

## Public Health Classics

This section looks back to some ground-breaking contributions to public health, reproducing them in their original form and adding a commentary on their significance from a modern-day perspective. To complement the theme of this month's *Bulletin*, Peter Brooks reviews osteoarthritis in the light of George E. Ehrlich's 1975 paper reporting on the importance of inflammation in a study of 170 patients. The original paper is reproduced by permission of the American Medical Association.

### Inflammation as an important feature of osteoarthritis

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George Ehrlich's paper "Osteoarthritis beginning with inflammation: definitions and correlations" emphasized the importance of inflammation as a component of osteoarthritis (1). In this paper, published over 25 years ago, Ehrlich described a cohort of predominantly menopausal females who presented with a deforming and inflammatory osteoarthritis, some of whom went on to develop changes characteristic of rheumatoid arthritis. Although the majority of patients were controlled with standard anti-inflammatory medications, a minority of the cohort suffered exacerbations of their disease and developed more extensive evidence of inflammation, including a positive rheumatoid factor. These patients presented initially with primarily interphalangeal involvement with clinical features of pain and inflammation. Large joints such as the shoulder and knee were also involved.

Ehrlich raised the issue that this particular syndrome might be at the "interface" between osteoarthritis and rheumatoid arthritis, and inflammation is now well accepted as a feature of osteoarthritis. A current working definition of osteoarthritis maintains that it is a condition of synovial joints characterized by cartilage loss and evidence of accompanying periarticular bone response. Examination of synovial tissues from patients with osteoarthritis clearly shows evidence of inflammation, though this is not as aggressive as that seen in the inflammatory arthropathies such as rheumatoid arthritis. A key feature of osteoarthritis is the cartilage loss and the accompanying periarticular bone response which leads to the development of osteophytes and subchondral sclerosis. This is also accompanied by a degree of synovitis. With ageing of the population, the importance of osteoarthritis as a cause of disability is increasing in both industrialized countries and the developing world.

Osteoarthritis remains one of the most common forms of musculoskeletal disease described in all countries of the globe. It is the fourth most common predictor of health problems worldwide in women and the eighth most common predictor of ill-health in males (2). Using a community-based questionnaire — Community-Oriented Program for the Control of Rheumatic Diseases (COPCORD) — nearly a third of participants reported current musculoskeletal pain in a Cuban population, with osteoarthritis being the most common diagnosis (3). The prevalence of radiographically defined osteoarthritis has been estimated in two studies representative of the United States population, the National Health and Nutrition Examination Survey (NHANES): NHANES-1 of

1971–75 looked at hips and knees, and NHANES-3 was conducted between 1992 and 1998. NHANES-1 reported radiographical evidence of osteoarthritis in more than 70% of persons aged between 55 and 78 years (4). The majority of persons over the age of 65 years of age have a least one joint involved with radiographically defined osteoarthritis. Women tend to be more affected than men and there are also regional differences described in the pattern of osteoarthritis across the world (5). For example, hip osteoarthritis seems to be less common in Africa and Asia than in Western countries (6).

Given the ageing population in the majority of countries around the world, the impact of osteoarthritis on public health and the significant costs that musculoskeletal conditions generate will affect all societies as we move into the future (7). These costs will be made up of a number of factors including loss of productivity, use of health services including physiotherapy, pharmaceuticals and the increasing burden of surgical treatment with arthroplasty.

Although there is evidence that the progression of osteoarthritis may be mechanically driven with varying degrees of inflammation, well-established risk factors including ageing, obesity, gender and, in selected subgroups, congenital abnormalities have been described (8). Local factors such as physical activity or injury are important, but other issues such as the strength of muscles around a joint, ligament laxity, and factors such as proprioception may also play a role in both the initiation and progression of osteoarthritis. Once the joint has been damaged, continuing use is likely to speed the pathological process, emphasizing the importance of prevention and early management of joint trauma.

Genetic factors determining the biochemical constituents of bone and cartilage may place individuals at an increased risk of osteoarthritis. Given the number of cell types in cartilage and bone, there is the potential for many genes to contribute to the predisposition to osteoarthritis.

The importance of obesity as a risk factor for development and progression of knee osteoarthritis, in particular, is relevant in that weight reduction can significantly lessen pain and disability (9). The association of weight with osteoarthritis of the hip is much weaker, though obesity will certainly exacerbate symptoms of hip osteoarthritis. Given the increasing prevalence of obesity around the world, obesity remains an important consideration in osteoarthritis prevention and management.

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Moderate exercise and regular physical activity, along with patient education programmes, have been shown to have a positive effect on the symptoms of osteoarthritis (10). The benefits of a moderate physical activity programme in osteoarthritis may be produced by a number of factors including weight reduction and increased strength and support of muscles around the joint. These beneficial features are also demonstrated in patient education programmes that tend to focus on self-management. Other interventions such as careful alignment of footwear with wedging of the insole and knee bracing have also been described (11). In many countries, acupuncture is widely used for the treatment of osteoarthritis; however, a recent systematic review of acupuncture describes methodical problems in many trials with the most carefully conducted studies, showing no benefit of acupuncture over sham treatment for osteoarthritis pain (12).

Although the practice guidelines endorsed by the American College of Rheumatology (ACR) recommend acetaminophen (paracetamol) as initial therapy for osteoarthritis, a number of studies have suggested that patients with osteoarthritis of the knee express a clear preference for non-steroidal anti-inflammatory drugs (NSAIDs) in terms of pain relief as opposed to analgesics (13). This probably depends on the degree of inflammation associated with the osteoarthritis and — since this may be intermittent — leads to the clinical observation that patients with osteoarthritis do not always take anti-inflammatory drugs on a continuing basis. Systematic reviews of the use of NSAIDs in rheumatoid arthritis continue to demonstrate that NSAIDs reduce short-term pain in osteoarthritis in comparison with placebos but there is limited evidence of benefit over simple analgesics (14). This has to be balanced by the significant gastrointestinal adverse events associated with NSAIDs, although such events are significantly fewer with the COX-2 selective inhibitors (15).

The widespread use of glucosamine for osteoarthritis reflects an increasing use of nutraceuticals in musculoskeletal

pain. An increasing number of studies concerning the benefit of glucosamine in osteoarthritis have been described and systematic reviews have demonstrated evidence of efficacy of glucosamine in relation to placebo (16).

The debate as to whether NSAIDs should be used as initial treatment for osteoarthritis continues to rage, with some patients clearly benefiting from their use. It is interesting that the efficacy of anti-inflammatory drugs in this common chronic condition could be predicted by the clinical observation by Ehrlich some 25 years ago that significant numbers of patients with osteoarthritis do have clinical evidence of inflammation, albeit intermittently.

Despite preventive, nonpharmacological treatment and drug therapy, some patients with osteoarthritis become significantly disabled. For patients with progressive joint destruction, modern surgical techniques with hip and knee replacements provide enormous relief in terms of pain alleviation and reduction of disability. These operations are among the most cost-effective surgical procedures available, with a cost per DALY (disability-adjusted life year) in the order of Australian dollars 8000 and Australian dollars 12 000 (approximately US\$ 4800 and US\$ 7200) respectively (17).

Given the increasing prevalence of osteoarthritis, health systems around the world will need to develop strategies to focus on this epidemic. By developing a range of approaches, including primary and secondary prevention, the majority of patients can be managed without resort to surgery. However, in those patients with significant pain causing interference with lifestyle, arthroplasty offers significant and lasting relief.

The report from George Ehrlich on inflammation in osteoarthritis in 1975 is as relevant now as it was then. Osteoarthritis is a disease that causes significant pain and disability and leads in many cases to lasting joint damage: all countries need to focus on preventive and treatment strategies to reduce the burden it causes in the community. ■

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