Letters to the editor

Complications of Chymopapain Injection

To THE EDITOR: I read with interest the article by Dr. Davis and his colleagues (Davis RJ, North RB, Campbell JN, et al: Multiple cerebral hemorrhages following chymopapain chemonucleolysis. Case report. J Neurosurg 61:169–171, July, 1984). I am sorry that such an event occurred, but it stresses once more the importance of precise needle placement during chymopapain injection.

Review of the discograms (their Fig. 2) shows that the needle inserted at L5–S1 was not in the disc space. The dye (Renografin) entered the subarachnoid space and collected on the left side because the patient was in the left lateral decubitus position (the contrast material itself is neurotoxic when injected intrathecally). This was followed by injection of the enzyme into the same intraspinal space, which explains the poor result achieved.

In my opinion, this case emphasizes a very basic clinical point: needles should be accurately placed into the disc nucleus. There are several techniques for needle placement and each surgeon should use the one he feels most comfortable with. Besides the classic lateral position generally taught at workshops (which I personally find difficult to apply), there are at least three other techniques of which I am aware, including a stereotaxic one. I use the prone position, with the C-arm television monitor adjusted for oblique views of the spine. The needle is aligned with the disc center as shown in Fig. 1. No measurements are required with this technique.

Review courses, videotaped material, and training sessions are widely available for instruction on correct insertion of the needle into a lumbar disc.

MAURICE ROMY, M.D.
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RESPONSE: As noted by Dr. Romy and as discussed in our report, the appearance on our patient's x-ray films (obtained from another institution) of discographic dye in a myelographic pattern suggests intrathecal extravasation. Presumably both contrast material and chymopapain entered the subarachnoid space. Both American manufacturers of chymopapain, in their July 19, 1984, letters to the medical community, warned that the two agents together are significantly more neurotoxic than either alone. Accordingly, they have recommended avoidance of discography as part of the chemonucleolysis procedure. They further note a potential role of multiple disc injections and general anesthesia in the neurological complications reported to date.

On the available x-ray films of our patient, the lateral view (our Fig. 2 left) shows that the needle at L5–S1 overlies the disc space, which apparently contains contrast material. On the slightly oblique anteroposterior view (our Fig. 2 right), its position is less clear, and appears suboptimal. The films may not be simultaneous and, in any event, represent only moments in a continuing process. Even when the needle is in the center of the nucleus pulposus, extravasation around it or along other needle tracts may permit entry into the subarachnoid space. Dr. Romy and both drug manufacturers properly note the importance of verifying correct needle placement.

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Complications of Chymopapain Chemonucleolysis

To THE EDITOR: In the recent article by Artigas, et al. (Artigas J, Brock M, Mayer HM: Complications following chemonucleolysis with collagenase. J Neurosurg 61:679–685, October, 1984), the authors reported that eight of their 11 patients required laminectomy less than 75 days following injection and, of the eight, five were operated on in less than 14 days. No postoperative results were given. Extensive alterations were found after injection of collagenase, including "digestion" of the nucleus pulposus and anulus fibrosus,
and damage to the end-plates, bone, ligaments, and epidural fat.

At the present time, intradiscal injections of collagenase in the United States are under strict monitoring by the Food and Drug Administration. I am one of five investigators, including two neurosurgeons and three orthopedic surgeons, who have operated on 82 of 410 patients previously treated with collagenase injections. Our attention has been focused on any changes that differed from those following a routine laminectomy for disc protrusion. None of us has found the reported changes in any of the 82 patients. Artigas, et al., reported that 73% of their previously collagenase-injected patients required laminectomy, whereas our combined figure was 20%. A detailed report on our experience with collagenase is being submitted for publication.

ROBERT G. FISHER, M.D., PH.D.
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RESPONSE: We thank Dr. Fisher for his comments on our article. The fact that none of the investigators "has found the reported changes in any of the 82 patients" treated with collagenase is not in disagreement with our assumption that the severe alterations observed in our patients were due to the use of a "hyperaggressive" batch of the enzyme. This occurred because the methods of titrating the activity of collagenase were too inefficient. All investigators involved in chemonucleolysis hope that it will be possible to "tame" collagenase for the benefit of our patients.

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Constant-Current versus Constant-Voltage Stimulation

TO THE EDITOR: With regard to the article by Drs. Møller and Jannetta (Møller AR, Jannetta PJ: Preservation of facial function during removal of acoustic neuromas. Use of monopolar constant-voltage stimulation and EMG. J Neurosurg 61:757-760, October, 1984), we agree that cerebrospinal fluid (CSF) shunting is an important potential source of false-negative stimulation. Such false-negativity is unacceptable when stimulation is used as a guide to tumor dissection in the posterior fossa. Based upon theoretical considerations and on their experience, the authors advocate the use of a low-impedance constant-voltage source as opposed to constant-current in order to minimize the effects of CSF shunting. However, this comparison was not well documented in their paper.

Based upon our experience with an animal model, we would like to propose the use of stimulus probes with insulation carried flush to the tip (the "flush-tip" probe) as an alternative solution to the problem of CSF shunting. Under conditions of CSF shunting, such probes were observed to have several advantages over "bare-tip" probes, which have more uninsulated conductor at the tip than is in direct contact with the tissue to be stimulated.

Our preliminary findings may be summarized as follows: 1) When constant-current stimulation was used in the presence of CSF, flush-tip probes consistently required the least amount of current to achieve a given response level. 2) When constant-voltage stimulation was used in the presence of CSF, flush-tip probes usually required the least voltage to achieve a given response level, although probes with approximately 1 mm or less of uninsulated terminus required the same or slightly less voltage in some preparations. 3) When either constant-current or constant-voltage stimulation was used in the presence of CSF, flush-tip probes required the least power (current \times voltage) to achieve a given response level. 4) The impedance of flush-tip probes was relatively independent of the presence of CSF, allowing the power delivered to the tissues to be maintained within a narrow range under a wide range of shunt conditions. 5) At a given response level, when either constant-current or constant-voltage stimulation was used in the presence of CSF, stimulus artifacts were always of smallest amplitude with flush-tip probes. 6) When flush-tip probes were used in the presence of CSF, no practical advantage of constant-voltage over constant-current stimulation could be demonstrated.

We used a rat sciatic-nerve model in our nerve stimulation studies. Electromyographic activity was recorded in the quadriceps muscles while the corresponding nerve fascicle, dissected free from the main sciatic trunk, was stimulated under various conditions. In order to simulate CSF shunting, the nerve was approached from behind and the gluteal muscles were divided in such a way as to create a reservoir surrounding the sciatic nerve. The fascicle to the quadriceps was supported away from muscle and other nerve tissue with a nonconducting porous synthetic material (Perfund), and the field was flooded with normal human CSF. Under these "worst-case" shunting conditions, stimulation was relatively inefficient with either constant-current or constant-voltage when a significant area of the stimulus probe was bare other than that in direct contact with the nerve. With 5 mm of bare tip at the terminal end of a No. 28 probe, half-maximal responses were obtained at 0.5 to 1.0 mA with constant-current and 0.1 to 0.3 V with constant-voltage stimulation. (Current levels were estimated indirectly using Ohm's law. A cathode ray oscilloscope was used to determine the voltage drop across a 100-ohm resistor in series with purely resistive loads, matched to various electrode impedances encountered in this study. Current levels were approximately equal to expected values, based upon the dial setting, when 50 V or greater was delivered to the stimulus isolation unit.)

When constant-current stimulation was used under the above conditions, flush-tip probes consistently required the least amount of current to obtain a given response level. Half-maximal stimulation of nerve fascicles, with diameters approximating those of the probe (No. 28), was achieved with 0.03- to 0.1-mA pulses of 100-\mu sec duration. When constant-voltage stimulation

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