

# VALUE OF INTRA-ARTICULAR INJECTIONS IN OSTEO-ARTHRITIS

## A CONTROLLED SERIES

BY

M. H. L. DESMARAIS

*From the Rheumatism Research Unit, Royal National Hospital for Rheumatic Diseases, Bath*

(RECEIVED FOR PUBLICATION OCTOBER 10, 1952)

In view of the controversial reports on the value of intra-articular injections in the treatment of osteo-arthritis conditions it was decided to carry out a clinical experiment under strict control to investigate this problem.

For that purpose groups of cases suffering from osteo-arthritis of the hip and knee were treated by intra-articular injections using different types of solutions at different pHs, and the results obtained were compared with those in a control group.

Waugh (1938) was the first to treat arthritic joints by the intra-articular injection of a stable solution of procaine lactic acid at pH 5.0. He based this treatment on previous observations that synovial fluid of arthritic joints was consistently alkaline, and on the observations of Starling (1932) that the hydrogen ion concentration in a haematoma around a fracture was strongly acid in reaction. This acid shift was a physiological mechanism for the solution of bone calcium and for tissue regeneration. Waugh (1936) suggested that the acidity possibly acted as a stimulus to polymorphonuclear leucocytosis and later to local mesoblastic proliferation. This assumption was also based on his work on the pH values of purulent discharges in cases of osteomyelitis and compound fractures. He found that the normal pH of synovial fluid of joints was around 7.4. Twenty-four hours after an injury the pH became acid, and it returned to normal or slightly to the alkaline side of neutrality within 7 days. He assumed that the acid, identified as sarcolactic acid, was derived from local cell tissue damage and degeneration. On the above observations he stipulated that the joint acidity was a physiological response to trauma designed to excite local leucocytosis and repair. Procaine lactic acid intra-articular injections were therefore used in an endeavour to imitate this physiological reaction.

Nicholson (1948) strongly criticized these views on the ground that Waugh's experimental observations were limited in number and that the methods

used for estimating the pH values were crude. Estimation of the pH of body fluid could only be measured accurately *in vivo*.

Coste and Morin (1939) tried different solutions in the treatment of 24 cases of osteo-arthritis of the hip joint and reported equivocal results with a concentrated solution of procaine. Various other solutions have also been tried: Fletcher (1943) reported very good results with lipiodol and gomenol injections. Of twenty cases thus treated thirteen (65 per cent.) became symptom-free and maintained the improvement at the end of 3 years; two other cases were also improved.

Crowe (1944), using a 1 per cent. solution of acid potassium phosphate, treated 284 painful and swollen rheumatic joints and reported recovery of full function and complete disappearance of pain in 68 cases (24 per cent.). In 102 cases (36 per cent.) deformity and swelling were reduced and range of movement increased. In 114 cases (40 per cent.) only temporary subjective alleviation of symptoms was experienced. The best results were obtained in quiescent cases with a normal E.S.R. Usually one injection sufficed to produce the improvement.

Baker and Chayen (1948), in an attempt to compare the effects of procaine lactic acid solution and a neutral solution of procaine in isotonic saline, obtained equally satisfactory results with both solutions. They attributed the benefit to the psychological effect of the prompt relief of pain by the procaine in conjunction with the lubricating action of the fluid injected. There was a tendency to recurrence of symptoms a fortnight after the injection. R. Kron (1948) reported encouraging results with an isotonic solution of sodium bicarbonate.

Lawther (1949), using solutions of procaine lactic acid and 2 per cent. procaine hydrochloride in the treatment of degenerative disease of the hip, reported equally satisfactory results in both series. The relief of pain was more marked than the increase in range of movement.

Waugh (1945) reported his further experience of the treatment of over 1,200 cases of different types of arthritic joints by the intra-articular injection of procaine lactic acid. Though he gave no statistical analysis of his results, he estimated that 70 per cent. of cases were rendered free from pain with sufficient restoration of function to allow them to return to their normal occupation.

Mawson (1946) and Heald and Martin (1947) also reported encouraging results in cases of mixed arthritis treated by the Waugh method.

The majority of reports in the literature have been concerned with the effects of intra-articular injections of the hip joints; in this joint, for anatomical reasons, it is not easy to be certain that the injection is truly intra-articular.

Dobson (1948), checking the anatomical accuracy of intra-articular injections of the hip in cadavers, used a solution of carmine in glycerine and found at dissection that 65 per cent. of the injections were successful. In a second series she obtained a 67 per cent. success and recommended the anterior approach as giving slightly better results (Dobson, 1952).

Many theories have been put forward in an attempt to explain the reported relief of symptoms following various intra-articular injections. Tarsy (1938) suggested that the effects of procaine lactic acid were due to the anaesthetic and analgesic properties of the procaine, which acts by interrupting the vicious circle of pain, spasm and congestion. Waugh (1938), on entirely empirical evidence, concluded that the swing of the alkaline pH of the joint to the acid side stimulated local leucocytosis and repair by mesoblastic proliferation.

Sacks (1949) attempted to explain the mechanism of relief of symptoms on physical and biochemical grounds. In articular cartilage, chondroitin sulphate is combined with protein to form a glyco-protein. Chondroitin sulphate can be extracted from this protein linkage by dilute alkali, the molecule being easily depolymerized or broken down. The molecule is therefore extremely sensitive to the pH of the surrounding fluid, and it is this factor which is of fundamental importance in cartilage physiology. Since all acid substances would tend to reduce depolymerization of chondroitin sulphate in the cartilage matrix, the relative value of acid substances alone or in combination with procaine becomes obvious.

The origin of joint pain has for long been a controversial subject. The anatomy of the innervation of the knee and hip joint has been well demonstrated by Gardner (1948). This knowledge was applied by Fell (1952) to show on human volunteers that localized referred pain from the hip

corresponded to the anatomical pattern of the innervations of the joint capsule. On the assumption that pain in arthritic joints arises largely from fibrosis of the capsule, the regions corresponding to the localized referred pain were injected with procaine, with good results but temporary relief. Kellgren (1950), investigating the pain pattern of the knee joint, found that the fibrous capsule and its ligaments played an important role in articular sensation and appeared to be the major source of joint pain. The synovial membrane was poorly supplied with pain end-organs but was rich in autonomic nerve fibres.

#### Methods

In an attempt to find an answer to some of the problems referred to above, especially the part played by the pH of the solutions injected into joints of cases suffering from osteo-arthritis of the hip or knee, joints were allocated to four different treatment groups by random sampling. The joints were treated with solutions of

- (i) lactic acid at a pH of approximately 5.4,
- (ii) 2 per cent. alkaline procaine at a pH of 7.4,
- (iii) normal saline buffered to a pH of 7.2.

In addition a control group was included in which the joints were penetrated by the needle but no fluid injected. All cases received physiotherapy as indicated. The course of treatment consisted of a total of six injections each of 10 ml. given twice-weekly for 3 weeks. In the case of the hip the anterior approach was invariably used; for the knee joint the antero-lateral approach either below or above the patella was commonly chosen. When either of these latter was technically difficult the medial mid-patella route was used. None of these techniques was found to be unduly difficult or unpleasant to the patient.

The clinical condition of the joint was assessed before each injection, at the end of treatment, and 3 months and 6 months after completion of treatment.

The main criteria used in the assessments were the change in the degree of pain as reported by the patient and the change in range of movement of the joint. Swelling, tenderness, and any improvement of function were also noted.

The clinical change in pain and movement after treatment was recorded as "no change", "slight improvement", or "marked improvement". An increase in range of movement of 10-20° was considered as "slight improvement", and an increase in range of 20° or above as "marked improvement". As the range of movement in the majority of the knees at the onset of treatment was full, only the change in mobility which occurred in the hips could be analysed. All assessments were made by the same observer using the same criteria of improvement throughout.

In cases with small effusion, only sufficient fluid required for laboratory examination was aspirated. In a few cases with a large effusion the pH of the fluid was examined before injecting 10 ml. lactic acid, and then again at 2-, 4-, and 10-minute intervals, and in some

cases again at the end of 3 and 7 days. All pH estimations were carried out almost immediately after aspiration in a room adjoining the theatre. The pH values in the last four cases were examined at first by the Comparator method, but they were estimated by a pH meter.

In the present series the effects of intra-articular injections were studied in 189 osteo-arthritic joints (108 hips and 81 knees).

**Results**

**Pain.**—There was a tendency to improvement as judged by pain during the period of treatment in all groups, including the controls. At completion of treatment there was little difference in the number of improved in each group. After 3 months the knees treated with lactic acid or procaine, and the hips treated with procaine showed slightly better results than the other groups (Table I). The fact

that the procaine-treated hips progressed better than those injected with lactic acid might be explained by the procaine having had a direct analgesic effect on the capsule through part of the injection being extra-articular.

On statistical evaluation, however, using the four-fold  $\chi^2$  test, it becomes obvious that the above impressions of the effect of intra-articular injections on pain may have been due to chance and are not proven (Table I).

**Movement.**—On examining the effect of treatment on movement, there appeared to be some increase in range in the groups injected with lactic acid, procaine, or saline as compared with the controls. In other words the use of any fluid may sometimes assist in the promotion of movement in the hip (Table II).

TABLE I  
CHANGE IN DEGREE OF PAIN IN KNEES AND HIPS

Joints	Treatment	No. of Joints Treated	Change in Degree of Pain										p Value 3 Months after Treatment
			After 3 Injections			After 6 Injections			3 months after Treatment			6 months after treatment Improvement Maintained	
			No change	Slight Improvement	Marked Improvement	No Change	Slight Improvement	Marked Improvement	No Change	Slight Improvement	Marked Improvement		
HIPS	Lactic Acid	28	22	6	0	14	12	2	18	8	2	5	0.90 > p > 0.80
	Alkaline Procaine	29	21	7	1	12	13	4	13	13	3	13	0.30 > p > 0.20
	Saline	25	20	4	1	12	12	1	18	7	0	6	0.50 > p > 0.30
	Needle Prick	26	17	9	0	10	14	2	17	8	1	8	—
KNEES	Lactic Acid	23	15	8	0	8	12	3	8	11	4	11	0.50 > p > 0.30
	Alkaline Procaine	19	17	2	0	7	9	3	6	9	4	13	0.70 > p > 0.50
	Saline	21	17	4	0	12	7	2	13	6	2	7	0.50 > p > 0.30
	Needle Prick	18	12	5	1	7	7	4	10	6	2	5	—

TABLE II  
CHANGES IN RANGE OF MOVEMENT OF HIPS

Treatment	No. of Joints Treated	Change in Range of Movement (hips only)								
		After 3 Injections			After 6 Injections			3 Months after Treatment		
		No Change	Slight Increase	Marked Increase	No Change	Slight Increase	Marked Increase	No Change	Slight Increase	Marked Increase
Lactic Acid .. ..	26	22	4	0	18	7	1	20	6	0
Alkaline Procaine ..	27	24	3	0	17	10	0	19	7	1
Saline .. .. .	24	20	4	0	17	6	1	18	5	1
Needle Prick .. ..	25	24	1	0	21	3	1	20	4	1

TABLE III  
pH VALUES OF SYNOVIAL FLUID OF KNEE JOINTS BEFORE AND AFTER 10 ml.  
LACTIC ACID INJECTED INTRA-ARTICULARLY

Diagnosis	Case No.	pH Values					
		Before Injection	2 Minutes After	4 Minutes After	10 Minutes After	3 Days After	7 Days After
Osteo-arthritis	79	7·6	7·5	7·4	—	7·6	—
Osteo-arthritis	66	7·5	—	7·5	—	7·5	7·5
Osteo-arthritis	95	7·4	7·4	6·8	—	—	—
Osteo-arthritis	77	7·6	7·4	7·4	—	—	—
Osteo-arthritis	62	—	—	—	—	7·5	—
Osteo-arthritis	147	7·5	—	—	—	7·5	—
Osteo-arthritis	87	7·5	—	—	—	—	—
Osteo-arthritis	164	*7·35	*7·45	*7·48	*7·50	—	—
Osteo-arthritis	180	*7·46	*7·34	*7·23	*7·30	—	*7·40
Osteo-arthritis	181	*7·35	*7·30	*7·28	*7·28	—	*7·35
Osteo-arthritis	182	*7·30	*7·25	*7·45	*7·30	—	*7·30
Rheumatoid Arthritis	88	7·40	—	—	—	—	—
Rheumatoid Arthritis	166	—	—	—	—	7·4	—
Rheumatoid Arthritis	95	7·40	—	—	—	7·40	7·40

\* pH values estimated directly by a pH meter.

**Effusion.**—The degree of effusion was measured in thirty knee joints, before and 3 months after treatment. The injections appeared to have no appreciable effect when compared with the control group.

#### Discussion

The improvement in pain obtained in all groups, including the control group, immediately after treatment suggests the psychological effect on the patient of a new treatment. It seems that the use of intra-articular injections of lactic acid in the treatment of osteo-arthritis of the hip and knee is of less value than that of alkaline procaine. Any beneficial effects of alkaline procaine cannot be ascribed to the alkalinity of the solution, as a saline solution of approximately the same pH failed to produce any sustained improvement. The anaesthetic property of the drug is likely to be the mechanism whereby the pain is relieved.

The average pH value of the synovial fluid of the knees in ten cases before treatment was 7·45 (range 7·30 to 7·60) (Table III). Two minutes after an injection of 10 ml. lactic acid solution there was a very slight fall in the pH value of the fluids in all but two cases, the average being then 7·27. A slight fall in the pH was also noted after 4 and 10 minutes. The values after 3 and 7 days respectively were all normal.

In two cases, the effects of adding the solutions of lactic acid to synovial fluid *in vitro* in the dilution of 1 in 4 and 1 in 2 had no effect in changing the

original pH value of the fluid. In each case the pH remained constant at 7·40.

The pH values obtained in cases of osteo-arthritis of the knee were all within the normal range and did not agree with the high values of 8·0 and 8·8 reported by Waugh (1938). The small changes in the pH values after the injection of 10 ml. lactic acid was not significant and was well within the range of experimental error. It is well appreciated that the *in vitro* methods used do not reflect the true *in vivo* pH values, but the strong buffer action of synovial fluid has been demonstrated by the failure of the lactic acid added to synovial fluid to alter the pH value in two cases at the low dilutions of 1 in 4 and 1 in 2. Synovial fluid, by virtue of its chemical composition and physical state, is a strong buffer, and it is not surprising that the injection of such a weak acid as lactic acid should fail to alter the pH of the joint fluid to any appreciable extent.

In conclusion it is considered that intra-articular injections in the treatment of osteo-arthritis are of very limited value and should be reserved for cases who have failed to respond to other forms of treatment. In such cases a simple local anaesthetic is probably the solution of choice.

#### Summary

A series of 189 osteo-arthritic joints was injected with alkaline procaine, lactic acid, or saline, or needled without injection.

Some cases in each group improved, but the

differences between those receiving lactic acid or procaine, and those used as controls were not statistically significant. There was a suggestion that in some cases procaine relieved pain, especially in the hip, and that the injection of any fluid might increase the range of hip movement.

The pH of the joint fluid was normal before treatment in ten cases, and no large or lasting change in pH followed the injection of lactic acid.

I wish to thank Dr. G. D. Kersley for suggesting this work and for his helpful criticism and assistance. Dr. Bradford Hill co-operated in organizing the statistical planning of the experiment. My thanks are also due to Mr. J. Bastow for supplying many of the cases and to Messrs. Brady and Martin Ltd. of Newcastle-upon-Tyne for their trouble in preparing the special alkaline procaine solution used in this trial.

This work was done during the tenure of a Nuffield Research Scholarship in Chronic Rheumatic Diseases.

REFERENCES

Baker, D. M., and Chayen, M. S. (1948). *Lancet*, 1, 93.  
 Coste, F., and Morin, H. (1939). *Bull. Soc. med. Hôp., Paris*, 55, 1009.  
 Crowe, H. W. (1944). *Lancet*, 1, 563.  
 Dobson, M. (1948). *Annals of the Rheumatic Diseases*, 7, 172.  
 — (1950). *Ibid.*, 9, 237.  
 Fell, W. A. (1952). International Congress of Physical Medicine 1952. (*Annals of the Rheumatic Diseases*, 11, 232.)  
 Fletcher, E. (1943). *Post. Grad. med. J.*, 19, 193.  
 Gardner, E. (1948). *Anat. Rec.*, 101, 109.  
 — (1948). *Ibid.*, 101, 353.  
 Heald, C. B., and Martin, A. J. (1947). *Lancet*, 2, 110.  
 Kellgren, J. H., and Samuel, E. P. (1950). *J. Bone Jt Surg.*, 32B, 84.  
 Kron, R. (1948). *Schweiz. med. Wschr.*, 78, 80.  
 Lawther, K. (1949). *Annals of the Rheumatic Diseases*, 8, 178.  
 Mawson, R. (1946). *Brit. med. J.*, 2, 691.  
 Nicholson, D. P. (1948). *Annals of the Rheumatic Diseases*, 7, 28.  
 Sacks, S. (1949). *S. Afr. med. J.*, 23, 475.  
 Stirling, R. I. (1932). *Trans. med.-chir. Soc. Edin.*, N.S. 46, 203.

Tarsy, J. M. (1938). *Med. Rec.*, 148, 269.  
 Waugh, W. G. (1936). *Lancet*, 2, 976.  
 — (1938). *Ibid.*, 1, 487.  
 — (1945). *Brit. med. J.*, 1, 873.

Valeur des injections intra-articulaires dans l'ostéoartrite. Série contrôlée.

RÉSUMÉ

On a injecté dans 189 articulations ostéoarthritiques de la procaine alcaline, de l'acide lactique, du sérum physiologique, et on a fait des piqûres sans rien injecter.

Il y a eu quelques améliorations dans chaque groupe, mais les différences entre ceux qui avaient reçu de l'acide lactique ou de la procaine et les témoins furent insignifiantes du point de vue statistique. On est porté à croire que dans quelques cas la procaine aurait procuré un allègement de la douleur, surtout à l'articulation sacro-iliaque, et que l'injection d'un liquide quelconque tendrait à augmenter l'étendue du mouvement de cette articulation.

Le pH du liquide synovial, normal dans dix cas avant le traitement, ne subit pas de modification appréciable ni durable après l'injection d'acide lactique.

Valor de inyecciones intra-articulares en la osteoartritis. Series controladas.

SUMARIO

En 189 articulaciones se inyectó procaina alcalina, ácido láctico y suero fisiológico, y se introdujo agujas sin inyectar.

Hubo algunas mejoras en cada grupo, pero las diferencias entre los que recibieron ácido láctico o procaina y los testigos no tuvieron significancia estadística. Hubo indicaciones de que en ciertos casos la procaina aliviara el dolor, especialmente en la cadera, y que una inyección de cualquier líquido pudiera aumentar la extensión del movimiento en la articulación de la cadera.

El pH del líquido sinovial, normal antes del tratamiento en diez casos, no sufrió alteración apreciable o durable después de la inyección de ácido láctico.