Osteoarthritis

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Background—where do we stand today?

Historical background

At the beginning of this century, chronic arthritis was differentiated into two main categories through a combination of radiographic and pathological criteria (1). Hypertrophic arthritis, characterised by new bone formation around the damaged joint, was differentiated from atrophic arthritis, which featured bone erosion and inflammatory synovitis. Subsequently atrophic arthritis attracted much attention and interest, spurred on by inflammatory and immunological phenomenology, whereas the much commoner hypertrophic form was associated with aging and trauma, and was equated with previous descriptions of joint destruction in the elderly, such as "malum coxae senelis". Thus the disease that we now call osteoarthritis (OA) became labelled as "degenerative" and "a wear-and-tear condition," resulting in negative attitudes amongst both patients and doctors. The recent revival of research interest in OA has owed more to connective tissue biology than to clinical interest (OA has become a cartilage disorder instead of a degenerative disease), but growing recognition of the enormity of the health care problem caused by OA should result in it now becoming a clinical priority.

Prevalence, morbidity and cost for society

The prevalence of OA is huge (2,3,4), although difficulties in definition, as well as discrepancies between the radiographic evidence of joint damage (the main tool used to detect OA) and clinical problems, result in variations in the quoted figures. The main morbidity and impact on society arise in older people with OA of the lower limbs (knee and hip disease) or spine. Some 25% of people over the age of 60 have significant pain and/or disability from these conditions (2,3,4).

The problem is a world-wide one, and its frequency is rising as populations become generally older and otherwise fitter. The recent WHO publication on the burden of disease (5) show that OA is one of the world's largest health care problems. Using calculations based on years lived with disability (YLDs), OA comes out as being predicted to become the 4th most important condition in women and the 8th in men in developed countries. Using disability adjusted life years (DALYs), OA remains the 4th most frequent predicted cause of problems world-wide in women, and the 8th in men.

The economic implications vary in different countries, depending on the amount of work loss, as well as the care provided, and in particular on the provision of hip and knee joint replacements (globally, some 80% of all joint replacements are done for OA of the hip or knee). However, it is clear that the economic consequences of OA are also enormous - it is, for example the first rated cause of work loss in the USA, in spite of being a condition which causes most problems to populations of retirement age (6,7).

Pathophysiology

OA is characterised by focal areas of loss of the articular cartilage of synovial joints, combined with hypertrophy of marginal and underlying bone, mild synovitis and capsular thickening.

- Risk factors include a variety of intrinsic factors that confer a predisposition to the disease (age, sex, race) and extrinsic factors that can damage joints (occupation, injury, sport etc.). These risk factors carry different weight for varying joints (8).
- Initiation depends on the balance between tissue resistance to injury, and degree of mechanical insult—this results in three distinct forms of OA: 1) rare early, widespread disease due to a genetic abnormality resulting in poor tissue resistance (e.g. alkaptonuria, Col 2A1 abnormalities); 2) post-traumatic OA in single joints (e.g. after anterior cruciate ligament rupture) and 3) the most common form, due to age-related OA due to accumulation of injury in older people, and age-related loss of tissue integrity (9).

- Progression is less well understood, but appears to be a mechanically driven but biochemically dependent phasic disease process, involving all joint tissues (bone, synovium, capsule etc., as well as cartilage), and mediated by cytokines and proteases. It is becoming clear that different factors drive progression from those responsible for initiation of OA (10,11), which is very important to the future basic research agenda.

Diagnostic procedures

Early diagnosis is difficult for two reasons: 1) patients tend to present late because of the gradual onset of pain and disability, which many people regard as an inevitable part of aging that they can adapt to; 2) early joint damage is difficult to detect without very invasive or expensive procedures (such as arthroscopy or magnetic resonance imaging respectively). The diagnosis of late disease is easy on both clinical and radiographic grounds, although the impact of attendant pain and disability is less easy to assess and quantify.

Treatment modalities

Current therapy is palliative, being designed to reduce pain and disability rather than altering the disease process. However, there has been a huge recent awakening of interest in the management of OA within science and industry, which has already helped to increase the number of options and quality of care that can be provided to help people with OA. One of the current challenges is to find ways of making sure that the huge numbers of people in the community who could benefit from such interventions get them—and this could be one of the objectives of the "Decade" campaign, which, from the point of view of the OA sufferer, is timely.

Guidelines to treatment have been developed (12). A pyramidal approach is recommended, starting with simple measures such as education and empowerment, advice about joint protection etc., footwear alterations and exercises; then going on to drugs (local and systemic), injections and other therapies in more severe cases; reserving surgery for the worst affected. However, therapy needs to be better individualised to patients problems of pain or restrictions of activities/ participation, and it is clear that many patients could benefit more if "fast-tracked" to the more invasive interventions such as surgery. There appears to be widespread ignorance of the large range of options available, especially in primary care.

Outcome

Surprisingly little is known about the natural history of OA. However, it is clear that the outcome, both in terms of the joint damage and the impact of patients, is very heterogeneous. Joint damage can be stable or rapidly progressive, and is accompanied by very variable degrees of bone reaction (atrophic and hypertrophic forms of OA). Clinical outcomes depend on a large number of variables that include age, the joint site involved, degree of joint damage, many psychosocial variables (such as anxiety, depression, isolation and poverty), and attendant periarticular and muscular problems, as well as co-morbidities in older people (age-related muscular weakness and neuromuscular lack of co-ordination may be amongst the most important determinants of OA outcomes).

Some patients develop severe joint damage, pain and disability, despite conservative therapy, necessitating joint replacement surgery. Progression to this point is probably inevitable after joint damage has reached a critical point (a hypothetical "point of no return"), but it is not yet clear how this point can be defined, or how we can identify the critical sub-group of patients who are going to progress. Although a small percentage of the total number of those with OA, this sub-group still constitutes a large number of people, and it is the main cause of the huge personal and economic burdens arising from OA, including hip and knee replacements (13). However, another current issue in OA outcome and management is the diversity of prostheses available and the absence of evidence based indications for joint replacement surgery.

Future perspectives

Epidemiology

OA is already a huge problem, and it is bound to become an even bigger one unless major progress can be made towards prevention, cure, or both. The aging populations (particularly the huge predicted increase in the global population over 50 years old over the next few decades), and quite appropriately increasing demands for good health amongst older people, is bound to result in an increase in the burden of pain, disability and economic costs caused by OA. There is no justification for OA being a low health care priority, either morally or economically.

Prevention and treatment

OA has been described as one of the "age-related disorders of evolution" (14)—a condition that we get because of our longevity, the way in which we use our joints (which is not that for which they are well designed) and the lack of genetic investment in the repair of age-related tissue damage. If this paradigm is correct, then it may be inappropriate to look for a sim-

ple biological cures. Furthermore, the high frequency of the condition, which often affects older people with intercurrent disease, suggests that relying on the development of expensive options such as drugs that interfere with the body's repair mechanisms, or cartilage transplants, are not sensible ways to forward in the global perspective. Primary prevention may be a better way to go.

Primary prevention: There is much current interest in the genetic predisposition to OA (15), and we can expect further developments in this area - although it is not clear how this will help in prevention of such a common phenomenon. At a global level, environmental risk factors would appear to be a better target for intervention, and we should be looking for population based strategies which will protect our joints from OA. Risk factor analyses offer us lots of potential targets, including:

- Reduction in the prevalence of severe obesity (a major risk factor for knee OA).
- Reducing life-long impact loading on joints through improved footwear.
- Avoiding certain occupational activities which confer a high risk, such as working in the squatting position, and habitual heavy loading.
- Maintaining general fitness, a full range of motion of all joints, and the strength of all muscles acting on vulnerable joints.
- Reducing the incidence of specific injuries which predispose to OA, such as anterior cruciate ligament rupture.

In general "what is good for the heart is good for the joints" (keep slim, fit and active, without overdoing it or being susceptible to high impact activities). However, it is not clear how such strategies for the prevention of OA can be successfully implemented at the population level.

Therapeutic developments: Lots of putative disease modifying agents are in development or clinical trial. These might work, but most depend on either reducing tissue breakdown or enhancing repair, and it is not yet clear what that will do to older people or other diseases, and the biological approach based on the belief that we can understand and reverse the cellular and chemical causes of joint damage may not work.

Developments in surgery: We can expect continuing technical developments and improvements in minimally invasive approaches (for uni-compartmental knee prostheses for example), as well as increasing high quality of surgical interventions.

Improvements in the control of pain and disability: Some recent research has thrown new light on the mechanisms that lead to the pain and disability that are the main causes of patient related problems in OA. We can expect and should promote more strategies aimed at reducing pain and disability, irrespective of joint damage.

Interventions for activity impairment should get better—e.g. by understanding and treating the attendant loss of muscular control around OA joints. For example, better muscular control around the knee joint may help prevent the initiation and progression of knee OA, as well as reducing the burden of pain and disability in those with established disease (16,17).

Goals for the next decade

A suggested agenda of health priorities for osteoarthritis:

- Increase the understanding of the size of the problem and impact of OA in both the public sector, and amongst purchasers of health care and policy makers—if we are to reduce the huge burden of pain and disability amongst older people, OA must come higher up the health care agenda than it does at present, and should be represented in health care with the same priority ranking that it receives as a cause of ill health in the recent WHO report (5).
- Improve public awareness that increasing age does not have to result in pain and disability, that they are both preventable and manageable, and that there are many different approaches to treatment available.
- Better use of current management, with improved delivery of currently available and new strategies that can reduce pain and disability, irrespective of joint damage; improving the access of all to these treatments, and increasing the likelihood that the right treatment is made available to each individual patient.
- The parallel development of evidence based indications for major interventions such as joint surgery.
- Research on the implementation of population strategies that are likely to reduce the incidence of OA by removal of environmental risk factors. This would involve developing and exploring strategies for the primary prevention of joint damage in the community with packages of education, advice, physiotherapy, footwear changes, weight loss etc., and trials of these packages for both the primary and secondary prevention of OA.
- Further research on strategies to alter the process of OA, with the particular aim of investigating the effectiveness and cost-effectiveness of these strategies, and their effects on other systems in the frail elderly who suffer most from OA.

- Better understanding of the pathogenesis of joint pain and lower limb disability in older people, and their relationships to both joint damage and to psychosocial factors that interact with pathology and help determine the burden to the individual (i.e. complement current targets of research (centred on joint damage) with the key patient related problems).
- Emphasise the fact that OA is both preventable and treatable, and concentrate on the appropriate delivery of simple cost-effective interventions at societal and community level, as well as the high technology, industry-driven solutions.

Specific research protocols can be developed to help take each of these objectives forward

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