. Anatomical abnormalities (n = 17)
4. Other reasons (n = 30) (previous surgery, private patients, repeat injections)

Randomized into trial (n = 120)

with discography. Informed consent was obtained from them to enter the trial.

All discographies were done as day case procedures under awake sedation and using a left posterolateral approach with fluoroscopic guidance by the two senior authors. At discography, if there were concordant pain on pressurization of a degenerate disc, each patient was randomized to the steroid or saline group, by opening a sealed envelope, and the appropriate injection was given. The surgeon was aware of the contents of the injection, which was either 1 mL containing 40 mg of Depo-Medrone (Pharmacia Ltd., Milton Keynes, U.K.), or 1 mL of normal saline. The patient remained unaware of the substance injected.

The patients were prospectively followed up in clinic and by postal questionnaire for 1 year. The response to the injection was assessed using a Visual Analogue Score for pain[17] and the Oswestry Disability Index.[18]

The primary outcome measures were the change in disability, *i.e.*, baseline percentage disability minus follow-up percentage disability,[19] and the change in pain score. Assuming that the randomization was successful in providing two comparable groups, we compared the average change in disability in the two groups using the independent samples *t* test and the change in pain score using the Mann-Whitney U test. Other secondary outcome measures were also recorded.

■ Results

These are reported using the CONSORT[20] criteria for randomized controlled trials. Between 1997 and 2000, a total of 274 patients had discography procedures in our unit. Of these, 120 patients were recruited into the trial; 154 patients could not be recruited for the reasons outlined in Table 1.

Randomization allocated 60 patients in each group. All randomized patients received the injection as planned, *i.e.*, methylprednisolone acetate 40 mg in 1 mL or 1 mL of normal saline. The two groups were comparable with respect to gender, age, pain, and percentage disability (Table 2).

Table 2. Descriptive Statistics for Baseline Data

Variable	Treatment Group	Control Group
Male: number (%)	29 (49.2)	26 (42.6)
Age: mean (SD)	45.0 (8.8)	42.5 (9.3)
Pain: median (IQR)	3 (3,4)	3.5 (2,4)
Oswestry Disability Index: mean (SD)	50.8 (14.4)	49.8 (16.6)

Table 3. Flow Chart of Patient Progress Through the Trial

	Steroid Group (n = 60)	Saline Group (n = 60)
Received intervention as allocated	60	60
Did not receive intervention	0	0
Followed up	60	60
Timing of primary and secondary outcomes	1 year	1 year
Withdrawn	14	8
Reasons for withdrawal		
Intervention ineffective—had surgery within 1 year	6	4
Lost to follow-up	3	1
Other (incomplete records)	5	3
Completed trial	46	52

At the end of 1 year on the trial, primary outcome data of 98 patients were available for analysis: 46 of 60 in the steroid group and 52 of 60 in the saline group. The reasons for withdrawal are outlined in Table 3.

There was no significant difference in primary outcome between the two groups ($P = 0.71$). Those given steroid had a mean change of 2.28 (SE 2.49) in percentage disability, while those in the saline group had a mean change of 3.42 (SE 1.79) (Figures 1 and 2).

Secondary outcome data were available for 98 patients. There was no significant difference between the two groups in the change in pain score ($P = 0.72$). Those given saline had a median change in pain score of 0 (interquartile range −1 to 1), whereas those given steroid treatment had a median change in pain score of 0 (interquartile range −0.25 to 1) (Figure 3).

Ten patients, 6 from the steroid group and 4 from the control group, failed to complete the study at 1 year because they needed an operation. Five patients had a fusion, three had a nerve root decompression, and one each had a discectomy and chemonucleolysis. These patients were not included in the analysis of primary outcome.

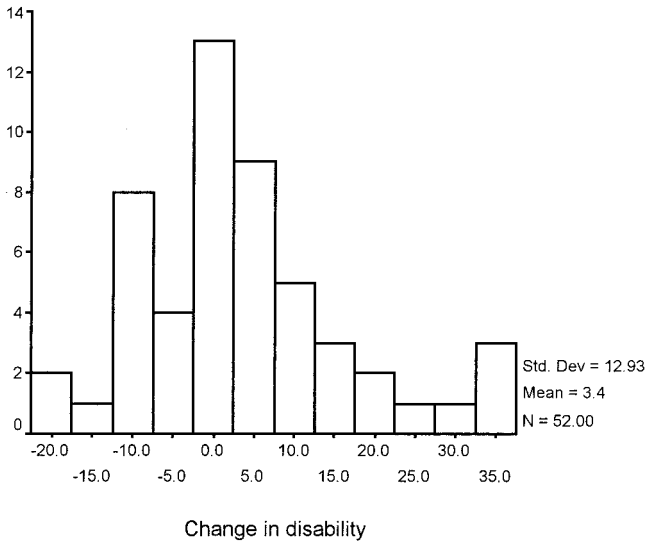

Figure 1. Change in disability for the saline group.

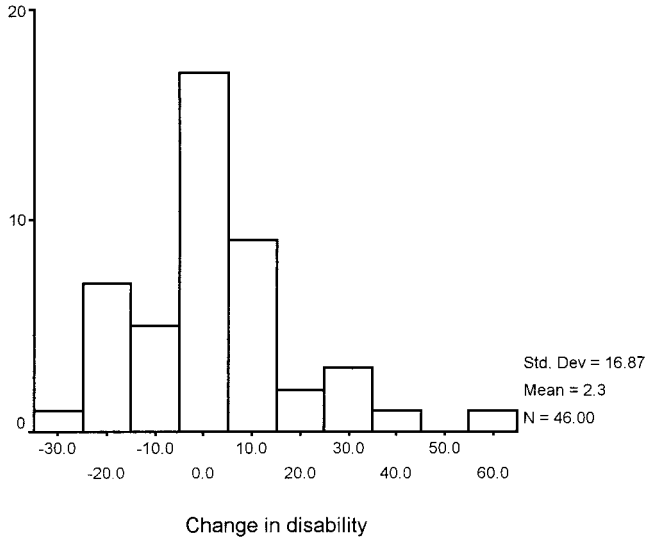

Figure 2. Change in disability for the steroid group.

■ Discussion

Discogenic pain has caused controversy in spinal surgery for many years.[21] Acceptable criteria for diagnosis are variable, and there are many different approaches to management. Discography has, however, become generally accepted as a diagnostic tool, and the presence of concordant pain on pressure studies can be used as a reliable indicator of discogenic pain.[5]

Although steroids have been used in spinal disorders for many years, their efficacy and mechanism of action have not always been proved. Theoretically, steroids have been presumed to have an anti-inflammatory action.[22] When the symptom of pain is thought to result from inflammation, it is natural to think that an anti-inflammatory agent will work. McCarron *et al*[23] discussed the inflammatory potential of the nucleus pulposus, and since then, many studies have shown that the nuclear material does possess the ability to irritate the nerve root by inducing inflammation.[24–26] This has led to the use of steroids around the nerve root, either as an epidural or as a nerve root foraminal injection,[27] to decrease symptoms of nerve root pain, and this has been proved to be effective.[28]

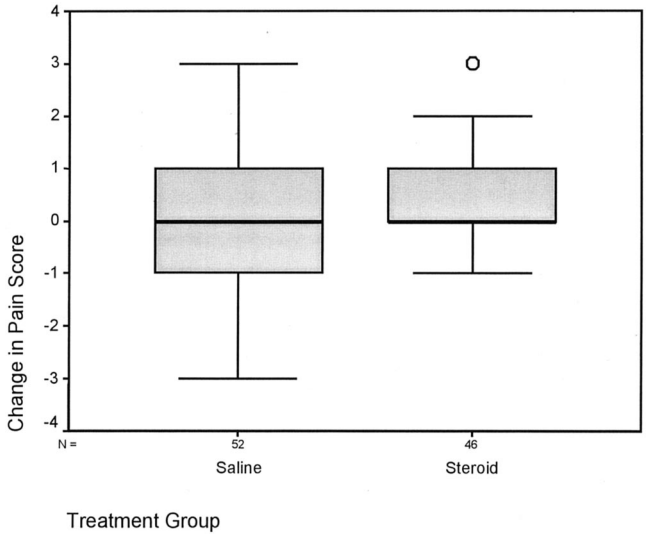

Figure 3. Boxplot for change in pain score for the saline and steroid groups.

However, within the disc, the theoretical basis for the therapeutic use of steroids is not so well established. Leao[11] discussed the polymerizing effect of steroid within the disc but admitted that it was possibly due to vasoconstriction or cellular modification of the inflammatory process. Feffer[22] also used hydrocortisone to induce a reversal of degenerative inflammatory change within the disc space and added that the polymerizing effect of steroid would help the disc heal itself and reduce the symptoms of low back pain and sciatica.

This is an attractive theory to use in discogenic low back pain. If steroids have a beneficial effect, it would be a useful method to avoid major surgery. On this basis, therapeutic intradiscal steroids have been used in the treatment of low back pain. Feffer[22] reported that 46.7% (114 of 244) of patients had remission of symptoms and commented that 54.5% of those who got better had primarily back pain compared with 45.6% who improved with symptoms of radicular pain.

Wilkinson and Schuman[14] used steroids as an alternative to chymopapain and reported a series of 29 patients with lumbar disc disease; 54% of patients with low back pain symptoms had no relief after the injection, with only 31% reporting some improvement. Graham[12] reported a small series from his own practice, comparing the effectiveness of chymopapain with hydrocortisone. The two groups of patients had symptoms of back pain (17 of 40) and back pain with leg pain (23 of 40). His results did not show any significant difference between the two groups. The two groups were also too small to compare the results separately for effectiveness of the injection for back pain and for leg pain. Eight of the nine patients who improved with the injection of hydrocortisone were private patients.

Simmons *et al*[15] have reported a randomized controlled trial of intradiscal steroids in 25 patients with back pain with and without sciatica. They had 14 patients in the steroid group and 11 in the placebo group, which had local anesthetic (bupivacaine). The inclusion criteria were strict, but their results were based on a small number of patients with only a 2-week follow-up period; 21% (3 of 14) in the steroid group and 9% (1 of 11) in the anesthetic group showed improvement, with no statistical difference between the two groups. They concluded that there was no apparent benefit from intradiscal steroid injection. Kato *et al*[29] studied the MRI changes in a specific group of 31 of 38 patients who improved clinically after an intradiscal injection of steroid. This group is a subgroup of 77, 39 of whom did not improve and needed further treatment. They have shown that steroids cause accelerated degeneration within the

disc space, and this correlated well with clinical improvement in their group of patients.

A large randomized controlled trial was therefore needed to answer the question regarding the clinical effectiveness of intradiscal steroids. Our results, derived from analysis of 98 of 120 patients, show that there is no difference in the clinical outcome after injection at 1 year as compared with a saline placebo, as measured by the Visual Analogue Pain score and the Oswestry Disability Index. These are both validated instruments used in studies discussing clinical outcomes in treatment of low back pain.[17,30]

The dropout rate in this analysis is a combination of several factors as outlined in Table 3. The low numbers of patients lost to follow up probably reflect the relatively stable population in our area and the lack of other local spinal services. This dropout rate was higher in the steroid group (14 *vs*. 8). We think that this was unfortunate but would not influence the analysis.

Animal studies by Aoki *et al*[31] have shown that both methylprednisolone and glycol, which is a carrier in the insoluble preparation, cause degeneration and calcification within the disc space in rabbits within 24 weeks of injection. They proposed this as the basis for the reported clinical improvement in patients where steroids were used within the disc space for the treatment of low back pain and sciatica.

This trial therefore demonstrates that steroids are not effective in improving the clinical symptoms in this patient group. The evidence concerning steroid-induced disc degeneration is not translated into either clinical benefit or worsening of symptoms at 1 year.

We therefore cannot recommend the use of steroids as an intradiscal injection in patients with discogenic low back pain. Not only are steroids ineffective as a therapeutic option in discogenic pain, but there are also increasing concerns in the literature that they may have a deleterious long-term effect.

■ Key Points

- The use of steroids in the disc space has been empirical.
- The clinical benefit of using intradiscal steroid therapy is not proven by a randomized control trial in patients with discogenic back pain.

Acknowledgments

The authors thank Mrs. Alison Bullard and Sr. Helen Vernau for their help in collecting the data and Barbara Arch and Eleanor Pinto at the Centre for Applied Medical Statistics, Cambridge, for helping with the statistical assessment.

References

1. Lindblom K. Diagnostic puncture of intervertebral discs in sciatica. *Acta Orthop Scand*. 1948;17:213–239.
2. Hirsch C. Studies in the pathology of low back pain. *J Bone Joint Surg Am*. 1959;41:237–243.
3. Moneta GB, Videman T, Kaivanto K, et al. Reported pain during lumbar discography as a function of anular ruptures and disc degeneration: a re-analysis of 833 discograms. *Spine*. 1994;19:1968–1974.
4. Simmons EH, Segil CM. An evaluation of discography in the localization of symptomatic levels in discogenic disease of the spine. *Clin Orthop*. 1975;57–69.
5. Guyer RD, Ohnmeiss DD. Lumbar discography: position statement from the North Am Spine Society Diagnostic and Therapeutic Committee. *Spine*. 1995;20:2048–2059.
6. Gunzburg R, Parkinson R, Moore R, et al. A cadaveric study comparing discography, magnetic resonance imaging, histology, and mechanical behavior of the human lumbar disc. *Spine*. 1992;17:417–426.
7. Heggeness MH, Doherty BJ. Discography causes end plate deflection. *Spine*. 1993;18:1050–1053.
8. Weinstein J, Claverie W, Gibson S. The pain of discography. *Spine*. 1988; 1988:1344–1348.
9. Holt EP, Jr. The question of lumbar discography. *J Bone Joint Surg Am*. 1968;50:720–726.
10. Simmons JW, Aprill CN, Dwyer AP, et al. A reassessment of Holt's data on: "The question of lumbar discography." *Clin Orthop*. 1988;120–124.
11. Leao L. Intradiscal injection of hydrocortisone and prednisolone in the treatment of back pain. *Rheumatism*. 1960;16:72–77.
12. Graham C. Chemonucleolysis: a preliminary report on a double blind study comparing chemonucleolysis and intradiscal administration of hydrocortisone in the treatment of back-ache and sciatica. *Orthop Clin North Am*. 1975;6:259–263.
13. Bosacco SJ. Lumbar discography: redefining its role with intradiscal therapy. *Orthopedics*. 1986;9:399–401.
14. Wilkinson H, Schuman N. Intradiscal corticosteroids in the treatment of lumbar and cervical disc problems. *Spine*. 1980;5:385–389.
15. Simmons JW, McMillin JN, Emery SF, et al. Intradiscal steroids: a prospective double-blind clinical trial. *Spine*. 1992;17(suppl):172–175.
16. Bull T, Sharp D, Powell J. The efficacy of intradiscal steroid injection compared to Modic changes in degenerate lumbar discs. *J Bone Joint Surg Br*. 1998;80:47.
17. Roland M, Fairbank J. The Roland-Morris Disability Questionnaire and the Oswestry Disability Questionnaire. *Spine*. 2000;25:3115–3124.
18. Fairbank JC, Couper J, Davies JB, et al. The Oswestry low back pain disability questionnaire. *Physiotherapy*. 1980;66:271–273.
19. Little DG, MacDonald D. The use of the percentage change in Oswestry Disability Index score as an outcome measure in lumbar spinal surgery. *Spine*. 1994;19:2139–2143.
20. Altman D. Better reporting of randomised controlled trials: the CONSORT statement. *Br Med J*. 1996;313:570–571.
21. Boden S, McLain RF. Lumbar disc disease with discogenic pain: what surgical treatment is most effective? *Spine*. 1996;21:1836–1838.
22. Feffer HL. Therapeutic intradiscal hydrocortisone: a long term study. *Clin Orthop*. 1969;67:100–104.
23. McCarron R, Wimpee M, Hudkins P, et al. The inflammatory effect of nucleus pulposus: a possible element in the pathogenesis of low back pain. *Spine*. 1987;12:760–764.
24. Kang JD, Georgescu HI, McIntyre-Larkin L, et al. Herniated lumbar intervertebral discs spontaneously produce matrix metalloproteinases, nitric oxide, interleukin-6, and prostaglandin E_2. *Spine*. 1996;21:271–277.
25. Matsui Y, Maeda M, Nakagami W, et al. The involvement of matrix metalloproteinases and inflammation in lumbar disc herniation. *Spine*. 1998;23: 863–868; discussion 868–869.
26. Virri J, Gronblad M, Seitsalo S, et al. Comparison of the prevalence of inflammatory cells in subtypes of disc herniations and associations with straight leg raising. *Spine*. 2001;26:2311–2315.
27. Hildebrandt J. Relevance of nerve blocks in treating and diagnosing low back pain: is the quality decisive? *Schmerz*. 2001;15:474–483.
28. Karppinen J, Malmivaara A, Kurunlahti M, et al. Periradicular infiltration for sciatica: a randomised controlled trial. *Spine*. 2001;26:1059–1067.
29. Kato F, Mimatsu K, Kawakami N, et al. Changes in the intervertebral disc after discography with intradiscal injection of corticosteroids observed with magnetic resonance imaging (MRI). *J Neurol Orthop Med Surg*. 1993;14:210-216.
30. Fairbank JC. The use of revised Oswestry Disability Questionnaire. *Spine*. 2000;25:2846–2847.
31. Aoki M, Kato F, Mimatsu K, et al. Histologic changes in the intervertebral disc after intradiscal injections of methylprednisolone acetate in rabbits. *Spine*. 1997;22:127–131; discussion 132.

Point of View

C. J. M. Getty, MA, FRCS(Eng), FRCS(Ed)

Earlier literature on the use of intradiscal steroid therapy contains little scientific evidence to support their use. Some of the earlier studies compared chymopapain with steroids. Usually, no clearly defined pathology for the use of these substances was established. The symptoms experienced were those of back pain and leg pain.

With the introduction of more sophisticated imaging, our understanding of disc pathology has improved. With that in mind, the authors of this paper felt that there was a lack of a properly defined study to assess the effectiveness of intradiscal steroid injection at discography.

They noted that intradiscal steroids in the rabbit disc caused disc degeneration over 6 weeks while MRI studies following intradiscal steroids showed a progressive degeneration in the disc, milder than that which occurred after chemonucleolysis. This raised concern as to the effects of intradiscal injection in humans both short and long term.

They designed a prospective randomized study of the therapeutic effect of intradiscal steroid injection compared with a saline placebo. They restricted the study to patients presenting only with discogenic low back pain excluding those with root pain in the leg. Additionally, the MRI findings demonstrated degenerative disc disease. They allowed a 6-week trial of conservative treatment before entering the patient into the study. Furthermore, to enter the trial, at discography there had to be concordant pain on pressurization of the degenerate disc.

They were clearly strict in the criteria that they used in the trial.

There was a good follow-up percentage. They demonstrated that: 1) steroids were not effective in improving the clinical symptoms in this particular patient group; 2) the evidence concerning steroid-induced disc degeneration was not converted into either clinical benefit or worsening of symptoms at 1 year; and 3) intradiscal steroid injections carried no benefit over a placebo saline injection.

This is an important study because it shows quite conclusively in this group of patients that there is little to support the use of intradiscal steroids for the management of discogenic pain, bearing in mind the potential unknown side effects in the longer term.

Previously, the authors had identified that patients with Type 2 Modic changes on the MRI may have an inflammatory process that responds to steroid injection in a significant number of patients. Further prospective randomized studies are required to confirm this and dependent on the result to identify the reasons for such an outcome.

In the absence, however, of any scientific evidence at this moment in time, there seems little justification for the use of intradiscal steroids in patients with discogenic back pain.

From the Department of Orthopaedics, Northern General Hospital, Sheffield, UK.
The manuscript submitted does not contain information about medical device(s)/drug(s).
No funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.
Address correspondence to C. J. M. Getty, MA, FRCS(Eng), FRCS(Ed), Great Gilling, 11 Chorley Road, Sheffield S10 3RJ, U.K.; E-mail: info@johngetty.co.uk