Hand Osteoarthritis — Clinical Presentation, Phenotypes and Management

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1. Introduction

Osteoarthritis (OA) is the most common arthritic disorder, affecting increasing numbers of people in an ageing population [1]. Nearly 27 million people are estimated to have OA among US adults [2]. OA of the hand is known to cause significant morbidity and can have a severe impact on patients' functional capacity. For example, the US Framingham study found that 27% of adults aged over 26 have hand OA (HOA) [2]. In addition, a large European study of 7983 people demonstrated that 25% of participants with hand pain showed significant hand disability [3]. Hand OA can lead to the development of chronic pain, causing significant emotional and financial burden to those affected, impacting on carers and on society as a whole [4]. Treatment of HOA currently comprises analgesia with analgesic drugs including topical or oral nonsteroidal anti-inflammatory agents (NSAIDs), opioid analgesics and rehabilitative hand physiotherapy [5]. However, large numbers of people continue to experience impaired hand function and pain.

Pathologically, OA is typified by cartilage degradation, osteophyte formation and underlying subchondral sclerosis. More recently, imaging-detected synovitis and bone marrow lesions have also been found to correlate with OA inflammation and pain. In this chapter we discuss the recognised clinical phenotypes of hand OA, typical features of hand OA, including Heberden's nodes, radiographic correlates of the clinical features observed and new insights into treatments for this chronic painful arthritic condition.

2. Clinical phenotypes of hand OA

2.1. Nodal hand OA

Nodal hand OA characteristically involves the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints of both hands. A typical swelling of the interphalangeal joints evolves, which can enlarge to a maximum size during its development (Figure 1). At the early to mid-stages when enlargement occurs, DIP joints can become painful, erythematous and difficult to mobilise. The underlying pathogenesis of this process includes bony enlargement of the underlying interphalangeal joints, synovitis and soft tissue swelling of the region affected [6]. When involving the DIP joints, the enlargement may give rise to an often typical feature described as a 'Heberden's node'. The historical context of the description of Heberden's nodes is given further below. The PIP joints are also a recognised feature of nodal hand OA. They can be associated with a very similar pathological process to the joints described in DIPs as above and are sometimes called 'Bouchard's nodes' [7]. The radiographic features of nodal hand OA are demonstrated in Figure 2. Interestingly, the presence of Heberden's and Bouchard's nodes can occur with or sometimes without associated symptoms of pain, stiffness and disability.

Figure 1. Distal interphalangeal (DIP) joint swelling of the index, middle and ring fingers demonstrating Heberden's nodes in a patient with hand OA. The patient also has involvement of the proximal interphalangeal joints (PIP) of the index, middle and ring fingers (Bouchard's nodes).

Figure 2. Radiographic features of nodal hand OA demonstrating DIP joint involvement (index and ring fingers especially) with joint space narrowing and osteophyte formation. This patient also has involvement of the first carpometacarpal (CMC) joint of the thumb. The metacarpophalangeal joints are spared, which is often a characteristic finding.

2.2. First carpometacarpal joint OA

The first carpometacarpal (CMC) joint is a distinct recognised feature of hand OA. It is often seen bilaterally in people affected and is often a major cause of symptomatic joint pain. Risk factors for first CMC joint hand OA include mechanical factors and manual occupations [8]. The typical radiographic features of CMC joint OA are demonstrated in Figure 2. They often give rise to a 'square-shaped' hand in people affected by this condition. Interestingly nodal hand OA can co-exist with first CMC joint OA.

2.3. Erosive hand OA

The erosive phenotype of hand OA is a particularly aggressive form of hand involvement. It is associated with erosions particularly in the DIP and PIP joints [9]. It is important to exclude other forms of inflammatory arthritis in its management. Typical radiographic features of this

condition are shown in Figure 3. Historically, clinicians have considered the use of disease-modifying anti-rheumatic drugs (DMARDs) in this variant to avert the progression of this erosive form of the disease [10].

Figure 3. Typical radiographic features of erosive hand OA are shown. There has been aggressive erosive damage to the proximal and distal interphalangeal joints (PIPs) and (DIPs) respectively. A central erosion is observed in several of these joints with a corresponding characteristic 'gull-wing' deformity and osteophytes observed laterally on either side. The interphalangeal (IP) joint of the thumb is also involved and characteristic joint space narrowing at the first carpometacarpal (CMC) joint is observed. The metacarpophalangeal joints are characteristically spared.

Other rarer forms of hand OA are also observed in the context of underlying conditions e.g. inflammatory arthritides, where hand OA can be a secondary phenomenon. The may include rheumatoid arthritis or the crystal arthropathies including gout and pseudogout. In the crystal arthropathies, clinical and radiographic appearances can be very similar and may also respond to similar therapies [11], giving prolonged episodes of joint inflammation and pain. Other underlying conditions which may give rise to chronic OA of the hands include genetic conditions such as Stickler's syndrome, and others such as haemochromatosis, hyperparathyroidism and acromegaly.

3. Risk factors for hand OA development

The risk of OA rises with increasing age, with the prevalence of OA increasing over the age of 50 [4]. With respect to the question of whether heavy physical work is associated with hand OA, some researchers have suggested that heavy occupational work was not associated with the presence of OA [12] and other studies have favoured a positive correlation of manual work with OA [13]. Obesity has also been investigated as an independent risk factor for hand OA with occasionally conflicting results. Hochberg *et al.* previously suggested that age and not obesity, were the main risk factor for hand OA [14]. In contrast, Denisov *et al.* suggested that obesity was associated with the progression of knee and hand OA in a cohort of almost 300 patients [15]. Cicutinni *et al.* have also suggested that there is a 9 to 13% increase in knee and hand OA for every kilogram increase in body weight [16].

Since the range of presentation of hand OA is varied, with several clinical phenotypes recognised, it is perhaps not surprising that a number of genes have been identified as risk factors for hand OA. These have been summarised in a recent review [17]. The main themes which have arisen from genetic studies include the observation that the genetic associations for hand OA cover a broad nature of genes, perhaps reflecting the multifactorial risk factors in this condition. Reported genetic associations include a female preponderance carried in many family cohorts, OA susceptibility loci mapping to chromosome 6 for hip and knee OA. Recently a group reported a significant association between hand OA and susceptibility loci on chromosome 6 [18]. In a UK cohort, Zhang *et al.* have investigated four putatively functional genetic variants in the KLOTHO gene, which is a strong ageing-related gene [19]. The group suggested that one variant in the KLOTHO gene was associated with hand OA susceptibility and especially with osteophyte formation rather than cartilage damage. Further studies have reported four SNPs in the IL-1R1 gene suggesting an association between the gene encoding the IL-1R1 and hand OA. Since IL-1 is a cytokine that has catabolic effects on cartilage, this may be particularly relevant in human disease [20]. Recent work has also focused on the extracellular matrix protein found in cartilage: aggrecan. Kamareinen *et al.* [21] showed that patients homozygous for the most common aggrecan VTNR (variable number of tandem repeats) allele, A27, had a significantly lower risk of hand OA. People who carried 2 copies of the aggrecan alleles with less than 27 repeats or more than 27 repeats demonstrated a higher risk of hand OA. The link between hand OA and extracellular matrix proteins found in cartilage has received further attention with the recent reports that single nucleotide polymorphisms (SNPs) in the asporin (ASPN) gene are associated with hand OA progression [22]. A recent genome-wide association study in an Icelandic population has shown that variants within the ALDH1A2 gene was associated with hand OA. The variants within the ALDH1A2 gene were confirmed in replication sets from The Netherlands and UK [23].

Although the studies above suggest a strong familial association with hand OA, the broad nature of clinical presentation and phenotypes suggests that strong genetic associations with hand OA are difficult to identify. In future it would be useful to accumulate larger populations of specific phenotypes to establish genetic associations in greater detail.

4. Mechanisms of pain in hand osteoarthritis

Osteophytes, which are a pathognomonic feature of OA, are often observed to create a physical barrier to optimal range of movement and can give rise to severe joint pain as well. Recently, inflammatory changes have been found to relate to higher risk of structural damage in a study which looked at 2 years follow-up [6]. Kortekaas and colleagues showed that inflammatory features, defined by synovial thickening, effusion and increased power Doppler signal on ultrasound scan (demonstrated in Figure 4), when they persisted, were related to increased radiographic progression of OA after 2 years. The presence of synovitis by ultrasound may therefore guide treatment decisions such as corticosteroid-guided intra-articular injection in hand joints affected by OA.
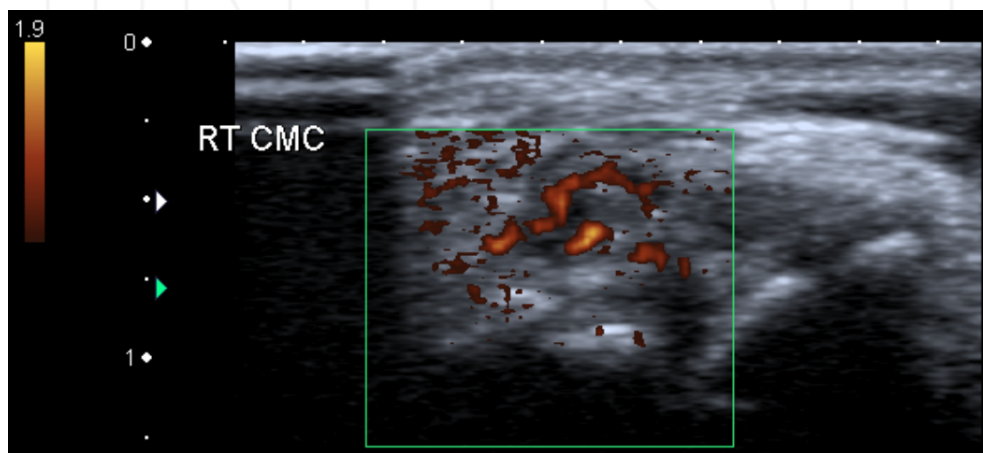

Figure 4. Ultrasound image of the right first carpometacarpal joint, showing evidence of synovial thickening and increased vascularity on power Doppler imaging.

Recent work has demonstrated the evidence of bone marrow lesions (BML), which are defined as high density signal lesions on MRI with T2-weighted imaging, especially in the knee [24], have also been observed in people with hand OA [25]. In their study, Haugen *et al.* showed that bone marrow lesions, synovitis and erosions were associated with joint tenderness. It is therefore possible that synovitis and bone marrow lesions could be future targets for therapeutic interventions in hand OA.

5. Heberden's nodes: A historical perspective

"What are those little hard knobs, about the size of a small pea, which are frequently seen upon the fingers, particularly a little below the top, near the joint? They have no connection with the

gout, being found in persons who never had it; they continue for life; and being hardly ever attended with pain, or disposed to become sores, are rather unsightly, than inconvenient, though they must be some little hindrance to the free use of the fingers." [26]. These were the observations of William Heberden whose philosophy in medicine was that one must always be guided by their own direct observations. Heberden's nodes, which are classical lesions of osteoarthritis, were initially described as 'digitorum nodi' in Latin by Heberden himself, which led him to make the important distinction between gout and osteoarthritis [27]. OA remains a common disabling condition worldwide and the most common form of arthritis [28]. However, there are few diagnostic tests and unfortunately current treatments for OA have not been able to successfully eliminate pain from the clinical manifestations of the disease [5].

In addition to Heberden's description further observation of the nodes have led them to be classified according to the location (Figure 1). Nodes either appear on the lateral aspect on the dorsolateral margins or in the central midline where occasionally they fuse with the lateral nodes to form a ridge. They can also be classified as idiopathic or traumatic, with the latter most commonly resulting in a solitary Heberden node [29]. Idiopathic nodes are easily identifiable from the clinical history, which usually consists of a node, which slowly and gradually increases in size on one finger and then spreads to other fingers. Reports from patients about pain associated with the nodes are inconsistent, with some reporting painful growth of the nodes whereas others report the growth as painless [30]. Stecher [29] described the progression of Heberden's nodes having observed around 7,000 individuals with Heberden's nodes. He noted that the progression could be divided into three stages. The initial stage consists of a visible enlargement of the joint; this enlargement is also palpable at the proximal end of the distal phalanx as two spherical nodules or as prominent ridge. In some people it was noted that the enlargement was so severe that the nodules were palpable at the sides of the joint and on the palmar surface. The second stage consists of palmar flexion of the distal phalanx in addition to the enlargement. In addition to the previous two stages the third stage consists of lateral deviation of the distal phalanx from the midline (see Figure 1) [29].

It is well established that Heberden's nodes are associated with underlying radiographic changes [30]. More recent studies have shown that Heberden's nodes, which are more developed and affecting both sides of the joint show joint space narrowing as opposed to Heberden's nodes in their initial stages. This can be attributed to the slow growth of Heberden's nodes and that joint space narrowing is possibly a late manifestation of the disease [31]. With this knowledge it can be assumed that Heberden's nodes affecting both aspects of the joint can be used as a clinical marker for radiographic change [31].

OA is a process of cartilage and bone damage in which changes are eventually irreversible. However it seems that Heberden's nodes have a different process governing their formation and they are histologically different depending on the location on the joint. Midline nodes are traction spurs growing in the extensor tendon, this growth is usually found in athletes as a physiological response to excessive tension. It is important to note that this spur is not a true osteophyte and that it can be identified by its location and the lack of a cartilage cap. Conversely, the lateral node has shown to have a constant presence of osteophyte, which arises from one or both of the phalanges and is located lateral to the extensor tendon. These histo-

logical findings are supported by radiological observation. Radiography of Heberden's nodes shows that there is evidence of osteophyte formation in the lateral node and a traction spur in the middle node [31]. Osteophytes consist of both new bone and cartilage formation, which arise from progenitor cells, indicating that the sequelae of joint destruction induces a pluripotent cell response [32]. The exact function of osteophytes in osteoarthritis is yet be understood but can been seen as an adaptive mechanism against joint injury to stabilize the joint [33, 34]. Analysis of osteophytes at different developmental stages has shown a sequential process of differentiation and the presence of the anabolic factor transforming growth factor-beta (TGF-β) [32]. Osteophyte growth usually occurs in the direction of least resistance; in joints such as the shoulder and ankle the strong capsules restrict osteophyte growth. At the distal interphalangeal joint the only obstruction is a thin capsule, which holds in synovial fluid. This obstruction is not sufficient to restrict osteophyte growth hence the presence of such prominent Heberden's nodes. To what extent the osteophyte causes deviation of the distal phalanx is dependent on the strength of the collateral ligament, which is genetically determined [31]. Extensive research by Stecher has shown that there may be a single autosomal gene responsible for the inheritance of Heberden's nodes however it seems to exhibit a sex-linked pattern as it is dominant in females and recessive in males [29].

Although Heberden's nodes were first described over 150 years ago and despite extensive research their exact mechanism and purpose has not been fully understood. They are part of the clinical picture of osteoarthritis but it seems that their pathophysiology and genetic inheritance somewhat differs to our current understanding of generalised osteoarthritis.

6. Treatments for hand osteoarthritis

A range of treatments have been used in hand OA, including physical techniques such as taping and splinting to reduce pain and improve function [35, 36]. Such treatment is often administered through physiotherapy and/or occupational therapy units and can be repeated during flares.

Pharmacological treatments are often focused around symptomatic pain relief including paracetamol, topical and oral non-steroidal anti-inflammatory drugs such as ibuprofen, naproxen and others, which have been shown to be efficacious over and above other analgesic treatments in large scale meta-analyses [4]. Such treatments are now recommended within several international guidelines for the treatment of OA [36]. Recent imaging studies which have shown synovitis and bone marrow lesions to correlate with painful progressive hand OA have led to renewed interest in considering disease-modifying anti-rheumatic agents for hand OA.

Previous studies have shown that intra-articular injections of corticosteroid can be particularly beneficial in hand OA, particularly at the first CM joint [37]. However, repeated injections are not without significant side-effects, including local tissue damage and skin atrophy. The general consensus is that, if not straightforward, local injections may best be performed under

ultrasound guidance. Some reports have suggested intra-articular hyaluronic acid may also be a potential therapeutic option, but such studies have not yet been subjected to large scale clinical trials [38]. With respect to systemic steroid, a recent study showed improvement in synovitis following intramuscular depomedrone injection of steroid for hand OA, which was sustained for 4 weeks [39]. However, the effects of systemic corticosteroid treatment were relatively short-lived and synovitis returned by ultrasound measures after 12 weeks of treatment.

With respect to the use of other disease-modifying agents, a recent trial of hydroxychloroquine has been conducted for the treatment of hand OA [40] and the results of this study are now awaited. Other groups have investigated the use of bisphosphonates e.g. intravenous clodronate in the treatment of hand OA with beneficial outcome for pain in their study [41]. However, a recent meta-analysis by our group did not show overall significant benefit overall for pain and function after use of bisphosphonates across several phenotype of OA, including hip, knee and hand [42]. Future studies targeted at specific stages of disease with proven synovitis and bone marrow lesions may be more helpful in establishing the potential future therapeutic use of bone-modulating agents in the clinic.

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References

[1] Hunter, D.J and Felson, D.T. (2006) 'Osteoarthritis'. *British Medical Journal.* 18(332): 640-642

[2] Lawrence, D. J. et al. (2008) 'Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II.' *Arthritis and Rheumatism* 58(1): 26-35.

[3] Dahaghin, S. et al. (2005) 'Prevalence and determinants of one month hand pain and hand related disability in the elderly (Rotterdam study)'. *Annals of the Rheumatic Diseases.* 64(1): 99-104

[4] Zhang, W. et al. (2007) 'EULAR evidence based recommendations for the management of hand osteoarthritis: report of a task force of the EULAR Standing Committee

for International Clinical Studies Including Therapeutics (ESCISIT)' *Annals of the Rheumatic Diseases*. 66(3):377–388.

[5] Sofat, N., Ejindu, V. and Kiely, P. (2011) 'What makes osteoarthritis painful? The evidence for local and central pain processing', *Rheumatology (Oxford, England),* 50 (12), pp. 2157-2165.

[6] Kortekaas, M.C., et al. (2014) 'Inflammatory ultrasound features show indeppendent associations with progression of structural damage after 2 years of follow-up in patients with hand osteoarthritis'. *Ann Rheum Dis*. Doi: 10.1136/annrheumdis-2013-205003

[7] Rees, F. et al. (2012). 'Distribution of finger nodes and their association with underlying radiographic features of osteoarthritis. *Arthritis Care Res (Hoboken)* 64(4): 533-8

[8] Jensen J.C., Sherson, D. (2007) 'Work-related bilateral osteoarthritis of the first carpometacarpal joints'. *Occup Med (Lond)* 57(6): 456-60

[9] Marshall, M. et al. (2013) 'Erosive osteoarthritis: a more severe form of radiographic hand osteoarthritis rather than a distinct entity?' *Ann Rheum Dis*. doi: 10.1136/annrheumdis-2013-203948

[10] Bryant LR, et al. (1995) 'Hydroxychloroquine in the treatment of erosive osteoarthritis'. *J Rheumatol.* 22(8): 1527-31

[11] Rothschild, B.M. (2013) 'Distinguishing erosive osteoarthritis and calcium pyrophosphate deposition disease. *World J Orthop*. 4(2): 29-31

[12] Goekoop, R.J et al. (2011) 'Determinants of absence of osteoarthritis in old age'. *Scan J Rheum*. 40(1): 68-73

[13] Snodgrass SJ, Rivett DA, Chiarelli P, Bates AM, Rowe LJ, Aust J Physio 2003; 49(4): 243-50

[14] Hochberg, M.C. et al. (1993) 'Obesity and osteoarthritis of the hands in women'. *Osteoarthritis Cartilage* 1(2): 129-35

[15] Denisov, L.N. et al. (2011) 'Role of obesity in the development of osteoarthrosis and concomitant diseases'. *Ter Arkh*, pp 34-7

[16] Cicuttini, et al. (1996) 'The association of obesity with osteoarthritis of the hand and knee in women: a twin study. *J Rheumatol* 23: 1221-6

[17] Gabay, O and Gabay, C. (2013) 'Hand osteoarthritis: new insights'. *Joint Bone Spine*. 80(2): 130-4

[18] Jakowlev, K. et al. 'Search for hand osteoarthritis susceptibility locus on chromosome 6p12.3-p12.1'. *Human Biol*. 79(1): 1-14

[19] Zhang F, et al. 'Association between KLOTHO gene and hand osteoarthritis in a female Caucasian population'. *Osteoarthritis Cartilage* 2007; 15: 624-9

[20] Nakki, A. et al. (2011) 'Allelic variants of IL1RI gene associated with sever hand osteoarthritis'. *BMC Med Genet* 11: 50

[21] Kamarainen, O.P. (2006) 'Aggrecan core protein of a certain length is protective against hand osteoarthritis'. *Osteoarthritis Cartilage*, 14: 1075-8

[22] Bijsterbosch, J. et al. (2013) 'Association study of candidate genes for the progression of hand osteoarthritis'. *Osteoarthritis Cartilage* 21(4); 565-9

[23] Styrkarsdottir, U. et al. (2014) 'Severe osteoarthritis of the hand associates with common variants within the ALDH1A2 gene and with rare variants at 1p31. *Nat. Genet.* 46(5): 498-502.

[24] Crema, M. D. et al. (2013) 'Prevalent cartilage damage and cartilage loss over time are associated with bone marrow lesions in the tibiofemoral compartments: the MOST study'. *Osteoarthritis Cartilage* 21(2):306-13

[25] Haugen, I.K. et al. (2012) 'Associations between MRI-defined synovitis, bone marrow lesions and structural features and measures of pain and physical function in hand osteoarthritis'. *Ann Rheum Dis*. 71(6): 899-904

[26] Heberden, W. (1818) 'Commentaries on the History and Cure of Diseases', pp. 119

[27] Lian, T. Y. and Lim, K. K. (2004) 'The legacy of William Heberden the Elder (1710-1801)', *Rheumatology (Oxford, England)*, 43 (5), pp. 664-665.

[28] WHO (2014) *Chronic diseases and health promotion.* Available at: http://www.who.int/chp/topics/rheumatic/en/ (Accessed: 3/13 2014).

[29] Stecher, R. M. (1948) 'Heberden's Nodes: The Clinical Characteristic Of Osteo-Arthritis Of The Fingers', *Annals of the Rheumatic Diseases*, 7 (1), pp. 1-8.

[30] Swanson, A. B. and de Groot Swanson, G. (1985) 'Osteoarthritis in the hand', *Clinics in Rheumatic Diseases*, 11 (2), pp. 393-420

[31] Alexander, C. J. (1999) 'Heberden's and Bouchard's nodes', *Annals of the Rheumatic Diseases*, 58 (11), pp. 675-678

[32] Sandell, L. J. and Aigner, T. (2001) 'Articular cartilage and changes in Arthritis: Cell biology of osteoarthritis', *Arthritis Research*, 3 (2), pp. 107-113

[33] Pottenger, L. A., et al. 'The effect of marginal osteophytes on reduction of varus-valgus instability in osteoarthritic knees', *Arthritis and Rheumatism*, 33 (6), pp. 853-858

[34] Fassbender, H., G (2002) *Pathology and Pathobiology of Rheumatic Diseases*. 2nd edn. Germany: Springer.

[35] Brandt KD. Diagnosis and Nonsurgical Management of Osteoarthritis

[36] Hochberg, M.C. et al. (2012). 'American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip and knee'. *Arthritis Care Res (Hoboken)* 64(4): 465-74

[37] Maarse, W. et al. (2009) 'Medium-term outcomes following intra-articular corticosteroid injection in first CMC joint arthritis using fluoroscopy'. *Hand Surg* 14(2-3): 99-104

[38] Fuchs, S. et al. (2006) 'Intra-articular hyaluronic acid compared with corticosteroid injections for the treatment of rhizarthrosis'. *Osteoarthritis Cartilage* 14(1); 82-8

[39] Wenham, C.Y. (2012). 'A randomized, double-blind, placebo-controlled trial of low-dose oral prednisolone for treating painful hand osteoarthritis. *Rheumatology (Oxford)* 51(12): 2286-94

[40] Kingsbury, S.R. et al. (2013). 'Hydroxychloroquine effectiveness in reducing symptoms of hand osteoarthritis (HERO): study protocol for a randomized controlled trial'. *Trials* 14:64

[41] Saviola, G. et al.(2012) 'Clodronate and hydroxychloroquine in erosive osteoarthritis: a 24-month open randomized pilot study'. *Mod Rheumatol.* 22(2): 256-63

[42] Davis AJ, et al. (2013) 'Are bisphosphonates effective in the treatment of osteoarthritis pain? A research synthesis and meta-analysis'. PLOS ONE, 8(9):e72714