A history of the Arthritis Research Campaign Epidemiology Unit, 1954–2004

A. J. Silman

The founders of the Arthritis Research Campaign (arc) Epidemiology Unit were Kellgren and Lawrence. Their initial work was conducted in miners and then in the general population. They pioneered standardized methods of interview, examination and X-ray evaluation. They also played a key role in the early development of classification criteria for use in epidemiological surveys. The second director, Philip Wood, focused on understanding the impact of rheumatic diseases on the individual and on society. He was largely responsible for the International Classification of Impairments Disabilities and Handicaps. In the last 30 yrs, developments in statistics, computing and genetics have enabled the basic questions of disease aetiology to be re-examined. The third director, Alan Silman, took over in 1988. The Unit now has three research divisions: Genetics and Genomics, Outcome Studies and Population Surveys.

Historical background

The Centre for the Study of Chronic Rheumatism, at Manchester University Medical School, was opened in 1947, the first academic department of rheumatology in Great Britain. Its first director was a pathologist, Professor Stephen Baker, and its first clinical director was a rheumatologist, Professor Jonas Kellgren. From the very start, this centre was multidisciplinary in outlook and included an epidemiology section whose first task was to investigate the prevalence of musculoskeletal complaints amongst coal miners. This work was supported by the Ministry of Health, which at that time recognized that this was a substantial cause of sickness/absence from work and thus a subject worthy of investigation. As the early pioneers of this work, Professor Kellgren together with Dr John Lawrence, undertook these investigations of miners, it became clear that there were few or no data on the prevalence of the major musculoskeletal and rheumatic disorders in the general population. Kellgren therefore persuaded the then Empire Rheumatism Council (now the Arthritis Research Campaign, arc) to establish a mobile field unit for undertaking population-based investigations. Lawrence was appointed as its first director and secured funding for the initial studies.

Early population studies

These first population studies on the prevalence of the rheumatic disorders were carried out in Leigh, a small working-class town in Lancashire, and in Wensleydale, ‘James Herriot country’, in Yorkshire. The aim of these studies was to investigate the prevalence of both the individual features of the rheumatic diseases and the proportion of the population which could be classified as suffering from defined disorders. Subsequent surveys in the same populations allowed an estimate of incidence based on the occurrence of new cases in the interval between surveys.

Problems to be faced

These early studies faced a number of problems. Although it was relatively easy to identify population samples for study, it was much harder to achieve high response rates. It was recognized early on that home visits, by bringing the survey to the individual rather than relying on the participant travelling to a distant centre, would encourage greater participation. The arc caravan, fitted out with the latest X-ray equipment as well as facilities for examination and blood-taking, therefore became a regular sight in both Leigh and Wensleydale (Fig. 1). Forms were designed for the collection of symptoms by interview as well as for recording abnormalities of joints, including swelling and deformity, by examination. Kellgren and Lawrence were well aware of the importance of consistency and reliability in clinical measures. The same was also true in the laboratory assessment, and Professor Johnny Ball was responsible for adapting the sheep cell agglutination test for large-scale population studies to produce consistent results.

The full investigation of key disorders, such as erosive rheumatoid arthritis and osteoarthritis, required X-ray data gathering and interpretation. At that time the only method for evaluating X-rays was clinical impression; thus, to make these data appropriate for epidemiological studies, it was necessary to develop a standardized system for grading X-rays across a number of different disease dimensions. The Atlas of Standard Radiographs of Arthritis was developed during the first decade of the unit’s existence and was published in 1963 [1] (and reprinted in this supplement). This Atlas, together with the Kellgren and Lawrence scoring system, remains in widespread use today particularly for grading osteoarthritis.

Data analysis at that stage was also rudimentary. Data were punched on to cards and initially analysed by hand and subsequently using mechanical card sorters, which were capable only of counting the number of individuals by different characteristics. Using these totals and the simple statistical techniques available at the time, these pioneers were able to undertake fairly limited investigation of the relationship between risk factors and disease.

The final component necessary to make sense of the individual clinical laboratory and radiological data was the development of agreed criteria for the classification of individuals by the main disorders, such as rheumatoid arthritis and osteoarthritis. Prior to the development of criteria, diagnosis was based on clinical impression but it was soon realized that this would be inappropriate for epidemiological investigation. An international
effort, co-ordinated by Kellgren and Lawrence, resulted in meetings in Maryland in 1957, Rome in 1961 and New York in 1966, at which criteria were developed and refined, particularly for rheumatoid arthritis and for osteoarthritis [2]. The results from these epidemiological studies were published in several scientific publications but were very usefully brought together, together with a detailed methodological evaluation of the problems involved, in Lawrence’s classic monograph *Rheumatism in populations* [3].

**Genetic factors**

Kellgren and Lawrence readily appreciated that genetic factors were going to be important in explaining differential susceptibility in the various rheumatic diseases they investigated. At that time genetic markers were in their infancy and the study of them comprised predominantly the examination of characteristics such as blood groups. However, these early investigators undertook detailed investigations of familial clustering both in terms of the prevalence of disease in first-degree relatives of index cases compared with that in first-degree relatives of controls, and in terms of aggregation in twins. Thus, one of the earliest studies of the occurrence of rheumatoid arthritis concordance comparing monozygotic and dizygotic twins was conducted by the arc Unit. In data collections in 1962 and 1967, 594 twins were studied [4].

**Health services research**

Doctor, subsequently Professor, Phillip Wood became the second director of the unit in 1968, although Lawrence continued to work on the data he had collected, reading X-rays and analysing data well into the late 1980s.

Wood, however, recognized that there was a deficiency in knowledge of the impact of rheumatic diseases on both the individual and on society. The impact in terms of impairment was only one part of the problem. It was important to assess impact in terms of functional ability as well as the subject’s participation in society or lack of it due to handicap. These issues transcended several areas of medicine, and Wood completed, during his time as director, the monumental task of producing for the World Health Organization the *International classification of impairments, disabilities and handicaps* [5], which provided the cornerstone for those wishing to quantify the impact of disorders on health and function. He also, together with Dr Elizabeth Badley, initiated a major study of the impact of musculoskeletal diseases and related disorders explaining disability at a population level in the Yorkshire borough of Calderdale [6], the very first population study of its kind. Wood also was the first to recognize that epidemiological tools could be used to assess health-care needs in rheumatology. Thus, by providing robustly collected data on rheumatological manpower in the UK he was able to argue cogently for a massive expansion in the number of rheumatologists. The fruit of his efforts can be seen in the UK by the substantial growth in the number of consultants in this specialty.

**Changes in epidemiology 1960–1990**

The 30-yr period between 1960 and 1990 represented, for epidemiologists, a period of growth of the discipline with several major advances, both conceptual and technical. The principal change was the development of statistical tools to allow multivariate analysis, by determining the relationship between an individual exposure and an outcome after allowing for the confounding effect of other exposures. Thus, the development of the Mantel–Haenszel test in 1959 [7], logistic regression in 1962 [8] and the proportional hazards and regression analysis for survival type data [9] has provided the basis for all key epidemiological analyses subsequently. These statistical advances required the development of appropriate computing facilities, available and accessible to the individual epidemiological researcher. Indeed, the rapid growth of computing power went hand in hand with these statistical advances. Although the initial analyses were undertaken using batch processing methods which were laborious, by the mid-1980s real-time data analysis of epidemiological data had become a reality for departments of epidemiology such as the arc’s Epidemiology Unit.

As discussed above, the investigation of the role of genetic factors seemed to be the key to understanding the background susceptibility to most of the important rheumatological disorders. Familial and twin clustering, however, could be explained by shared environmental factors. It was particularly with the...
The discovery of HLA as a key genetic marker for diseases such as ankylosing spondylitis [10] that epidemiological investigations could begin to examine the role of specific genetic factors in disease occurrence. Early studies on HLA were based on serological investigation but modern DNA techniques, particularly based on the PCR method, allowed more rapid, accurate and high-throughput investigations to be done. Obviously in the past 10 yr there has been an explosion in understanding of other sources of genetic variation within the genome and the ability to identify the role of genetic factors in disease occurrence has increased enormously. In parallel with these advances grew the appreciation that epidemiological methods could be applied not only in a traditional way to explaining the relationship between putative risk factors and disease but also, given the presence of disease, to the understanding of what factors contribute to a good and a poor outcome. More recently the same tools have also been applied in terms of pharmaco-epidemiology in understanding why, given the use of a particular therapeutic agent, some individuals do well and others do not, or conversely some individuals develop a side-effect and others do not. A key modern example of this kind of epidemiology is to be found in the British Society for Rheumatology’s Biologics Register, currently co-ordinated by the arc Epidemiology Unit.

**arc Epidemiology Unit 1988–2004**

Alan Silman was appointed as the third director of the arc Epidemiology Unit in 1988 and, together with Bill Ollier, Deborah Symmons, Peter Croft, Gary Macfarlane, Jane Worthington, Wendy Thomson, Terry O’Neill, Ariane Herrick, Ian Bruce and Mark Lunt, the arc Epidemiology Unit in the past 16 yrs has moved to take advantage of the advances mentioned above to revisit key questions relating to the prediction of both the onset and the outcome of the major rheumatic diseases.

The unit has focused its attention on the collection of high-quality clinical data, supported by genetic material where appropriate, frequently as a springboard for prospective studies. Key patient cohorts include the Norfolk Arthritis Register, the arc Twin Study and National Repository for multicase rheumatic disease families, the European Vertebral Osteoporosis Study, the South Manchester Low Back Pain study and the Altrincham Pain study, which are discussed elsewhere in this supplement.

As the unit moves into the 21st century, its work has been divided into three separate but overlapping research divisions. The first is a Genetics and Genomics group, with a particular remit to take advantage of recent advances in high-throughput genotyping to investigate the genetic basis of both disease occurrence and disease outcome using both targeted, candidate gene approaches and wide-scale whole-genome investigations. The unit is now positioned to take forward genetic hints resulting from these investigations by undertaking functional studies. The second research division is the Outcome Studies division, which, building on the early work of the Norfolk Arthritis Register, is looking at long-term outcomes of rheumatoid and related forms of arthritis, particularly the role of treatment. The unit has recently established a multicentre prospective study of childhood arthritis, the Childhood Arthritis Prospective Study, in collaboration with colleagues from Manchester, Liverpool, Newcastle and Glasgow, to try to investigate the role of the same factors in the outcome of childhood arthritis, which have been so successfully identified in adult rheumatoid arthritis. The Outcomes Division has also taken under its wing the responsibility for the British Society for Rheumatology’s Biologics Register. The third division within the unit is the Population Surveys Division. Current studies, detailed elsewhere in this supplement, focus on the factors associated with the occurrence of pain, particularly early life factors, and the development of osteoporosis and related disorders in the ageing male for the European Male Ageing study. The unit is currently actively involved in the early stages of the UK Biobank project, which represents a serious investment in the UK in a study of the role of genetic and environmental factors in the causation of major chronic diseases. The UK is unique in having a large national dedicated research unit devoted to studying the epidemiology of the rheumatic diseases. The strong tradition of epidemiology in the UK, the centralization of its health service and the support of the rheumatological community have all been major contributors to the unit’s success.

**Acknowledgement**

I am very grateful to Mary Ingram, the arc Epidemiology Unit Librarian and Information Officer, and Jacqui Oliver, Postdoctoral Research Associate, for their substantial contributions in researching the early years of the arc Unit. That the unit has achieved all it has is dependent in large part on the major contribution of its founding fathers, particularly Professor J. H. Kellgren, its first director, Dr John Lawrence, its second director and deputy director, Professor Philip Wood and Dr Elizabeth Badley respectively. The arc's generous financial support over half a century for dedicated epidemiological research is without equal in the world of rheumatology.

The author has declared no conflicts of interest.

**References**