**Osteoarthritis Knee Pain: Applying the Evidence to the Person**

This is an outline of an evidence-based approach to Knee Osteoarthritis in the real world, with reference to diagnosis, management and innovation from a Sport and Exercise Medicine perspective.

**DIAGNOSIS**

Patients can be reliably diagnosed with knee Osteoarthritis on clinical grounds. The assessment is mainly about exclusion of other diagnoses. There is a wide variety of presenting features, but usage related joint pain in a patient over 45 without mechanical features or prolonged morning stiffness is OA until proven otherwise.

A clinical assessment holds the most weight in diagnosis. Plain “standing x-rays” can be performed to provide baseline information about the joint space, but don’t make the diagnosis. Special alignment x-rays may be helpful in assessing whether the medial (inner) or lateral (outer) knee compartment is under more pressure, particularly when there is visible mal-alignment. Bow-legged patients have increased medial compartment stress, while knock-kneed patients have increased lateral compartment stress. Further advanced imaging is usually unnecessary unless there are unusual features.

Clinical questionnaire scores are recommended to obtain a baseline measure with which to assess the effects of treatment. Validated measures include the KOOS (Knee Osteoarthritis Outcome Score) and WOMAC (Western Ontario McMaster University Osteoarthritis Index) questionnaire. Functional tests, such as the “Timed Up and Go”, or a timed 40-meter walk test, are usually undertaken with the Physiotherapist or Sport and Exercise Physician, to gain more objective information.

**Is an MRI needed?**

While advanced imaging is not recommended for OA, MRI is much more sensitive to identify early osteoarthritis, since once loss of joint space and bony changes are present on x-ray, the condition is fairly advanced. If you wish to obtain an MRI for diagnostic purposes, Medicare will not cover the costs and you must pay privately. Even meniscal tears as a part of the OA process are very commonly seen as horizontal tears in the older age group. The commonness of these tears and the lack of effective surgical treatment (4–6) means an MRI doesn’t really change the treatment if there is a clear diagnosis of OA.

## MANAGEMENT

### Understanding your goals is the starting point

Control over your treatment is critically important to getting the best outcomes. Things we are interested in knowing about you include:

- What do you want to be able to do on your knee?
- What exercise do you love?
- What have you done to date to manage your knee?
- What else do you think would help you?
- How do you think that would help?

### Why we need to Treat You and not just Your Joints

Osteoarthritis is a complex condition. It was initially also called “degenerative joint disease”, in reference to the progressive loss of articular cartilage. Then the emphasis changed; with the knowledge that there is more than “wear” related cartilage loss involved, and that both inflammatory and degradative pathways are involved that affect the whole joint, including periarticular tissues. More recently, the medical community are coming around to the notion that osteoarthritis is commonly an issue of general health, as both a sign and consequence of poor metabolic health.

### The Foundations of Treatment

To understand which treatments are likely to be effective for you, it is important to understand the different mechanisms underlying osteoarthritis. The harsh reality is that there are no disease-modifying agents for osteoarthritis, largely because the condition follows many complex pathways that are not fully understood. It is no longer true to say that osteoarthritis represents a simple “wear and tear” process, as part of normal ageing. It is true that ageing is a factor, but only part of the process involves joint wear from mechanical and traumatic factors. The arthritic process is also strongly driven by pro-inflammatory mediators that promote “Matrix Metallo-Proteinases” (MMPs), enzymes that progressively and irreversibly degrade articular cartilage, and also the other joint tissues including the meniscus and ligaments. These MMPs are thought to represent a final common pathway to joint damage, and inhibition of this process has proven difficult due to problems with toxicity and lack of clinical effectiveness.

Different “phenotypes” or classes of OA are thought to exist, which potentially changes the way treatment is directed.

**Inflammatory OA**
Most patients with osteoarthritis that affects multiple joints tend to be older. When it particularly affects the hands, hips and knees are said to have "Nodal OA", which seems to be mostly genetic and age related. In contrast, patients who have one or up to a few joints with significant morning stiffness and fluctuating, variable pain are likely to have a more "inflammatory OA" phenotype. There is some suggestion that this fluctuating, inflammatory phenotype may involve crystals in the joint, which can be treated differently.

**Trauma**
Post-traumatic osteoarthritis represents another common pathway to Knee OA. Cartilage injury may start the process of continued joint breakdown. Bone marrow swelling that is seen on MRI following significant knee injury (such as ACL rupture), correlates with the development of osteoarthritis.(8) Researchers have found that the injured bone under the cartilage releases chemicals and enzymes that lead to articular cartilage breakdown- raising the idea that the process of osteoarthritis may start in the bone.

**Metabolic OA**
There is a relatively new type; "metabolic associated OA". This is well supported studies showing overlap with features of the "metabolic syndrome".(9) The metabolic syndrome is a term that describes the condition when the body starts producing too much of the fat storage hormone called insulin, and diet and genetics mostly underlie it. It is known that abdominal fat produces circulating chemicals and cells, which are powerful promoters of inflammation.(10) This certainly supports the role of diet and exercise in promoting insulin sensitivity and reduction of central fat (the "pot-belly").

As we age, all of these processes gain momentum. Cellular ageing results in reduced responsiveness of joint cells and cartilage cells to growth and repair factors, and reduced cell turnover. At the same time, matrix ageing results in the accumulation of chemicals called AGEs (Advanced Glycation End-products),(12) which increases brittleness of articular cartilage. This has overlap with the "metabolic syndrome", as we age in a metabolically challenged society.

**Can we slow the progression?**

It is important to realise that symptomatic progression is generally slow in osteoarthritis. Not all patients are inevitably going to require joint replacement surgery. In fact, the symptoms of Knee Osteoarthritis tend to be stable over several years, with sudden deterioration being rare.(13) Therefore, you must learn to manage your symptoms, accommodate your lifestyle and daily activities to your joints and maintain some form of physical activity to stop the harms of a sedentary lifestyle.

We are currently still uncertain as to how to prevent deterioration in osteoarthritis. Despite many years of pre-clinical and clinical studies on a range of biological agents, there are no treatments that have a confirmed disease-modifying effect for osteoarthritis. Given that twin-studies suggest that 40% of OA is explained by genetics,(14) the future of prevention may be in manipulating this fact. SIRT-1 is an epigenetic protein and is responsible for multiple wide-reaching downstream effects, via increasing "gene expression" for the genes

that code metabolic health, inflammation and cell repair and death. It is seen to be inhibited in the metabolic syndrome. Ways of modulating SIRT-1 are being explored as an overarching means of managing many of the health concerns of modern society- including osteoarthritis. The good news is that SIRT-1 appears to be upregulated by the things we do to improve general health- exercise and diet (caloric restriction).(15–17) The future may hold therapeutic agents that are able to upregulate it (the so called “Exercise in a Pill” concept). Although this seems convenient, I wouldn’t hold my breath for this.

**What is the most effective type of exercise?**

Progressive resistance training appears to have the most benefit for pain and function. It must involve both the hip girdle and upper thigh musculature. The skill is to provide adaptive training stimulus without exacerbating symptoms. Dynamic or high velocity movements impart high levels of shear and compressive forces and should be avoided. Static exercises are a safe point to start with. It is critical to allow at least one day of rest between strength sessions to provide time for muscle protein synthesis and repair.

The evidence suggests that general aerobic exercise is effective for pain management. Walking or cycling are straight forward and easy to do. Experienced clinicians prefer cycling because intensity can be increased without impact or high peak loads. Tai Chi and aquatic exercise are also excellent options.(18) The key is to find exercise you enjoy and are likely to adhere to. You should aim to build up to the recommended guidelines of 30 minutes, 5 days per week; to accumulate at least 150 minutes of moderate intensity exercise weekly.

**Activity Modification- Striking the right balance**

Patients commonly ask us whether they can continue to play their sport. This is difficult to answer scientifically because there is limited and conflicting data on whether impact sports (running in particular), accelerates osteoarthritis. For the development of knee OA, the best available evidence suggests that normal knees are actually protected with repetitive, low impact exercise such as recreational running. Risk of OA increases with repetitive high impact exercise (such as competitive running or sport, which may be due to increased injury risk).(19–22) However, abnormal or injured knees (whether there is osteoarthritis, malalignment, pre-existing injury, meniscus injury or nerve problems) appear to have increased risk of progression to osteoarthritis even with repetitive, low impact exercise such as recreational running. All tissues in the body are dynamic and resilient, but once there is joint damage, the repair process cannot keep up.

**Balancing Evidence with Accessibility- what Adjunctive treatments are worth considering?**

Beyond education, weight loss and exercise, which should be prescribed to all patients, other treatments are optional, but likely to be of value if they can promote useful exercise. These treatments can be tailored to the individual depending on the severity of their symptoms, and perhaps the "phenotype" of their knee OA. Some of the treatments with evidence of effectiveness include topical and oral Anti-inflammatories, Strontium, Colchicine and Injections- including Cortisone, Platelet-rich plasma and Hyaluronic Acid. **A checklist summarising each treatment is included below.**

Recently, Mesenchymal Stem Cells (MSCs) obtained from blood, fat or bone marrow have been used in clinical practice. These have evidence of effect in clinical trials of non-healing ulcers and fracture non-unions.(58,59) Similar to the evidence for PRP injections, there are promising results but high risk of bias among all of the RCTs to date. MSC injections appear to pose little risk of physical harm with no major adverse effects reported. (60–62) A recent systematic study reveals the high risk of bias of all smaller studies that have been performed, and recommended against clinical use of these injections.(63) The Australasian College of Sport and Exercise Physicians (ACSEP) position, is that stem cell therapy should not yet be offered as a part of routine clinical practice, but should continue in research settings until safety and efficacy are demonstrated.(64,65) This treatment costs around $10,000 for the harvesting, processing and re-injection of stem cells. Currently, stem cells might be a justifiable last resort for joints that don't have better surgical options (like ankle joints).

**When is it time for surgery?**

There is no role for knee arthroscopy in knee OA unless you have knee locking and giving way and your symptoms have not responded to a proper 6-week course of physiotherapy. Well conducted studies have consistently shown that the outcomes for surgery are no better than physiotherapy alone,(4,6,66–71) with the caveat that some patients do fail physiotherapy and cross over to the surgical arm. Whether a meniscal tear or mechanical symptoms are present does not seem to make a difference to the long-term outcomes. While an arthroscopy is very easy to book in for, it usually doesn't help and also has significant risks (clots, bleeding, joint damage and even death).

High Tibial Osteotomy (HTO) is a realignment procedure that is initially painful, but effective. It involves breaking the medial side of the tibia, holding it open with a plate, and allowing bone to fill the defect so that the leg is less bow legged. It gives an average of 12 years of pain relief before patients require total knee replacement.(72) It is generally offered to active patients under the age of 55, with isolated medial compartment knee OA.

Uni-compartmental joint replacement can be done for either compartment. Again, this provides long-term improved pain and function in these patients.(72) Overall patients are very satisfied at an early stage following the procedure. Very active patients may be at risk of early prosthetic wear or loosening. The conversion to total knee replacement is made slightly harder due to loss of some bone around the components.

**Future directions**

There are many innovative treatments under investigation that aim to target the pain generators, inflammatory and catabolic processes involved in knee OA.

Patients often come to Sport and Exercise Physicians for injections. Before offering anything invasive, a checklist of the evidence based treatments should be completed. Review of the KOOS score change from baseline helps quantify the effects of treatments on pain and function.

**KNEE OSTEOARTHRITIS TREATMENT CHECKLIST**

**Essential**

□ Monitoring progress with KOOS score
□ Weight Loss (with formal support)
□ Exercise (with formal support)
□ Activity Modification to find optimal joint load
□ Topical Voltaren or Capsaicin gels
□ Alignment correction- Trial of Valgising Knee brace

**May be Trialled (if no contra-indications)**

□ Physical agents like acupuncture or TENS
□ Short course NSAIDs for flares of pain
□ Paracetamol (3g/day) if NSAIDs contraindicated
□ Nutraceuticals (Fish Oil, ASU, Glucosamine/Chondroitin)
□ Colchicine (if evidence of CPPD)
□ Duloxetine (if moderate/severe pain)
□ Strontium (if evidence of bone marrow oedema)

**More Invasive Adjuncts**

Injectable agents including:
□ Cortisone
□ HA
□ PRP
□ ACS are all options to facilitate function
□ Joint sparing surgery (HTO or Uni-compartmental Knee Replacement)

□ Last Resort- Total Knee Replacement

**Not Recommended**

Arthroscopic lavage or meniscectomy
Bisphosphonates
Biological agent injections (FGF-18 or Tanezumab)
Mesenchymal Stem Cells (unless under research conditions)

If you decide to go ahead with an injectable treatment, it needs to be combined with specific post-injection instructions. In my practice, patients must take 5 days off any formal exercise. They must meet their rehabilitator 1 week following the injection to re-commence progressive strengthening. A review in 4 weeks generally allows an accurate assessment of the effect on any injection.

If there are any concerning symptoms (mainly locking), a lack significant improvement or severe deterioration in symptoms and function, as measured by the KOOS score in 6-8 weeks of conservative treatment, a surgical opinion is worthwhile.