Prolotherapy for Podiatrists - part 2
Basic Premise, History, Agents and Techniques

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Introduction
In the first part of this article we examined the mechanisms of injury and normal physiological repair in Dense Connective Tissue (DCT). The common misconception of treating what may often be a virtually non-inflammatory condition with anti-inflammatoryms and further compromising the chance of a physiological healing cascade developing in a reasonable timescale was also discussed.

Basic premise of prolotherapy
The simple basic premise of prolotherapy is that a sustained and physiologically structured healing cascade is required in order to repair damaged DCT. In instances where a healing cascade has not commenced, prolotherapy seeks to initiate and maintain one.

History
The term prolotherapy was suggested in 1956 by the American Physician Dr George S Hackett, in his book; *Ligament and tendon relaxation treated by prolotherapy*. There are much earlier references to the use of ‘sclerosing injections’ and ‘sclerotherapy’ to treat a variety of DCT pathologies, and Rice and Aratson in their 1936 work *sclerosing injections* and *sclerotherapy* to treat a variety of DCT. In instances where a healing cascade has not commenced, prolotherapy seeks to initiate and maintain one.

The concept of irritating tissue to stimulate healing by causing inflammation is much older, and can certainly be traced back to the writings of Hippocrates in the 4th Century BC(21). In this instance the inflammation was caused by using slim heated irons; *Kauterion*, which, in the case of lax ligaments in the shoulder, were thrust red hot into the tissue in order to cause scarring. The scarring (as we note in keloid scars today) promoted thickening and contraction of the tissue(22).

By the early to mid 20th Century, sclerosing therapy was being used to treat strained spinal and other ligaments, hernias and varicose veins(23). The importance of using a local anaesthetic, as an aid to patient comfort, was highlighted by Leriche in 1937, who identified the rich supply of sensory nerve endings in ligaments and articular tissues(24). Steindler and Luck, in their research into lumbarosacral pain, built on Leriche’s principles and in 1938 advocated infiltration of local anaesthetic into lumbarosacral ligaments in order to abolish pain in both the ligament and the dermatome served by its adjacent nerve root(25). They also established the principle of using local anaesthetic as a diagnostic tool to precisely identify the area of damaged tissue.

The ‘traditional’ prolotherapy method of Hackett and his followers is to induce an inflammatory response in the area of damaged tissue by introducing irritants that will ‘stress’ the cell population and initiate cytokine expression. It is important to differentiate here between the non tissue destructive stressing or shocking of a cell in prolotherapy and tissue destruction and subsequent formation of scar tissue which occurs in sclerotherapy. Perhaps the best known current example of sclerotherapy is its use for thread varicose veins. In this modality veins are exsanguinuated, injected with agents such as polidocanol or fibro-vein® and compressively bound. The corrosive agent damages the Tunica Intima of the vein and scar tissue is formed which closes the vein(27).

Glucose is currently the hyperosmolar agent of choice of many prolotherapy practitioners and research supports its efficacy as a cytokine expressant due to its interference with cellular osmolality. A solution of 20% W/V glucose for injection combined with 1% W/V Lidocaine Hydrochloride (formerly Lignocaine) is advocated by many acknowledged experts including the Australian prolotherapy tutor, Dr Margaret Taylor (Margaret’s website, Prolotherapy for Doctors, : www.drmartaylor.com.au contains much interesting information). In New Zealand the researcher and clinician Dr John Lyftogt advocates a stronger glucose component but in contrast Dr Gires Kanji a pain specialist from NZ advocates simple normal saline for injection plus an anaesthetic without glucose (Giresh’s website is: www.southerncrosspain.co.nz).

It is interesting to speculate whether 1% lidocaine hydrochloride, which also contains 0.7% of sodium chloride in its standard formulation may have a prolotherapeutic effect in its own right when used alone. This is perhaps an area that requires more research and properly constituted studies.

Other substances that may be used to good effect are the injectable homeopathic solutions such as Zeel or Traumeel (popular for sports injuries due to a lack of doping / drug test conflicts) which are manufactured in Europe by Heel GmBh of Baden Baden. Homoeopathy is a contentious subject in medicine with strong opinions being held by both its supporters and its detractors. The Author frequently uses homeopathic agents and must report that they do appear to have a significantly beneficial effect with virtually no possibility of side effects.

Direct application of growth factors
An additional way that is currently being explored by many researchers is to directly introduce growth factors or the cells carrying them, by injection into the area of damage. Cytokine research is one of the fastest growing areas of biological study and new information is being gleaned in this area almost daily. An insight into the vast amount of information already discovered can be assessed by visiting the famous website of Professor Horst Ibelgaufts ‘Cytokines and Cells online pathfinder encyclopaedia’ (http://www.copewithcytokines.de/). This monumental source of information is now in its 19.4th version and has tens of thousands of entries on these fascinating proteins and similar chemical messengers.

Commercially prepared growth factors are probably outside the remit of this article as costs are somewhat high, e.g. : the cost of frozen PDGF for...
Conditions to which prolotherapy could possibly be applied by Podiatrists

Examples of pathologies suitable for prolotherapy

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So we will concentrate on:

**Autologous whole Blood**

There is recent research that suggests that a few ml’s of a patients own blood, freshly harvested from a suitable vein (the inner brachial point is usual) can be infiltrated into sites of damaged DCT and used to initiate a healing cascade. Studies in both the UK and the USA have taken place on its use in lateral epicondylitis (tennis elbow) with encouraging results. Naturally, the limiting factor in this case is the speed with which fresh blood coagulates. To overcome this it is possible to mix an anticoagulant with the blood as it is withdrawn, in the same ratio as used in transfusion bags.

**Refined preparations from Autologous blood**

There is an increasing amount of published research appearing on the use of Platelet Rich Plasma (PRP), including its use in surgery, wound healing, osteoarthrits and dentistry plus its application in DCT pathologies such as plantar fasciitis.

The process of making PRP is briefly as follows, a sample of the patients own blood is collected and by a process which includes centrifugation, a platelet rich supernatant (the liquid above a sediment or precipitate) is prepared. The PRP fraction is withdrawn and injected using the prolotherapy method, under local anesthetic.

There are already commercial kits for this process but some involve ‘open processing’ which may give rise to the possibility of contamination of the products. However, Cascade Medical Inc supply a ‘sealed tube’ PRP preparation kit, which is CE marked that shows particular promise and a study of its use in pediatric prolotherapy is currently in hand. It is hoped that Chiroprapy Review may publish the results when they are completed.

**The method of prolotherapy solution application**

Once the needle has been inserted into the area to be treated it is repeatedly partially withdrawn and then repositioned in a slightly different part of the area of treatment with a tiny amount of the prolotherapy solution being deposited at each point. This is essentially the ‘peppering’ technique advocated for steroid injection by the British physician Dr James Cyriax. When the needle contacts bone it should be withdrawn very slightly before a deposition takes place. Bone contact should be done very gently because the periosteum surrounding a bone is rich in nerve endings and it is exceptionally painful if forcefully traumatised without adequate analgesia.

It is believed that the effects of ‘needling’ alone, apart from the solution used may be beneficial due to micro-haemorrhage and physical damage to cells causing growth factor release. This may be an explanation for the reported efficacy of the deep acupuncture technique known as ‘pecking the bone’. In certain instances ‘Dry Needling’ alone may be sufficient to provoke inflammation and subsequent healing. It is obviously more comfortable if done under local anaesthesia. Naturally, Podiatrists performing prolotherapy need to have an excellent knowledge of the structure that they are working upon. Also, all procedures should be carried out with due care and an aseptic injection technique.

**Examples of pathologies suitable for prolotherapy**

Conditions to which prolotherapy could possibly be applied by Podiatrists familiar with its mechanism of use include; hammer toes, hallux abducto valgus, neuromas, sprained ligaments in the tarsus, and ankle inversion sprains affecting the talofibular and deltoid ligaments. In the Achilles region it may help both acute tendinopathies and chronic tendinoses if administered outwith the tendon in the lateral and medial areas to bathe the paratenon. Currently (2007) the use of prolotherapy in tendinopathies is being further investigated by Kent Sweating, research fellow in Podiatry at Griffith University School of Medicine, Brisbane. Kent’s research has been funded by the Australian Podiatric Education and Research Foundation.

In the area of the Knee, the lateral and medial collateral ligaments and the coronary ligaments at the anterior lip of the tibial plateau are frequent sites of palpable pain and easily infiltrated with a prolotherapy solution.

In most cases the patient will suffer, at worst, a mild soreness at the site of prolotherapy as the healing cascade takes effect. A skilful technique can minimise this. The intelligent use of concurrent modalities that Podiatrists should be familiar with such as orthoses to minimise inappropriate joint movements, and advising on nutritional supplements such as Zinc and Manganese which are increasingly reported to benefit DCT healing can also be considered. Additionally, advice on footwear and exercise should be considered as part of an overall treatment strategy.

**Safety**

In examining the safety of such procedures, Dr Tom Dorman conducted a retrospective analysis of 494,845 patients and reported no fatalities. It is worth pointing out that the majority of the few problems recorded were overwhelmingly in areas of the body far outside the remit of the Podiatrist, i.e: pneumothoraces due to cannulation of the chest wall and spinal cord damage. Also, the study records that many of the procedures had used overt sclerosants rather than simple local anaesthetic and glucose or other agents with a low toxicity potential.

Even the use of sclerosants such as P2G and polidocanol has been identified by a 2006 report by the UK National Institute of Clinical Excellence (NICE) to be safe and entirely free from fatalities and again, the use of these far more potentially toxic agents is primarily in area’s of the body capable of much greater complications than the easily identified joints, peri articular ligaments, tendons and entheses in the lower limb.

It is also perhaps worth considering that UK Chartered Physiotherapists have been injecting joints, ligaments and tendons all over the body with local anaesthetics and steroids since around 1995. Whilst there was substantial opposition initially from entrenched medical opinion, and indeed the older more conservative elements in their own profession, this has gradually faded before the impressive safety record of the many hundreds of Physiotherapists performing tens of thousands of effective soft tissue injections for more than a decade.

**Availability of suitable prolotherapy substances**

The Local Anaesthetics currently permitted to Podiatrists trained and licensed in their use are entirely suitable for prolotherapy. The literature on the subject often suggests the use of a plain 1% solution of lignocaine (Lidocaine). The author usually uses this, often diluted to as little as 0.2% in the prolotherapy solution. Firm palpation with the thumb is the usual ‘tool’ used in identifying the exact location of damaged tissue in ligament damage and conditions such as plantar fasciitis. To subsequently find the exact point that is giving pain 3% Mepivicaine hydrochloride can be a useful ‘diagnostic analgesic’, due to its speed of action. When the patient reports that the pain has been ‘turned off’ the clinician knows the exact spot to concentrate their prolotherapy application in. The pre-existing analgesia will also make the multiple needling of the treatment itself much more comfortable if done under local anaesthesia, wound healing, osteoarthrits and dentistry plus its application in DCT pathologies such as plantar fasciitis.
more tolerable. In situations where longer duration of action is required then Ropivicaine or Bupivicaine Hydrochloride 0.5% plain (Marcaine) may be used additionally, possibly post - treatment. The long duration of Marcaine (up to 6hrs anaesthesia and 24hrs analgesia) may be useful to provoke de-sensitisation where 'pain wind up syndrome' (dorsal horn hyperalgnesia) is suspected. A local or Hospital pharmacy is a good source of some of the less commonly used analgesics that podiatrists can use, such as Ropivicaine or Marcaine, which is not stocked by many podiatry suppliers.

Glucose needs to be suitably diluted to around 20% W/V with water for injection or with the LA itself. At the time of writing (2007), glucose solution is a Prescription Only Medicine (POM) that is not on the list of POM’s available directly to podiatrists. However, its use can be supported by either a Patient Specific Direction (PSD) or a Patient Group Direction (PGD) from an independent prescriber. A discussion with the patients GP is recommended to obtain a suitable prescription.

As the glucose is manufactured for intravenous use and not for infiltration, prolotherapy is an ‘off label’ use. Again, it should be stressed that the fact of any substance being used ‘off label’ under a PSD or PGD by registered Podiatrists is perfectly permissible, and in pain medicine it is estimated that over 25% of all substances used are actually used ‘off label’.

The injectable homeopathic agents referred to here are available to LA qualified registered Podiatrists from BioPathica Ltd : (http://www.biopathica.co.uk/ . BioPathica Ltd PO Box 21, Ashford, Kent TN23 6ZU Tel: +44 01233 636678 Fax: +44 01233 638380).

Conclusions

Prolotherapy is a simple technique once the practical skills of administration have been acquired. It’s documented success rates and safety record suggests that it deserves consideration as a modality that may be suitable for trained Podiatrists to perform in a standard surgery situation.

A knowledge of the substances used, their methods of action and contra-indications, familiarity with the structures being treated and the mechanical techniques of administration can be acquired in suitable workshops by Podiatrists already trained in the safe injection of local analgesics which is the core skill required.

Further information, including details of prolotherapy workshops for LA qualified podiatrists is available from the author if required:

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References and Bibliography

21. “It deserves to be known how a shoulder which is subject to frequent dislocations should be treated ….. The cautery should be applied thus: taking hold with the hands of the skin at the armpit, it is to be drawn into the line, in which the head of the humerus is dislocated; and then the skin thus drawn aside is to be burnt to the opposite side. The burnings should be performed with irons, which are not thick nor much rounded, but of an obtuse form (for thus they pass the more readily through), and they are to be pushed forward with the hand; the cauterities should be red-hot, that they may pass through as quickly as possible, for such as are thick pass through slowly, and occasion sores of a greater breadth than convenient; and there is danger that the cicatrices may break into one another; which, although nothing very bad, is most unseemly, or awkward from: Hippocrates. Works – on the articulations; section VII. Francis Adams (trans) London 1849.