



**NAT PADHIAR**  
Centre for Sport & Exercise Medicine, Barts and the London School of Medicine and Dentistry, William Harvey Research Institute, Queen Mary University of London



**PAUL CHADWICK**  
Clinical Director, College of Podiatry



**ROBERT ASHFORD**  
past Dean, Faculty of Podiatric Medicine, Royal College of Physicians and Surgeons, Glasgow

Guidance on the safety of steroid injections during the pandemic for managing musculoskeletal problems encountered in podiatric practice.

# Stay safe with steroids

**M**embers may be concerned about the safety of using steroid injection for podiatric procedures during the pandemic. This article sets out the potential steroid risk and concerns during the current pandemic and considers the alternative injection therapy after balancing the risk to benefit ratio.

## Steroid risk

Steroid injection use is common in podiatric procedures for its powerful anti-inflammatory property of easing pain, increasing mobility and quality of life. Steroids' duration of effect is variable but can provide several months

of benefit. They stimulate T-cells to commit cell suicide (apoptosis) and thus also act as an immunosuppressant (Coutinho and Chapman, 2011), which is the universal concern. There is an increased risk of susceptibility to infection (Coutinho and Chapman, 2011). However, the immunological impact of steroids on patients with COVID-19 is unknown.

There is also a risk that asymptomatic patients who are carrying the virus could be treated, potentially putting them at increased risk of an adverse outcome from the virus. Higher-risk patient groups are the elderly and those with comorbidities resulting in higher mortality rates.

## Use of steroids and the possible impact with COVID-19

The current WHO guidance (2020) for the management of severe acute respiratory infection in patients with COVID-19 is to avoid the routine use of systemic corticosteroids (CS) unless indicated for another reason. Steroids have been associated with an increased risk for mortality in patients with influenza and delayed viral clearance in patients with Middle East respiratory syndrome (MERS) coronavirus infection (WHO, 2019).

Although they were widely used in the management of severe acute respiratory syndrome (SARS), steroids showed no good evidence of benefit,

and persuasive evidence of adverse short- and long-term harm (Russell et al, 2020). A recent study of patients with COVID in China reports that patients receiving CS did not affect mortality, but rather delayed viral clearance (Huang, 2020).

Newly published NHS England guidelines in March regarding the management of trauma and orthopaedic patients during the coronavirus pandemic highlight the need for a shift towards non-operative care as the system comes under ever-increasing pressure.

During this period of heightened burden, MSK patients with degenerative or traumatic changes to articular joints must be adequately cared for, and while treatment strategies are being revised – with recommendations for more conservative management and the deferral of orthopaedic elective surgery – the delivery of appropriate therapeutic options directed to the patient's symptoms remains essential.

Many NHS trusts have enforced a moratorium on intra-articular CS injections due to the associated and well-elucidated post-injection immunosuppressive effects (Oppong, 2015).

## Corticosteroids

CS serve to interrupt inflammatory and immune cascades, decreasing capillary permeability and vascularity and binding to glucocorticoid receptors, resulting in complex changes to gene transcription and inhibiting accumulation of inflammatory cells and mediators (Ayhan et al, 2014).

While CS may prove markedly effective in the management of inflammatory and autoimmune disorders, such inhibitory effects on multiple types of immune cells, especially in vulnerable patients, presents clinicians with a quandary during the pandemic – and the challenge to offer a viable alternative.

## Advice

Injections must not be given to patients with active infections. However, the potential also arises to do harm to those who may be incubating or who later develop COVID-19. Long-acting and usually insoluble steroid formulations are frequently used in procedures to manage pain. To put this into context, triamcinolone acetonide 40mg is equivalent to 10 times the normal daily physiological steroid production. Epidural steroids have been shown to cause a variable degree of adrenal suppression for at least some weeks (Friedly, 2018). The potential impact of this immunological suppression in a patient incubating COVID at the time or in the future is unknown. As with all podiatric procedures, a risk/

benefit balance has to be reached in discussion with the patient. Each case is unique, and no guidance will cover all eventualities.

Caution should be used when assessing patients for steroid injections. Balance the severity of the underlying disease, the potential benefit and the risks. These include immunocompromise, underlying comorbidities and further risk should the patient become infected in the period after injection when there is likely to be an ongoing effect on the immunological system. Patients should be fully aware of the potential increased risk, the lack of clear evidence, and be engaged in decision-making. Likewise, podiatrists should consider the risks and benefits of such injections and under which circumstances they will continue using them during the current clinical conditions.

## Recommendations

The College of Podiatry and the Faculty of Podiatric Medicine of the Royal College of Physicians and Surgeons of Glasgow (RCPSPG) jointly recommend, on the balance of current evidence and risk, that podiatrists should avoid the use of CS injections and to seek to employ clinical alternatives, such as delaying administration of the injection or use the alternatives wherever possible (CoP and RCPSPG, 2020). This is in keeping with advice and recommendations given by various NHS trusts and organisations.

The situation relating to the pandemic is rapidly changing, but it is thought that there will be several months of disruption and the potential for a significant proportion of the population to become infected. National guidance should also be followed and will be updated on a regular, often daily, basis.

## Common conditions requiring injection

Listed in Table 1 (overleaf) are some of the common conditions encountered in podiatric practice along with some suggestions for alternative treatments. Clinicians are encouraged to undertake a literature review and wherever possible adhere to evidence-based practice. They are

also encouraged to consider other treatment modalities, for example extracorporeal shock wave therapy, laser, therapeutic ultrasound, and so on.

## Alternative treatments

### 1. Viscosupplementation

– intra-articular hyaluronic acid (IAHA) (Pereira et al, 2018)

#### Conditions:

- Degenerative synovial joints, e.g. metatarsophalangeal (MTP), subtalar, ankle, knee.
- Positional tendon tendinopathy, e.g. tibialis posterior, peroneal, extensor, and flexor tendons. Always check that the product which is to be used is licensed specifically for tendons. Ostenil tendon is currently the only product that appears to have this licence.

- Mid-portion Achilles tendinopathy.

Viscosupplementation with IAHA offers patients and clinicians a non-immunosuppressive, physiologic treatment option for joint pain and loss of function. Crucially, this eliminates any concern over further jeopardising immunocompromised patients. IAHA negates other risks and contraindications associated with intra-articular CS usage, including such localised effects as chondrotoxicity, cartilage damage, post-injection flare, subcutaneous tissue atrophy and systemic effects such as flushing, osteoporosis, and hyperglycaemia – a serious consideration in patients with diabetes mellitus (Honcharuk and Monica, 2016; Choudhury et al, 2016).

Viscosupplementation offers a safe and effective treatment option for patients suffering from degenerative joint pain and loss of function. If conservative treatment and/or pharmacological management has failed to adequately resolve symptoms, and in accord with the current advice whereby CS injection is proscribed in immunocompromised patients, viscosupplementation should be the preferred mode of injection therapy.

There are many brand names (Synvisc, Orthovisc, Durolane, Hyalgan, Ostenil, and so on) on the market, but please use the one you are familiar with or that has shown favourable and beneficial outcomes. Ostenil products are particularly

CONDITIONS THAT AFFECT THE FOOT, ANKLE AND LEG THAT MAY REQUIRE AN INJECTION	
<b>FOREFOOT</b>	Morton's neuroma, stump neuroma, bursitis, synovial cyst, OA MTP joints, synovitis of MTP joints, gout, Freiberg's infraction, plantar plate injury.
<b>MIDFOOT</b>	OA midfoot joints in particular Lisfranc, cuboid-metatarsal and calcaneo-cuboid joints, cuboid compression syndrome, Crisp-Padhiar syndrome, Lisfranc ligament injury and enthesopathy.
<b>HINDFOOT</b>	Positional tendon tendinopathy (tibialis posterior, peroneal, long extensors and flexors), mid-portion Achilles tendinopathy, insertional Achilles tendinopathy, intra-substance tendon tears, Haglund's deformity, retro-calcaneal and pre-Achilles bursitis, anterior and posterior impingement syndrome, lateral ligament injury (ATFL, CFL and PTFL), sinus tarsi syndrome, plantar fasciopathy, plantar fascia partial tears, tarsal tunnel syndrome and medial calcaneal entrapment syndrome.
<b>LEG</b>	Medial tibial stress syndrome, superficial peroneal nerve entrapment, sural nerve entrapment syndrome, haematoma following muscle tear and myofascial tears.

useful in small joints e.g. Ostenil Mini for lesser MTP joints and Ostenil Plus for first MTP joint (Maher and Price, 2007).

### 2. Platelet-rich plasma (PRP)

(Wu et al, 2016)

#### Conditions:

- Osteoarthritis (OA) of first MTP joint, lesser MTP joint, ankle, and the knee
- Plantar fasciitis
- OA of the midfoot joints
- Intra-substance tears of the tendon, plantar fascia and ligaments.

PRP injections can be used in the treatment of many musculoskeletal (MSK) injuries, including that of tendons, muscles, and joints (Nguyen et al, 2011).

PRP and autologous blood have been used in the treatment of MSK injuries since 2003. They have proved immensely popular in the US and are becoming increasingly so in Europe, particularly with elite athletes. Although the use of PRP and autologous blood in sports medicine is a relatively recent development, PRP gels have been used in wound healing since the 1980s. Plasma is widely known for its role in haemostasis; however, it also has a key role in tissue healing and regeneration through the release of growth factors from alpha-granules (Lopez-Vidriero et al 2010; Stellos et al, 2010) In basic terms, PRP is a high concentration of platelets in plasma with a platelet count higher than the baseline. The average human platelet count in blood is approximately 200,000/ml and platelet levels in PRP have been reported to be between one and six times greater, depending on how the PRP is obtained (Delos et al, 2011).

The mechanism of action of PRP is not completely understood, but

platelet proteins are known to have a key role in healing (Lopez-Vidriero et al, 2010; Stellos et al, 2010). Platelets synthesise and release proteins that reside in the alpha granules, including platelet-derived growth factor, transforming growth factor B, vascular endothelial growth factor, cytokines and many more (Mishra et al, 2009; Borzini and Mazzucco, 2007). Much emphasis is placed on alpha granules; however, it is important to remember dense granules have a part in tissue regeneration including adenosine, serotonin, histamine and calcium (Mishra et al, 2009).

The evidence for the use of PRP in vivo is promising, especially in the treatment of tendon injuries; however, the treatment is not proven, and high-quality evidence is lacking. All studies agree that the risk of PRP is low (Mishra et al, 2009).

NICE and NHS England have published guidelines on the use of autologous blood and PRP in plantar fasciitis and tendinopathy which provide a review of current literature, but they do not offer any definitive evidence-based guidelines.

### 3. Prolotherapy

(proliferation injection therapy)

#### Conditions:

- OA of the non-synovial joints
- Stump neuroma
- Medial tibial stress syndrome (MTSS)
- Intra-substance and other tears (not complete rupture) of the tendon, plantar fascia, and ligaments
- Plantar plate tear
- Insertional Achilles tendinopathy
- Retinaculum tear with peroneal subluxation.

Proliferative injection therapy (prolotherapy, 15% to 25% glucose) has been used since the late 19th century.

The rationale behind prolotherapy is that injecting proliferants, such as hypertonic glucose solution, into damaged connective tissue initiates inflammation, which leads to a healing cascade resulting in fibroplasia, deposition of new collagen and tissue hypertrophy (Banks, 1991).

Animal studies have reported collagen proliferation, increased bone-ligament-bone junction strength, and ligament mass with prolotherapy injections compared with controls (Liu et al, 1983).

The periosteum is richly innervated with nociceptive nerve fibers (Safadi et al, 2009), therefore in MTSS, a prolotherapy injection may reduce pain by disrupting these sensory fibres as a result of the direct osmotic shock action of hypertonic dextrose on cells local to the injection site (Banks, 1991).

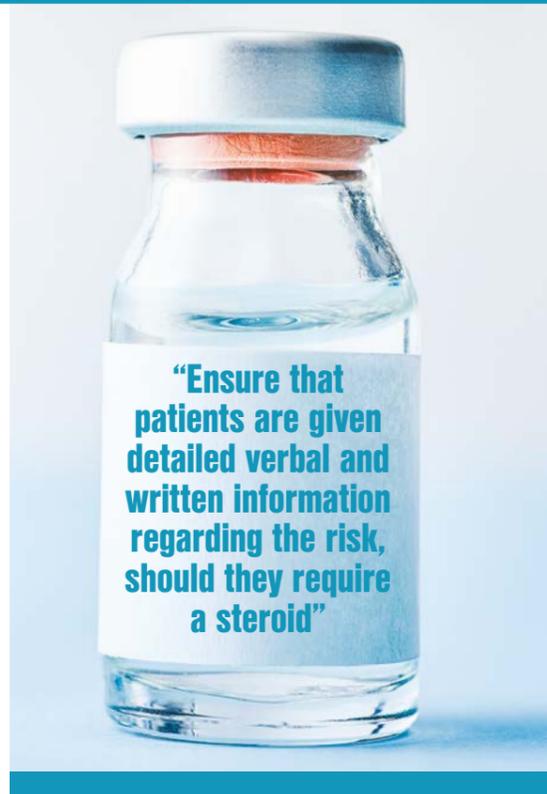
Most trials of prolotherapy are case series given the difficulty of recruiting adequate patient numbers not responsive to other treatments, providing level 4 evidence. There is currently no published literature investigating the use of prolotherapy in the management of MTSS.

**Practitioners are advised to carry out a thorough literature review for evidence before considering these three treatment modalities and ensure that they have the competency to perform these injections.**

## Conclusion

The pandemic has had a major impact in social and professional practice throughout the world. In podiatric practice, steroid injection is an integral and an important intervention in the management of MSK pathology. This guideline paper has considered the steroid injection risk during this pandemic along with recommendations, advice and guidance from various institutions. In conclusion:

- There is global concern regarding the immunosuppression property of steroids during this uncertain COVID-19 virus pandemic.
- There is no real evidence at this stage and the situation is changing all the time, sometimes on a daily basis. Clinicians are advised to be vigilant.
- Assess the risk to benefit ratio for each patient and follow the guidelines and advice set out in documents by various institutions.
- Ensure that patients are given detailed verbal and written information regarding the risk, should they require a steroid injection.
- Please be aware and follow the local COVID-19 rules, guidelines, and consenting procedures before performing the injection.
- Ensure that the robust informed consenting process is in place.
- There are various alternatives, which in many respects are better without compromising the immune response.



## WHAT ARE THE RECOMMENDATIONS?

The decision to resume injections should be based on a balance of risks and benefits for individual patients. Here is a summary of the recommendations of the joint guidance from the Faculty of Pain Medicine (FPM) and British Pain Society (2020)

- 1 The decision to resume injections should take into account the current COVID-19 situation in that region.
- 2 Injections should be prioritised according to the level of urgency suggested by the FPM guidance on the recovery of services.
- 3 An individualised treatment plan for difficult cases should be supported by the multidisciplinary team with a minimum of two clinicians involved.
- 4 All reasonable non-injection pain management measures should be explored before injections are started or resumed.
- 5 Protective measures should be taken by local protocol to minimise the risks to patients and staff.
- 6 Pain services must aim for the resumption of fully commissioned services when safe to deliver.

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