Osteoarthritis revisited and revived

Cinderella has emerged from her shadow. Osteoarthritis (OA) has for too long been regarded as a degenerative dead end, uninspiring, unimportant and as a result uninvestigated. This is beginning to dramatically change as a result of a revolution in methodology and a reappraisal of existing approaches to its research. A new wave of thinking about mechanisms of the disease has been triggered which provides an opportunity for the review that follows as a series in the Annals, on the potentials and problems of methodologies in research in OA.

This emphasises the diverse approaches to studying the condition and underlies why an application of basic science should make major changes in our understanding of a common, expensive cause of suffering. The series aims to reflect the different perspectives with contributions ranging from biochemistry to anthropology. There is a diverse interest in the problem, that in turn generates a variety of concepts and controversy. They share common problems.

Working and communicating on OA is confused by the poor definition of the condition. It is loosely and widely recognised as a joint disease characterised by osteophyte, bone sclerosis and cartilage disintegration. It has therefore proved difficult to apply rigid definitions. Conversely, there is a need to constraining definitions to enable workers to communicate findings about the osteoarthritis process. It is a classic ‘Catch 22’, and in trying to escape from the trap there has then been a risk of escaping into dogma. An example is the semantic confusion between osteoarthritis and osteoarthrosis—a condition that could perhaps do with a different name anyway.

OA as a concept was very much created by technological advance, in particular the radiograph. This enabled the changes to be seen in vivo, demonstrating the signs by which OA has come to be recognised: osteophyte and loss of cartilage associated with bone sclerosis. The technological advances in molecular biology and magnetic resonance imaging (MRI) may give even more dramatic insight. MRI reminds us of the anatomy, in vivo imaging of soft tissue and cartilage, and may allow understanding of in vivo physiology and dynamics of movement. Molecular biology permits a detailed new perspective on the biochemistry, which has already shown the importance of a genetic abnormality in OA, and has begun to suggest disease mechanisms. These new techniques need to be put in to the context of established methodology ... the basics of describing the epidemiology, insights from animal models and the perspective of other disciplines like anthropology.

All approaches need to break away from the established dogma of an inevitable wear and tear with age. A reappraisal of the nature of mechanical change and the nature of ageing in the joint have become legitimate areas for investigation. Ageing is part of the life cycle of the joint, raising the fundamental biological questions of how joints are developed and maintained, and how they involve. Solving the problem is compounded by any biological system’s capacity to respond to change. This response may be critical to the development of OA, suggesting that the response is maladaptive and results in joint failure. Conversely, it may be adaptive, it stabilises the system and results in the extraordinary high prevalence of asymptomatic OA in the population.

The question is, do injured joints heal? This can be answered in two ways. In the sense of whether a joint restores itself to a state it was in before injury, few tissues heal. They usually heal by scarring, and many of the tissues in the joint can do just that. The controversy is what happens to cartilage. Suggestions that cartilage does heal are countered by evidence that defects may persist for long periods—a level of biomechanical tolerance of the tissue that can get pretty ragged without producing failure. The second approach is to re-interpret healing as restored function rather than anatomy. In a functional sense partial healing is probably common.

The first major challenge is to clearly establish the natural history. Where studies have looked long term at this their findings have been relatively neglected. The limited studies available emphasise that the disease is variable. Qualitative and quantitative variation is very much a hallmark characteristic in clinical pattern, pathology and what is known of its aetiology. The clinical and pathological observations give us important constraints on understanding the disease which any solution to the enigmatic problem of OA must satisfy. Briefly, these are its variability, homogeneity, joint distribution and age association.

There are two basic concepts of the disease that meet these constraints. First, is the multiple disease hypothesis. A set of distinct ‘independent’ diseases make up OA. We just need to identify each one and gradually the problem will disappear into chapters of recognised different conditions. Second is the hypothesis that it is a final common pathway to joint disease. Any insult causing disruption to the joint will eventually trigger the process of osteoarthritis. This is characterised by attempts to repair
and with further damage, eventually leads to joint failure. OA is then seen as that failure. This funnel hypothesis—multiple insults feeding into a single final common pathway—emphasises the importance of OA in the widest sense to joint disease. The implication is that response may also be a key factor in the development of other joint diseases such as rheumatoid arthritis. Variation in the intrinsic characteristics of the response that make up osteoarthritis may be determinants of how a joint changes with the development of other types of arthritis. The funnel concept suggests a direction of cause as well as a set of necessary and sufficient conditions for developing OA. However, what if the direction does not necessarily need to be sequentially progressive, and if there is no unique set of necessary and sufficient conditions, the funnel becomes a web. A set of interlinked factors produce OA but they do not merge into a common pathway. The interlinking is more like a net or web. It allows a whole range of routes to produce osteoarthritis. There is no single route. OA results from a series of events that can be accumulated by a progressive walk through a variable set of changes. There is no unique set of necessary and sufficient conditions. This absence of such conditions would explain the features of OA but challenges the reductionist with a major problem. It makes it difficult to identify controllable points that would effectively allow intervention. A more complex approach is needed. Can existing methodology find ways into this?

The goal of greater understanding should not be just the intellectual satisfaction. There is no promise of identifying likely interventions that may allow some improvement of the clinical problems caused by osteoarthritis. Breaking away from a sense of degeneration’s inevitability and renewing confidence in the potential of the scientific approach to identify areas that can be safely and effectively changed, makes OA suddenly open up a new frontier for research into how joints work. Even if this yields little that is positive it will begin to enable us to review the current conventions and treatments. The technical fairy-godmother has Cinderella abandoning the rags of dogma on wear, age, degeneration and tear, making her suddenly look considerably more attractive.

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