Osteoarthritis in 2011: Many steps to climb

Osteoarthritis is a primary disorder of hyaline cartilage that results in secondary changes in subchondral bone and eventually joint failure.

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What is osteoarthritis?

Osteoarthritis (OA) is defined as a primary disorder of hyaline cartilage that results in secondary changes in subchondral bone and eventually joint failure.

Epidemiology and risk factors

OA is the most common chronic musculoskeletal disorder, and the leading cause of disability in elderly persons.[1] Symptomatic knee OA affects approximately 40% of adults over 70, and a quarter of these patients have difficulty carrying out their activities of daily living. The number of persons suffering from OA is increasing as people live longer, and as obesity escalates. Osteoarthritis-related pain, or complications of pain treatment, is a major reason for consultation of health care practitioners and a significant socio-economic burden.

Symptomatic knee OA affects approximately 40% of adults over 70, and a quarter of these patients have difficulty carrying out their activities of daily living.

Primary OA affects the knee, hip, hand, the first metatarsophalangeal joint of the foot and the lumbar and cervical spine (Fig. 1). The disease is said to be 'generalised' when 3 or more joints are affected. Of note is that the metacarpophalangeal, wrist, glenohumeral, temporomandibular, ankle and sacro-iliac joints are rarely affected in primary OA. Involvement of these joints should prompt a consideration of a secondary cause. Secondary OA may affect any joint, and causes include trauma, calcium pyrophosphate disease, rheumatoid arthritis and neuropathic arthropathy.

Hand OA affects the distal interphalangeal (DIP), the proximal interphalangeal (PIP) and the first carpometacarpal (CMC) joints, often associated with Heberden and Bouchard nodes, lateral deviation and flexion at the DIPs, and 'squaring' of the hand at the CMC joint. An aggressive subtype, erosive OA, is characterised by inflammatory episodes with severe pain and disability, and subchondral erosions on X-rays (Fig. 2).

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Primary OA is a multifactorial disease, with predisposing factors including age, female gender and abnormal joint mechanics resulting from, for example, ligament laxity, malalignment or muscle weakness. There is a genetic predisposition to certain types of OA: in hand and knee OA, genetic factors contribute a risk of 39% and 65% respectively.[2] The disease is polygenic, and both structural genes controlling cartilage and bone morphogenesis as well as genes involved in thyroid regulation, apoptosis and inflammation have been implicated.[3] Obesity is not only a risk factor for OA of weight-bearing joints (the knee in

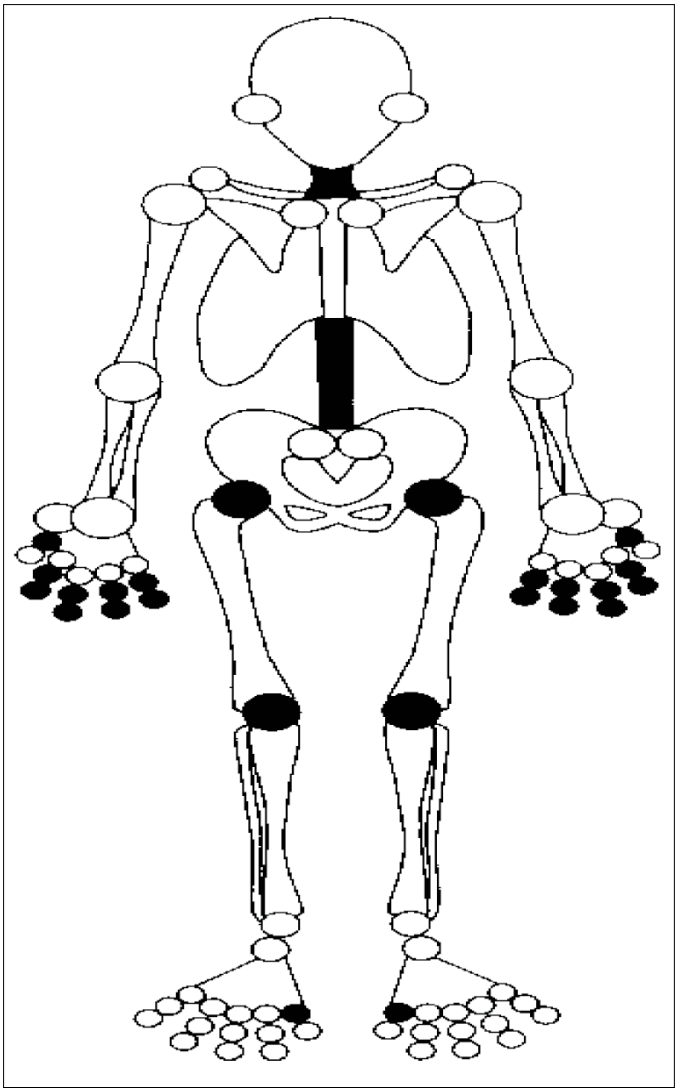

Fig. 1. Sites of primary osteoarthritis. These include the knee, hip, hand DIP, PIP and first carpometacarpal joints, the first metatarsophalangeal joint of the foot and the lumbar and cervical spine. Involvement of other joints should prompt consideration of an alternative diagnosis.

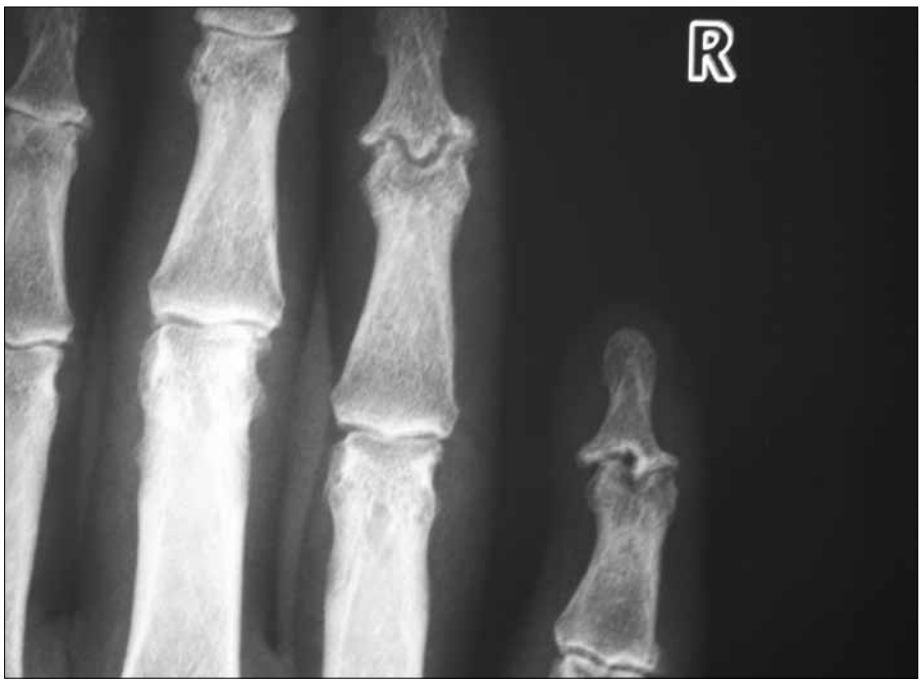

Fig. 2. Erosive OA of the hand.

Table I. Clinical features atypical of primary OA

Clinical feature	Diagnosis to consider
Atypical symptoms: acute, severe pain, swelling	Crystal arthropathy, sepsis, cartilage tear
Atypical joints involved, e.g. metacarpophalangeal joints	Haemochromatosis, rheumatoid arthritis
Prolonged stiffness after rest	Inflammatory arthropathy including rheumatoid arthritis
Rheumatoid factor positive	Rheumatoid arthritis but low titre RF is often seen in the elderly
Chondrocalcinosis on plain X-rays	Calcium pyrophosphate disease

particular), but also for hand OA. Each body mass index (BMI) increase above 27 confers a 15% increased risk of radiological OA and, conversely, weight loss results in improved pain and function.[4,5] These observations suggest that circulating metabolic factors like adipokines including leptin may play a role.

Obesity is not only a risk factor for OA of weight-bearing joints (the knee in particular), but also for OA of the hand.

In Africa, the epidemiology of OA is somewhat different to OA described in the West. Generalised OA is uncommon, and the oligoarticular forms of knee and spine OA are more frequently seen. Hip and hand OA and Heberden nodes are rare in African patients.[6] Mseleni joint disease, a rapidly destructive endemic OA, was first described in 1970 in northern KwaZulu-Natal, South Africa.[7] This disease predominantly affects the hips of middle-aged women, but can involve other large joints. No genetic or environmental cause has been found to date despite intensive investigation.[8]

Pathogenesis

There is increasing evidence that OA is an inflammatory process, with accelerated cartilage degradation coupled with a failure of adequate repair of damaged cartilage. Abnormal pressure on cartilage results in the release of inflammatory cytokines (IL-1, TNF, IL-6, IL-8) which activate chondrocytes prompting release of matrix metalloproteinases, leading to collagen and proteoglycan degradation. Dedifferentiated chondrocytes produce poor-quality extracellular matrix. Although the pathophysiology of OA has long since been considered cartilage-driven, recent work demonstrates involvement of both synovium and subchondral bone. Chronic patchy synovitis is seen in OA, and may be triggered by cartilage debris entering the synovial cavity, causing activation of synovial macrophages and resulting in further degeneration of cartilage, creating a vicious cycle of inflammation and degradation.[9] Bone changes occur early in the course of the disease, and may even predate cartilage changes, suggesting that alteration in bone metabolism may initiate cartilage damage.[10]

Diagnosis

The diagnosis of OA is based on a combination of clinical findings and radiological features. The typical history is one of chronic joint pain, worsened by activity, with or without brief stiffness occurring in the morning, after inactivity or in the evening. Inflammatory flares may occur during the course of the disease. Examination may reveal bony swelling, crepitus, joint line tenderness, possibly with a small effusion. X-ray changes include osteophyte formation, joint space narrowing and bony sclerosis. Table I outlines features atypical of primary OA, which should prompt consideration of an alternative diagnosis.

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Ultrasound, CT scans and MRI scans demonstrate details of the joint abnormalities, and are particularly informative in early pre-symptomatic disease, but their exact role in the clinical setting is not yet clear. Similarly, blood investigations are not indicated unless there is a suspicion of other diseases. Acute-phase reactants such as the erythrocyte sedimentation rate and C-reactive protein (CRP) are normal except rarely in the setting of erosive inflammatory OA, which can associated with a mildly elevated CRP, not

exceeding 20 mg/l. Biomarkers of cartilage degradation have been studied as diagnostic and prognostic tools but none has performed well enough to be of use in clinical practice.

Management

Pain is the first and predominant symptom of OA, and treatment of OA therefore focuses on reducing pain and maintaining and improving function. It should be remembered that non-pharmacological therapies are often as effective as pharmacological treatments.

Non-pharmacological therapy

Patient education is beneficial to patients living with a chronic illness. Knowledge of treatment options allows patients to better manage their disease and their pain, with positive effects on adherence to therapy and on health-related quality of life. Information on OA is available from various websites (see below).

Joint-specific exercise programmes can improve joint range of motion and muscle strength, which may alleviate pain. In addition, regular exercise has cardiovascular, weight reduction and psychological benefits for any patient. Because long-term adherence to a programme is critical, patients should be encouraged to select an exercise that they enjoy, bearing in mind that there is evidence for benefit of swimming, cycling, walking, tai chi and yoga, among other exercise regimens. Quadriceps strengthening exercises are important in the management of OA of the knee.

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Weight loss, even modest amounts in overweight or obese patients, can improve joint pain and function, and has been recently shown to improve cartilage structure and reduce inflammatory markers in the joint.

Assistive devices such as lateral wedged insoles redistribute weight on a lower limb joint compartment, and are of particular use in OA of the knee, and cushioning insoles may benefit both knee and hip OA sufferers. Simple elastic knee sleeves can reduce pain and instability in knee OA. Stiff braces reload mechanical stress on a symptomatic joint compartment, and may be made by a physiotherapist or occupational therapist. Walking aids including a cane, crutches or walking frame are of use, and in the case of unilateral knee or hip OA should be held in the contralateral hand. For thumb-base OA, resting splints have good effect on pain, disability and correction of lateral angulation.[11]

Acupuncture, thermotherapy and transcutaneous electrical nerve stimulation may significantly reduce pain and are worth exploring by a motivated patient.

Pharmacological therapy

Because of its safety, **paracetamol** is the oral analgesic of first choice, but many patients have been using the drug with limited effect before consulting their health care practitioner. A dose increase to the maximum of 4 g/day may be beneficial; although recent reports have questioned both the gastro-intestinal and renal safety of paracetamol.

Opioid analgesics (added to paracetamol), including codeine or tramadol, can be considered in a patient with severe pain despite paracetamol, but side-effects include drowsiness, confusion and constipation. A recent study in an elderly population found a paracetamol-tramadol combination to be both effective and safe.[12]

Non-steroidal anti-inflammatory drugs (NSAIDs) are superior to simple analgesics in relieving nocturnal pain and joint stiffness. However, they need to be prescribed with extreme caution because of the risk of potentially life-threatening adverse effects. They are a major cause of both upper and lower gastrointestinal (GI) tract events including bleeding, perforation and obstruction. Within 2 months of NSAID use 1 in 5 healthy patients can develop an endoscopic peptic ulcer.[13] Of note, there is no relationship between symptoms such as dyspepsia and the presence of endoscopic lesions, and the majority of lesions are asymptomatic. Hence, NSAIDs should be used in the lowest effective dose and for the shortest duration of time. In patients with high GI risk, either a non-selective NSAID with co-prescription of a proton pump inhibitor or misoprostol for gastroprotection, or a COX-2 selective agent (coxib) should be considered[14] (Table II).

Table II. Prescription of anti-inflammatory drugs based on cardiovascular and gastrointestinal risks (modified from Chan *et al. Am J Gastroenterol* 2008;103:221-227)

	Low GI risk	High GI risk*
Low CV risk	Non-selective NSAID	Non-selective NSAID + PPI or coxib as monotherapy
High CV risk#	Aspirin + naproxen + PPI	Avoid all NSAIDs

GI=gastrointestinal, CV=cardiovascular, NSAID=non-steroidal anti-inflammatory drug, coxib=selective cyclo-oxygenase-2 inhibitor, PPI=proton pump inhibitor.

*High GI risk defined as age ≥70, previous peptic ulcer disease and co-prescription of aspirin, corticosteroids or anticoagulants.

#High CV risk defined as established coronary artery disease, or Framingham risk score ≥ 20%.

There is also an increased risk of thrombotic events, strokes and coronary events, with all NSAIDs, both coxibs and non-selective NSAID agents, with the possible exception of naproxen.[15] These drugs should be used with caution in patients with cardiovascular (CV) risk factors. Co-prescription of aspirin may complicate matters further, as NSAIDs interfere with the antiplatelet activity of aspirin, and aspirin negates the GI-sparing effects of coxibs. Clearly many elderly OA sufferers have both GI and CV risks, placing their doctors 'between a rock and a hard place', and here alternatives need to be considered. Other side-effects of NSAIDs including hypertension, renal and liver dysfunction should not be forgotten. Blood pressure should be checked within a month of initiating NSAID therapy. Topical NSAIDs are safe but not widely used and are effective and helpful, particularly in patients with contraindications to oral NSAIDs.[16]

Recently, the CINODs have been developed by adding a nitric-oxide-donating group to

a NSAID, with early trials of naproxcinod showing good efficacy but less risk of CV and GI events.[17]

Over the past decade or two there has been much debate about the efficacy of **neutriceuticals** such as glucosamine and chondroitin in OA. Most studies show, at best, a modest beneficial effect on pain (particularly in the case of glucosamine sulphate), with a recent 5-year study showing a reduced incidence of total knee replacement in patients taking glucosamine compared with placebo.[18] The evidence for a structure-modifying effect of these drugs is less convincing, with some studies showing preservation of joint space but others disputing this. Given that these agents have no major side-effects, a practical recommendation is a trial of glucosamine sulfate 1 500 mg/day with chondroitin for 3 - 6 months; if no symptomatic benefit is experienced, the drug should be discontinued.

Intra-articular injections

Injections of long-acting **corticosteroids** are effective, particularly during inflammatory flares. Knee, IP and CMC joints of the hand may benefit from such an approach, possibly done under sonar guidance for accurate needle placement.

Hyaluronic acid injections repeated 3 - 5-weekly have shown improvements in pain and function for up to 6 months in knee arthritis. The drug has also been used in the CMC joint with some benefit.[19]

Surgery

Arthroscopic lavage and debridement is not effective treatment of OA and is indicated only where a cartilage or ligament tear is suspected.

Failure of medical management of symptoms is the major indication for **total joint replacement** (TJR), and a patient with severe pain, particularly nocturnal pain that is unresponsive to analgesics, or disability (unable to walk one block, climb one flight of stairs), should be offered joint replacement surgery. Trapeziectomy or CMC joint replacement may be considered for patients who have failed conservative treatment of base of thumb OA.

New horizons

Improved understanding of the pathogenesis of OA has opened the door to the possibility of developing new targeted treatments for the disease, and currently there are at least 33 clinical trials underway exploring novel therapies for symptom and structure in OA.[20] Drugs interfering with inflammatory cytokines (anti-IL-1 and IL-6, anti-TNF) or pain pathways (anti-nerve growth factor antibody), and subchondral bone molecules such as calcitonin and strontium ranelate, are possible future directions of therapy for OA.

Compared with the other rheumatic diseases, pharmacological treatment for OA is relatively unsatisfactory.[20] Clearly, with more than a quarter of people over the age of 65 suffering from OA, there is a need for new therapies. For now, much of the answer lies in avoiding the progression of OA, chiefly through non-pharmacological approaches: avoidance of obesity, exercise, podiatry and assistive devices to address joint malalignment with maintenance of muscle strength, and in sensible use of analgesics.

Useful websites with patient information on OA and its treatment

http://www.uptodate.com/contents/patient-information-osteoarthritis
http://www.hss.edu/conditions_14404.asp
http://www.patient.co.uk/health/Osteoarthritis.htm
http://www.arthritis.org.za

References available at www.cmej.org.za

IN A NUTSHELL

- Osteoarthritis is common, and a significant cause of disability and a major reason for health-care utilisation.
- The diagnosis of OA is clinical, and an alternative diagnosis should be considered if atypical features are present.
- Bony swelling, crepitus, and joint line tenderness are clinical features.
- X-ray changes include joint space narrowing, osteophytosis and bony sclerosis.
- The optimal management of OA requires a combination of non-pharmacological and pharmacological therapy.
- Non-pharmacological therapy includes education, weight loss if overweight, exercise and assistive devices including walking aids and orthotics.
- Patients with high GI risks should have either a non-selective NSAID with co-prescription of a proton pump inhibitor for gastroprotection, or a COX-2 selective agent.
- All NSAIDs, both coxib and non-selective agents, confer an increased risk of thrombotic strokes and coronary events.

SINGLE SUTURE

Drug driving test at your fingertips

A fingerprint is all you need to determine whether someone is under the influence of drugs.

Paul Yates from Intelligent Fingerprinting, a company spun out from the University of East Anglia in Norwich, and colleagues, have developed a hand-held device that police can use to detect breakdown products from drugs excreted through sweat pores in the fingertips.

The device applies gold nanoparticles coated with antibodies to a fingerprint. The antibodies stick to antigens on specific metabolites in the fingerprint. Fluorescent dyes attached to the antibodies will highlight the presence of any metabolites. The technique was first used to detect nicotine, but now works on a range of drugs, including cocaine, methadone and cannabis.

It is hard to prove that someone is drug driving, for example, says Yates, because existing tests are invasive, can be contaminated or are not sensitive enough. The new device could detect nanograms of metabolites in minutes, he says. The device was announced at the UCL International Crime Science Conference in London recently.

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