CHEMONUCLEOLYSIS

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A prospective study of 480 patients who underwent enzymatic dissolution of the nucleus pulposus with chymopapain is reported. Seventy per cent of patients with the clinical criteria for a disc herniation had a favourable response to chemonucleolysis. The commonest cause of failure was persistent back pain. In patients with sequestered discs or lateral recess stenosis surgical intervention was not made more difficult by chemonucleolysis. Those with a previous operation, spinal stenosis or psychogenic components to the disability had very poor results. Complications were few and easily managed.

Until Smith (1964) introduced the technique of enzymatic dissolution of the nucleus pulposus by chymopapain, the problem of the herniated lumbar disc had been resolved through conservative treatment or surgical excision. Removal of disc material by the use of chymopapain, without opening the spinal canal, was seen as a significant advance in the conservative treatment of sciatica (Parkinson and Shields 1973; Onofrio 1975; Wiltse, Widell and Yuan 1975). Others (Shealy 1967; Sussman 1971), however, ascribed neurotoxic qualities to the drug and described an apparent lack of effect in studies *in vitro* (Knighton and Reynolds 1976).

Early in 1975 two deaths from anaphylactic reaction to chymopapain occurred in the same North American centre. Subsequently, a preliminary report from four other American centres engaged in double-blind studies suggested that there was no difference in very early results between patients receiving chymopapain and those receiving a placebo (sodium iothalamate, cysteine hydrochloride and ethylenediamine tetra-acetic acid) (Knighton and Reynolds 1976). These events have left the use of chymopapain for chemonucleolysis in doubt.

The purpose of this paper is to describe the author's experience with chymopapain over the past seven years. A preliminary communication was first published in 1971 (Macnab, McCulloch, Weiner, Hugo, Galway and Dall 1971). This article reports a prospective study of 480 sequential patients who have undergone chemonucleolysis and describes the clinical presentation of those patients who tend to respond to chemical dissolution of the disc.

PHARMACOLOGY OF CHYMOPAPAIN

Chymopapain, derived from papaya latex, is a proteolytic enzyme which was first isolated by Jansen and Balls in 1941. The use of a proteolytic enzyme to dissolve disc material was first proposed by Hirsch in 1959, but it was

not until Smith published his paper in 1964 that the clinical potential of chymopapain was recognised.

Chymopapain catalyses rapid hydrolysis of the non-collagen ground substance of the nucleus pulposus (Stern 1969). The mechanism of the binding of chymopapain and nucleus pulposus is probably through the affinity of the positively charged chymopapain for the negatively charged acid mucopolysaccharides (Stern and Smith 1967). The exact mechanism by which enzymatic dissolution of the nucleus pulposus relieves the pain associated with disc herniation is not known.

It has been suggested that chymopapain hastens the natural ageing process of chondromucoprotein degradation (Stern 1969). The rapidity of this action *in vivo* is indicated by increasing urinary excretion of mucopolysaccharides in some patients within twenty-four hours after chymopapain injection (Stern, Cosmas and Smith 1968). Further rapid dissolution by chymopapain of parts of the water-insoluble components of the nucleus pulposus occurs *in vitro* over four hours (Stern and Smith 1967). This disruption of the fine structure of the chondromucoprotein destroys the water-binding capacity of the nucleus pulposus and thereby reduces the pressures which can be exerted by it.

Chymopapain effectively dissolved the nucleus pulposus of rabbits, dogs and cats when injected into intervertebral discs at doses of 50 to 500 units per disc (Garvin, Jennings, Smith and Gesler 1965). Much higher doses, of the order of 2,500 to 10,000 units per disc, had minimal effects on the inner portion of the annulus fibrosus. One hundred times the clinically effective dose of chymopapain was well tolerated by dogs and rabbits when administered epidurally, intradiscally or intravenously. Chymopapain was considerably more toxic when injected intrathecally, causing subarachnoid haemorrhage related to rupture of the fine blood vessels in the pia mater. Chymopapain had no effect on dural or nerve tissue, nor did it cause arachnoiditis in rabbits and dogs (Macnab *et al.* 1971).

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DEFINITIONS

The confusion surrounding terminology for low-back syndromes often creates difficulties in comparing the results of different methods of treatment. The following criteria represent the author's attempt to define and classify low-back disorders for the purpose of this study.

Disc herniation—There are many variations in annular disruption (Macnab *et al.* 1971), producing many variations in the clinical presentation of a disc herniation. However, each produces pressure on a nerve root, manifested as tension, irritation or compression. To enter the diagnostic classification of symptomatic disc herniation, a patient had to satisfy three or more of the following criteria. 1) Unilateral leg pain in a typical sciatic-root distribution, including discomfort below the knee. The leg pain had to be more severe than, or at least equal in severity to, the associated back pain. If the roots of the femoral nerve were involved, pain in the front of the thigh would be produced. 2) Specific neurological symptoms incriminating a single nerve—for example, numbness over the dorsum of the foot into the great toe region or flopping of the foot on walking, signifying involvement of the fifth lumbar nerve. 3) Limitation of straight-leg raising owing to pain in the leg, by at least 50 per cent of normal, or cross-over pain from the unaffected leg to the symptomatic leg, or radiating thigh or back discomfort or calf and foot numbness on bow-string pressure over the medial or lateral popliteal nerve. 4) At least two of four possible neurological changes: muscle wasting, muscle weakness, sensory alteration and reflex changes. 5) A positive myelograph showing a disc herniation at the level suspected clinically.

Any low-back syndrome with two or less of the above criteria was not considered to be due to disc herniation, but rather to disc degeneration or to stenosis affecting the cauda equina or individual nerve roots.

Disc degeneration—Changes within the disc, without displacement of disc material, interfere with mechanical integrity, leading to mechanical insufficiency of the spine and rendering it vulnerable to injury. The patient presents with a history of low-back pain provoked by activity, often punctuated by acute episodes of short duration. In its purest form none of the five criteria of disc herniation is present. The plain radiographs often, but not always, show narrowing of the disc space with or without osteophyte formation.

Stenosis syndromes—Exclusive of post-operative root fibrosis, two stenotic syndromes occur in the lumbosacral region. 1) *Spinal stenosis* from developmental narrowing of the bony lumbar vertebral canal causes bilateral leg symptoms in the form of tiredness or loss of power, a feeling of numbness in some lumbosacral dermatomes, or bilateral sciatica during walking or standing. The condition differs from a disc herniation in that the leg symptoms are bilateral and less severe than the back pain, straight-leg raising is almost always greater than 50 per cent of normal and the myelograph

shows a specific type of defect (Schatzker and Pennal 1968). It is possible for a small spinal canal to be compromised by a slight disc bulge, the significance of which will be discussed later. 2) *Lateral recess stenosis*: Disc narrowing, osteophyte formation or subluxation of a facet joint can encroach upon the limited space available to the nerve root in the lateral recess, causing back and unilateral leg pain which is often claudicant in nature. The back and leg pain can be equal in severity, but the back pain usually predominates; neurological symptoms (usually fifth lumbar) may be present with evidence of nerve-root compression (fifth lumbar). Straight-leg raising is not significantly reduced. Myelography with standard oil-based contrast media is usually negative. Clinically, it is often difficult to distinguish between lateral recess stenosis and disc herniation, and in fact the two conditions may coexist. However, pure lateral recess stenosis usually meets only two of the criteria for disc herniation.

Non-organic back pain—Pain in the back or leg may have minimal or no physical basis, but rather may represent a manifestation of tension (muscle spasm) or a conversion reaction. Symptoms are described in an atypical fashion. Examination reveals few physical changes, apart from tense muscles or numbness and weakness of the entire leg representing a conversion reaction.

On occasion, the prospect of compensation or of damages may focus the patient's attention on the commercial value of the illness. Such patients may demonstrate "physical" findings representing magnification behaviour, but the total clinical picture is characterised by minimal or no evidence of a structural disorder.

Patients with non-organic back pain were included in this series because of what was thought to be evidence of organic disease in association with their psychogenic reaction. This evidence was in the form of persistent root tension (as demonstrated on Pentothal pain study), a tendency for the numbness or weakness in the leg to be more pronounced in a radicular pattern, alteration in a reflex reaction and myelographic changes that were considered to be positive.

CLINICAL MATERIAL AND METHODS

Selection of patients—Patients were selected from the author's practice and were personally examined, treated and followed up. Basic requirements were 1) a history of symptoms for not less than three months and 2) a trial of conservative treatment (bed rest, anti-inflammatory medication) for not less than two weeks, with no improvement in leg pain or straight-leg raising; or 3) a course of ambulatory treatment, including bracing, anti-inflammatory medication and appropriate physiotherapy, for not less than three months.

The following patients were not selected: those allergic to papaya or meat tenderiser; those who had had a previous chemonucleolysis; those with neurological

affection of bladder or bowel function; patients with spinal cord tumours first evident on myelography; and pregnant women.

It is suggested in the product information that patients with a significant neurological deficit should not undergo chemonucleolysis. Nevertheless if the clinical picture was one of a disc herniation as the cause of the significant neurological deficit (exclusive of bladder or bowel involvement), the patient underwent chemonucleolysis as a method of decompressing an already damaged nerve root without the manipulation that occurs with surgical intervention.

Investigations of each patient included a standard history and physical examination, routine lumbo-sacral radiographs and appropriate laboratory studies to rule out arthritis, infection and tumour. With few exceptions, myelography preceded chemonucleolysis to verify the level and extent of disc herniation and to exclude spinal cord tumours. Myelography was not used as a method of diagnosis. Electromyography and psychological testing were not carried out as a routine. Discography was carried out on all patients at the time of chemonucleolysis.

TECHNIQUE

Chemonucleolysis is carried out in the operation theatre under local anaesthesia, image-intensifier control and with an intravenous needle in position. Although some investigators guard against anaphylaxis by routinely using general anaesthesia with endotracheal intubation, the author feels that this is unwise. Anaphylaxis is best treated at its onset, with neither its symptoms masked nor its management complicated by general anaesthesia. Further, the use of local anaesthesia allows the patient to respond during discography and facilitates the approach to the lumbo-sacral disc space without damage to the fifth lumbar nerve root.

A right postero-lateral approach to the involved disc space or spaces is facilitated by a portable C-arm image intensifier that permits antero-posterior and lateral radiography.

The L4-5 disc space is approached first from a site adjacent to the iliac crest and 10 centimetres from the midline. After the area has been anaesthetised with 1 per cent xylocaine, a 15-centimetre number 18 needle is advanced toward the disc space at a 50-60-degree angle. When the tip of the advancing needle reaches a line joining the posterior aspects of the vertebral bodies, as shown on a lateral radiograph (Fig. 1), the surgeon should obtain the gritty feel of the annulus. When the annulus is encountered, the needle is advanced into the centre of the disc and the position is verified with an antero-posterior radiograph. The tip of the needle should be in line with the spinous process and medial to the most medial aspect of the pedicle.

The lumbo-sacral disc space is approached from a site slightly cephalad and medial to that for the L4-5

disc space. Under similar local anaesthesia, a 10-centimetre number 18 needle is advanced to the posterior edge of the L5-S1 disc space. A 15-centimetre number 22 needle is then passed through the lumen of the 10-centimetre number 18 needle. The last 2 centimetres of the number 22 needle are bent, so that when it emerges from the end of the 10-centimetre needle, it curves towards the L5-S1 disc space. The number 22 needle is then advanced into the L5-S1 disc space in a similar fashion, and under similar control, as for the L4-5 disc space.

Fig. 1.

Lateral radiograph with line joining posterior vertebral borders showing location of needle tip when annulus is first encountered.

The major obstacles to proper placement of the needle are the nerve roots anteriorly and the vertebral elements posteriorly. Contact with a nerve root under local anaesthesia is very painful and indicates that the needle tip has been advanced too far anteriorly. Partial withdrawal and angulation from the horizontal closer to 60 degrees will eliminate this problem. Similarly, bony impingement signifies that the needle tip has been advanced too far posteriorly, and partial withdrawal and angulation from the horizontal closer to 45 degrees will eliminate this problem.

Discography is then carried out, using water-based contrast media such as Conray^R-60. Discography is

used to verify the position of the needle tip and to support the clinical impression.

To reduce the possibility of inactivation by a high concentration of radio-opaque contrast medium, fifteen minutes are allowed to elapse before chymopapain is injected. One to two millilitres or 2,000 to 4,000 units of chymopapain are injected into each disc space to a maximum of 5 millilitres or 10,000 units for each patient for multiple level injections. After injection and removal of the needles, the patient is turned to the supine position and observed for any adverse reactions. Since the procedure has been carried out under a local anaesthetic, the patient can signal any abnormal sensations which may mark the beginning of an anaphylactic reaction. These abnormal sensations include nausea, itchiness or tingling of the skin, a feeling of faintness and a constriction in breathing.

Anaphylaxis is treated by intravenous injection of 0.5 millilitre of 1 : 1,000 adrenaline. Further injections of 0.05 to 0.1 millilitre are given according to the blood pressure response. One gram of hydrocortisone is also given intravenously. A large replacement of circulating fluid is important, provided that the patient's heart and kidneys can tolerate the increased load.

POST-OPERATIVE CARE

In the hours immediately after injection, the patients usually have back pain and require analgesics. Relief of sciatica is usually apparent immediately: the patient will then describe new and less severe leg symptoms such as numbness, aching or cramping in the calf.

Within twelve to forty-eight hours of the injection, or when the back pain becomes tolerable, the patient is allowed up, with the support of a corset. Most patients leave hospital one or two days after injection.

Patients with jobs involving light duties are allowed back to work one to six weeks after injection, while those doing heavier work are allowed back to work after about three months.

For the purpose of this study, follow-up (including radiographic examination) was carried out at one, three and six months, and yearly thereafter. Occasionally, because of distance, a patient was followed yearly by an orthopaedic surgeon or neurosurgeon in his district, as well as by telephone calls by the author.

RESULTS

Four hundred and eighty patients* have undergone chemonucleolysis by the author during the past five years. The shortest follow-up was six months, the longest five years, and the mean eighteen months. There were 148 women and 332 men, with a mean age of 42.1 years. Two patients were lost to follow-up at six months and one year when they returned to their home countries.

Both showed excellent results when they left and are included in this report. The results were graded simply as success or failure (Table I).

The results are listed in Table II. Patients were divided into four groups: 1) those who had had previous spinal operations; 2) those with spinal stenosis; 3) those with psychogenic components to their pain; and 4) those with uncomplicated organic spinal pain. This last group of patients comprised the bulk of the study and included all patients with back pain of an organic nature, with or without radicular involvement.

Previous operation—Patients who had undergone operation previously did not do well after chemonucleolysis. Especially poor results were obtained in those patients whose symptoms had not been altered by operation. Chemonucleolysis was successful in patients who had previously undergone operation only when a successful result after operation many years previously had been followed by the sudden onset of sciatica caused by disc herniation at the same or another level.

Spinal stenosis—Chymopapain had little effect on patients with spinal stenosis uncomplicated by a disc herniation. The eight patients who did obtain a successful result had all had a sudden change in their symptoms associated with a unilateral increase in leg pain, significant limitation of straight-leg raising and focal neurological changes of a single nerve-root distribution. Most of the eight have some residual back or leg discomfort and are considered only good results.

Psychogenic pain—Owing to the author's initial lack of experience with chymopapain, a number of patients in this category were considered for chemonucleolysis. However, in spite of objective neurological changes and myelographic defects, such patients did not do well after chemonucleolysis.

Uncomplicated organic spinal pain—These patients were divided into two groups (Table III) according to the definitions outlined above.

One hundred and fifty-eight patients (70 per cent) with disc herniation obtained a successful result and sixty-seven (30 per cent) achieved a poor result. Within this group of 225 patients the result was not affected by the duration of pain, the age or sex of the patient, or the degree of degeneration of the disc before operation.

TABLE I
CRITERIA FOR ASSESSMENT OF RESULTS

Success	{	1 Completely free from all back and leg pain
		2 Minor, intermittent discomfort that did not interfere with normal activities
Failure	{	1 Improvement in symptoms, but persisting back-ache or sciatica that interfered with capacity to engage in full normal activity
		2 No change in symptoms

* See footnote to Table II.

As with most reported series, patients with the prospect of compensation for low-back pain did poorly compared with the rest of the group (Table IV), in spite of obvious clinical evidence of a disc herniation.

An important prognostic sign after chemonucleolysis was narrowing of the disc space. This occurred within the first week, was at its maximum within one month and did not change in either direction during the ensuing months (Table V). Those patients who lost their sciatica, went on to full straight-leg raising and developed disc-space narrowing, almost always achieved a successful result.

The number of disc spaces injected did not affect the outcome (Table VI).

FAILURES

The manifestations of failure in the forty-six patients from the select group (Table IV) are listed in Table VII.

The most common indication of failure was persisting back pain. Of six patients who subsequently underwent operative fusion for this problem, two obtained

relief of their back pain and four failed to do so. Fourteen patients were relieved of their sciatica, but had residual backache that produced functional limitations, although these were not severe enough to warrant consideration of operation.

In twelve patients a sequestered disc was the cause of failure; all went on to a successful result after operation. Six patients had lateral recess stenosis: four of these went on to a good result after operation, but the remaining two were only slightly improved. It is to be noted that these six patients fulfilled the criteria for disc herniation, yet the cause of continuing pain was lateral recess stenosis.

At operation after chemonucleolysis, little nuclear material was found within the disc space. The material that was obtained was not pathologically distinguishable from disc material removed from a disc space that had not received chymopapain. No changes were noted in the dura or nerve roots.

Five patients had either a sequestered disc or lateral recess stenosis as the suspected cause of failure, but have not accepted operation. One patient has a discitis as the

TABLE II
RESULTS

	Success		Failure		Total
	Number of patients	Percentage	Number of patients	Percentage	Number of patients
Previous operation	10	28	26	72	36
Spinal stenosis	8	31	18	69	26
Psychogenic pain component	12	11	97	89	109
Uncomplicated organic spinal pain	186	57	141	43	327
					498

(The total of 498 patients is produced by overlap between the first three groups.)

TABLE III
RESULTS IN UNCOMPLICATED SPINAL PAIN

	Success		Failure	
	Number of patients	Percentage	Number of patients	Percentage
Disc herniation	158	70	67	30
Disc degeneration and other clinical conditions	28	27	74	73

TABLE IV
RESULTS IN PATIENTS EXPECTING COMPENSATION COMPARED WITH OTHERS

	Success		Failure	
	Number of patients	Percentage	Number of patients	Percentage
Patients with compensation or other claims	28	57	21	43
Unencumbered patients (selected)	130	74	46	26

cause of continuing minor back pain. One patient was relieved of his sciatica, showed good disc-space narrowing and achieved full straight-leg raising, only to develop a conversion hysterical reaction.

Patients who did not fulfil the clinical definition of disc herniation did not do well following chemonucleolysis (Table III). Only twenty-eight (27 per cent) of these

NEUROLOGICAL RECOVERY

Of the 225 patients fulfilling the criteria for disc herniation, 178 had two or more neurological changes. Of these, seventy-one obtained full or significant neurological recovery. Occasionally, neurological recovery occurred on the day of injection. However, it was usual for it to

TABLE V
DISC-SPACE NARROWING RELATED TO RESULT

	Success		Failure	
	Number of patients	Percentage	Number of patients	Percentage
Narrowing . . .	111	78	31	22
No narrowing . .	47	57	36	43

TABLE VI
RESULT RELATED TO NUMBER OF SPACES INJECTED

	Success		Failure	
	Number of patients	Percentage	Number of patients	Percentage
One space	105	71	43	29
Two or more spaces	53	69	24	31

TABLE VII
MANIFESTATIONS OF FAILURE IN FORTY-SIX SELECTED PATIENTS

	Number of patients	Result of operation	
		Success	Failure
Persistent back pain . . .	21	2	4
Sequestered disc	12	12	0
Lateral recess stenosis . .	6	4	2
Suspected sequestered disc .	3	0	0
Suspected lateral stenosis .	2	0	0
Discitis	1	0	0
Conversion reaction . . .	1	0	0

patients obtained a good result and almost all of these had a component of leg pain to their disability, but did not have enough clinical characteristics for a diagnosis of disc herniation. Patients with back pain as their only complaint accounted for most of the seventy-four (73 per cent) failures. Again, age, sex, duration of symptoms and degenerative disc disease had no effect on the result. Similarly, those with compensation or other claims did poorly. Again, narrowing of the disc space after injection was usually associated with a good result, in that most of the patients in this group with disc-space narrowing were among the twenty-eight successful patients.

take weeks or months, with no pattern to the sequence of motor, sensory and reflex return. Muscle wasting usually took many months to recover. There was a tendency for neurological recovery to occur more often in younger patients and those with a shorter duration of sciatica, but this was not statistically significant.

COMPLICATIONS

One patient had an immediate anaphylactic reaction, with profound cardiovascular collapse within minutes of the injection. He was successfully resuscitated without

intubation, by injection of adrenaline, hydrocortisone and 4 litres of intravenous fluid.

Three patients manifested a delayed reaction in the form of a skin rash. This responded to treatment with anti-histamines. One patient had continuous mild back pain because of a non-pyogenic discitis. Since the procedures were done under local anaesthesia, no nerve roots were penetrated and thus there was no foot drop after injection. Occasionally, a patient developed pain in the opposite leg after injection, but this always subsided and did not account for any failures. One patient was found at later operation to have arachnoiditis about the cauda equina. In this case myelography had been very difficult; blood was aspirated during the examination and some of the contrast medium could not be removed. Initially, the patient obtained relief from his sciatica but, over two years, went on to increasing back pain, without evidence of root tension or irritation. At operation the cauda equina from L.3 to sacrum was involved with light adhesions. The dura and nerve-root sheaths had a normal appearance and this was verified by histological examination. The author feels that this complication represents the known risk of difficult myelography (Macnab *et al.* 1971) and does not represent an arachnoiditis caused by chymopapain.

RECURRENCE AND SYMPTOMS

Recurrent disc herniations causing sciatica did not occur in any patient who obtained relief of sciatica, regained full straight-leg raising and achieved disc-space narrowing. One patient had relief of symptoms for three years, but persistent limitation of straight-leg raising. She has recently had a sequestered disc removed after recurrence of sciatica. A number of other patients had persistent limitation of straight-leg raising, some with disc-space narrowing and some without. The author expects recurrent symptoms in some of these patients.

DISCUSSION

The concept of chemical dissolution of the intervertebral disc has many implications. The removal of offending disc material with a simple injection under local anaesthesia, without significant risk to the patient, and without a long hospital stay, is an important step forward in the management of low-back pain.

The mechanism of action of chymopapain is not clearly understood. Animal experiments (Macnab *et al.* 1971) have shown the dissolution effect on nuclear material of the intervertebral disc. The effect of chymopapain on human intervertebral disc material can readily be demonstrated by placing excised disc material in 2 millilitres of chymopapain. There is an instant appearance of milky fluid representing the dissolved chondromucoprotein. The remaining material represents the collagenous portion of the nucleus. This effect is often noticed clinically immediately following disc injection

with chymopapain when a milky fluid flows back into the syringe. A further clinical example of the effect of chymopapain is the instant relief of leg pain that often follows injection (Macnab *et al.* 1971).

Initially, the technique of postero-lateral approach to the disc space is difficult; however, with persistence it can be mastered (McCulloch 1977). The use of local anaesthesia does not increase the difficulty of doing the procedure. Chymopapain should be used as one would pursue surgical exploration in disc disease—that is, single disc herniations are more common than multiple herniations, therefore, single disc-space injections with chymopapain should be more common than multiple disc-space injections. The author purposely did multiple disc injections when there was any suggestion of disc degeneration at other than the clinically symptomatic level and noticed no beneficial result (Table VI). Similarly, the proposal for the use of prophylactic chymopapain has no scientific merit.

The leakage of contrast medium at the time of discography is not a contra-indication to chemonucleolysis. The phenomenon is very common and the site of the leak aids in placing chymopapain in contact with the extruded disc fragment. The safety of this has been adequately demonstrated in the laboratory (Macnab *et al.* 1971) and verified many times in this series.

The frequency of complications is low. Anaphylaxis occurred once in 480 patients (0.2 per cent). The occurrence of discitis in one patient is of concern. There has been no evidence to suggest that it was caused by a pyogenic infection, but it is causing continuing back pain in the patient in question.

Chymopapain will relieve symptoms in 70 per cent of patients with disc herniation causing sciatica (Table III). It is important to stress that only this type of patient will respond well to chemonucleolysis. Theoretically, chymopapain should not affect a sequestered disc which is predominantly collagen fibre. There are patients with sciatica who have significant neurological changes in an extremity, absence of back pain and large defects on myelography, suggesting a sequestered disc. A number of these patients obtained a successful result after chemonucleolysis. The author does not feel that the clinical suspicion of a sequestered disc is a contra-indication to chemonucleolysis.

Patients with symptoms persistent after operation and those with uncomplicated spinal stenosis will not respond well to chemonucleolysis, unless symptoms are due to a second protrusion or to disc herniation (Table II).

Patients with segmental instability and pain chiefly situated in the back as a result of disc degeneration do not do well after chemonucleolysis (Table III).

The role of non-organic reactions in low-back pain has always been difficult to understand. Despite obvious evidence of disc herniation, patients who expected compensation did not respond to chemonucleolysis as well as unencumbered patients (Table IV). Still, if the clinical

criteria for disc herniation were present, a reasonable result could be anticipated. However, the presence of any tension or conversion reaction historically or physically and the absence of obvious evidence of disc herniation, almost certainly precluded a good result (Table II).

Three patients with spondylolisthesis and a herniated L.4-5 disc underwent chemonucleolysis. All three had relief of sciatica, but two have persisting back pain. Chemonucleolysis in spondylolisthesis is probably not the treatment of choice, because of the skeletal instability.

The most important prognostic sign after chemonucleolysis is narrowing of the disc space. It is a useful guide to deciding whether treatment has failed. In two patients there was a significant increase in sciatica immediately after injection, and at operation three days later large sequestered discs were removed. In the series reported previously (Macnab *et al.* 1971) there was a tendency to operate early when sciatica was not instantly relieved. The author now recommends that, in the face of an apparent failure, operation should be delayed approximately six weeks. Narrowing of the disc space or improvement in straight-leg raising during that time are indications for further delay.

Operation for lateral recess stenosis or a sequestered disc is not made more difficult by chemonucleolysis. So little material is found in the disc space that it is recommended that only the sequestered fragment be removed, or that foraminal decompression be done without

curettage of the disc space with its attendant annular incision and additional nerve-root retraction.

On occasion, mild contra-lateral leg pain occurs soon after chemonucleolysis. In other series, in some patients injected under general anaesthesia, pain in the opposite leg was caused by penetration of the fifth lumbar root. In this series, this phenomenon was thought to be due to slight annular bulging during narrowing of the disc space. However, contra-lateral leg pain did not persist. Thus, the early occurrence of this phenomenon is not likely to be caused by movement of facet joints or pedicular kinking.

The ultimate role of chymopapain has not been established. It is clear to the author that the procedure is technically safe. Successful chemonucleolysis shortens the patient's stay in hospital and precludes the complications of a general anaesthetic and open operation.

There has been some criticism that the regime of conservative treatment outlined above is not adequate and that good results could be achieved simply by prolonging the period of complete bed rest. The author agrees, but feels that those patients who do not do well with the conservative treatment programme as outlined tend to follow one of two courses: failure to respond, or a prolonged course with recurrent episodes of sciatica. Successful chemonucleolysis in this group facilitates early resolution of symptoms. The real danger in this approach is the potential for indiscriminate use by elimination of all conservative treatment.

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