

J.S. Lawrence
Rheumatism in
Populations



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RHEUMATISM IN POPULATIONS

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To MIL

without whose persistence this work would not have seen the light of day.

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PREFACE

Epidemiology was described by Sir John Ryle in 1948 as the pathology of families, groups, societies or larger populations. In 1935 he had left a lucrative consultant practice for teaching and research as Regius Professor of Physics in the University of Cambridge, but felt that epidemiology was so important, that in 1943 he accepted an invitation to direct the new Institute of Social Medicine at Oxford.

My own involvement in epidemiology was less inspired but it has provided me with an insight into the rheumatic diseases which would not have been possible by any other means.

It has been said of epidemiology that it poses more problems than it can solve. Nevertheless there are many problems which can only be solved by this means and often the lead given by the epidemiologist can guide workers in other disciplines into a more profitable line of approach.

It is of interest that Heberden the elder included statistics among his many interests and in fact financed the reprinting of Graunt's book which gave the first description of methods of estimating populations by sampling.

Little reference will be found in the present work to acute rheumatism or rheumatic fever. It is concerned mainly with the more chronic disorders of the musculo-skeletal system and particularly with those which can be demonstrated by routine radiographs of population samples. However, certain systemic disorders such as systemic lupus erythematosus which frequently affect the joints are included. Because of the emphasis on radiography certain diseases of bone, such as Paget's disease and osteoporosis, which are not normally the concern of the rheumatologist are included.

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INTRODUCTION

An opportunity to undertake epidemiological studies first came in 1948 when, at the request of the Miners' Welfare Commission, the Departments of Rheumatism Research and Occupational Health of the University of Manchester agreed to conduct a survey of rheumatism in miners and I was put in charge of the investigation.

At that time little was known of the prevalence of rheumatic complaints in the population and it was decided to examine a group of miners working in the pits around Manchester and to compare them with non-mining employees of the National Coal Board at the Regional Offices of the Board in Walkden. It soon became apparent that rheumatic complaints were very common both in the miners and non-miners, the prevalence being of the order of 30%. Loss of work from this cause however was more frequent in the miners and it was decided to carry out a large scale survey. For this purpose the Bedford Colliery in Leigh was chosen since most of the one thousand employees lived in the town which was self-contained and would be used to study a random sample of the population for comparison with the miners.

A medico-social worker was appointed to visit the homes of the miners and of a one in ten sample of the adult population of Leigh and to enquire about rheumatic complaints. Those with complaints were seen by one of the physicians on the staff of the Rheumatism Research Centre in Manchester.

This complaints survey confirmed the greater loss of work in miners and showed that back and knee complaints were the main causes of incapacity in the miners. A subsequent x-ray survey of

miners and non-miners in the 40–50 age range indicated that intervertebral disc degeneration and osteo-arthritis were mainly responsible for the miners' greater incapacity.

An investigation of the factors in mining which were responsible involved the study of miners working at various seam heights and in wet and dry seams in mines in Lancashire and Yorkshire and also a group of dockworkers in Salford. From these it became clear that rheumatic complaints and incapacity were related to some extent to climate, being worse in damp conditions but that the x-ray changes of disc degeneration depended on the degree and duration of heavy lifting.

By this time we felt that we knew a great deal about rheumatic complaints in men but very little about women. Fortunately Professor Kellgren was able in 1954 to obtain a grant from the Medical Research Council to extend the population survey in Leigh to include women. A one in thirty sample of households was chosen for a detailed clinical, radiological and serological investigation of the 50–60 age group in these households. This survey, which was undertaken in co-operation with the Council's Pneumoconiosis Research Unit, confirmed the importance of disc degeneration and osteo-arthritis in men and indicated the greater importance of chronic polyarthritis and generalized osteo-arthritis as a cause of incapacity in women. This survey which was only 75% complete showed how difficult it is to persuade disinterested people to take part in a radiological survey.

Meanwhile the Arthritis and Rheumatism Council was becoming interested in epidemiological studies and in 1956 decided to set up a Field Unit for this type of investigation. I was fortunate enough to be appointed director of this unit and decided to extend the x-ray and serological study in Leigh to include all age groups from 15 upwards. Non-responders again proved a difficulty. Though some 90% of those approached agreed to attend the x-ray centre only 40% turned up and repeated visits with offers of transport did little to improve the completion rate. The problem was eventually solved by carrying out clinical and radiographic examinations in the home using a small portable x-ray set. With such a set, x-rays could be taken of the hands, feet, knees, pelvis and cervical spine but radiographs of the lumbar spine were impossible. However, quite often the respondent would agree at this stage to come to the x-ray centre for the final radiograph. With this technique it has been found possible to obtain completion rates in excess of 85% in most populations.

From this survey in Leigh the frequency and age and sex distribution of the commoner rheumatic diseases was ascertained and in 1958 it was decided to investigate a rural population sample in the same way. Advantage was taken of an area sample of the population of Wensleydale in Yorkshire investigated for rheumatic complaints by Dr. Joan Bremner of the University of Leeds. From her sample a

smaller area sample was selected for clinical, radiographic and serological investigation. This survey revealed the remarkable similarity between urban and rural populations for all the main rheumatic diseases, only gout being less frequent in the rural population. An incidental finding was the low frequency of rheumatoid factor in the rural population and this urban-rural difference was subsequently confirmed in other European populations.

During the surveys in Leigh and Wensleydale persons with rheumatoid arthritis, rheumatoid factor, generalized osteo-arthritis and hyperuricaemia were used as probands for family studies and with these it was possible to show the degree of familial aggregation which occurs in these various conditions.

By taking probands from population samples it is possible to avoid the uncertainties which may arise from incomplete ascertainment, but the method is unsuitable for the study of rare diseases or for the more severe forms of the commoner diseases and in 1959 it was decided to investigate familial aggregation of a wide variety of rheumatic diseases using as probands patients who had attended the Rheumatism Research Centre in Manchester. Included in this study were seropositive and seronegative forms of rheumatoid arthritis, psoriatic arthritis, spondylitis, gout, systemic lupus erythematosus, systemic sclerosis, dermatomyositis and periarteritis nodosa. All patients with these diseases who had attended during the previous 2-year period were included as probands in this family survey. Subsequently patients with other diseases were included—psoriasis without arthritis, discoid lupus erythematosus and scleroderma from the Skin Hospital in Manchester, Still's disease from the Canadian Red Cross Hospital in Taplow and the Hammersmith Hospital London who also supplied further probands with systemic lupus erythematosus, Reiter's disease from special clinics for the treatment of venereal disease throughout the United Kingdom. In 1963 probands with hypogammaglobulinaemia obtained from the MRC Working Party investigating this disease were added. The family survey was limited to first degree relatives and spouses living in the United Kingdom, except that grandparents were included in the Still's family survey. This was a joint project with Dr. Barbara Ansell from Professor Bywaters' department, and included as a control group a population sample in the town of Watford.

Apart from the Still's study these surveys were so designed that the clinician was unaware of the proband's diagnosis till he had made his clinical assessment of the relative, an important precaution if the clinical findings are to play an important part in the final assessment. Many of the relatives lived in the Manchester area and these were at first asked to attend for x-ray and clinical examination at the University but this was not found to be practicable since drivers would often be away for two hours or more when asked to bring in respondents from the outlying parts of the city. The scheme was

therefore adopted of taking an x-ray van to sites on the periphery of the town thus making a complete circuit during a two-year period. In this way the dense traffic in the city centre was avoided and travelling distances for respondents shortened. The x-ray van was subsequently taken to several of the larger towns in other parts of the United Kingdom but for the more scattered relatives this was not practicable and reliance had to be placed on the x-ray departments of local hospitals or on x-rays taken in the homes of the respondents. We were fortunate to obtain valuable co-operation from radiologists throughout the country who allowed us to use their departments in the evening or at weekends or, where the numbers to be x-rayed were small, arranged appointments for x-ray by their own staff and subsequently posted the films to Manchester. Pathologists were very helpful in allowing blood samples to be centrifuged in their laboratories and the sera stored in their refrigerators. It was usually possible to obtain supplies of cardice in the larger towns to enable the sera to be transported in a frozen state back to Manchester. The scheme adopted was to make a circuit of the United Kingdom heading north from Manchester, crossing to Northern Ireland from Stranraer and returning to that port. The subsequent course was along the west coast of Scotland to Glasgow and Fort William, across to Inverness, Aberdeen and the Orkneys and then south to Edinburgh and Newcastle and so to Manchester. A second circuit was completed by way of London, the south coast, the West Country, Wales, Birmingham and Coventry. Since many relatives were not available on the first circuit a second smaller and eventually a third circuit had to be made before an adequate completion rate (92%) was achieved. A control group in the town of Wantage was planned for this part of the family survey but had to be omitted owing to shortage of funds. In retrospect this was probably a mistake and it might have been better to reduce the number of relatives seen since a change in titres of rheumatoid factor at about this time made it difficult to assess the significance of titre distributions in the relatives.

This family survey in so far as it has been analysed has revealed familial aggregation of certain diseases, notably ankylosing spondylitis, seropositive rheumatoid arthritis, Still's disease, gout and psoriatic arthritis but up to 1964 doubt still existed as to the cause of this aggregation and in 1964 a survey of twins with rheumatic complaints was organized by Dr. Allan Dixon for the Arthritis and Rheumatism Council. This was included in the family survey from 1964 onwards and gave clear evidence of a strong genetic influence in seropositive rheumatoid arthritis.

Meanwhile further occupational surveys had been undertaken—cotton spinners and weavers in 1960, foundry workers in 1961 and electricians in 1963. The influence of climate on rheumatic complaints was investigated in Montana in 1961 in conjunction with the National Institute of Arthritis and Metabolic Diseases of the United

States, and in Jamaica in 1962 with the Medical Research Council's Epidemiological Unit in Kingston.

Longitudinal surveys in Leigh and Wensleydale in 1963–4 and Oberhörlen in West Germany in 1968 have sought to probe the incidence of rheumatoid arthritis in persons with high and low titres of rheumatoid factors and the cohort effects involved in rheumatoid factor production. The influence of various infections on arthritis and on rheumatoid factor titres has also been investigated in these follow-up surveys.

Statistical analysis of the data of these later surveys is still in hand. As epidemiology becomes more sophisticated, the analysis of simple clinical records is necessarily more elaborate if the results are to be meaningful. We look forward to the conclusions reached by Dr. P. H. N. Wood, the present Director of the Arthritis and Rheumatism Council's Epidemiological Research Unit since 1968.

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The Department of Medical Illustrations of the University of Manchester under Dr. R. Ollerenshaw is responsible for most of the illustrations and has given much useful advice.

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Chapter 1

HISTORY OF EPIDEMIOLOGY

Though population surveys were introduced as a research tool only some 30 years ago, the statistical approach to disease is of much longer standing.

As long ago as 1670 the value of tabulating vital statistics was recognized by John Graunt and by William Petty. Despite the paucity of official data these investigators were able to measure differences in mortality between urban and rural populations and indeed made valuable contributions to our knowledge of disease (Greenwood, 1941 and 1948). For their tabulations these early workers had to depend on data derived from christenings and from bills of mortality and had little information with which to define the populations they were studying. This was remedied at the beginning of the 19th century by the introduction of the National Census and by the official registration of births and deaths. But although *mortality* statistics were thus placed on a stronger foundation there was little information on *morbidity* and on the frequency of the non-fatal diseases. This was partially remedied with the advent in the present century of sickness benefit societies and national insurance schemes, which made available a vast mass of data relating to morbidity.

These schemes, by ensuring that at least a fair segment of the male population registered with their family doctor, provided a defined population from which morbidity statistics could be obtained. Advantage was first taken of this by Sir James MacKenzie, a London cardiologist, who in 1918 devoted himself to this type of research. He realized the value of accurate recording of clinical data by the family doctor as a means of advancing knowledge of the large mass of

non-fatal diseases many of which are never seen by the hospital physician. The St Andrews Institute of Clinical Research was founded by him to aid family doctors in collecting this information (Ramsay, 1926). Meanwhile, following a report by Kahlmeter in 1923 of the heavy toll of rheumatism in industry, this type of epidemiological research was being applied specifically to the rheumatic diseases by Alison Glover in co-operation with Sir George Newman. In 1924 the results of their survey of rheumatism in England and Wales were published by the Ministry of Health. This survey was based on a study of patients attending over a period of one year a picked group of general practitioners scattered throughout the country. It was followed by a similar study in the north of Scotland in 1937 (Scotland Medical Advisory Committee 1944). It was revealed that in England and Wales alone rheumatic diseases accounted for nearly a sixth of the total industrial disability, a yearly expenditure of £2,000,000 on sickness benefit and a loss of 21,000,000 days of working time. In Scotland 3,000,000 working days were lost by an insured population of 1,800,000.

Though of limited scientific importance, these studies were nevertheless of great practical value, since they drew attention to the economic impact of this group of diseases. The formation of the International Committee against Rheumatism in 1925 and of national committees in most European countries between the years 1926 and 1928 may well have been stimulated by the results of these earlier reports. As a result of the deliberation of the International Committee the *Ligue Internationale contre le Rheumatisme* was founded in 1928. Under the aegis of this league a number of studies on the prevalence of rheumatic disease were undertaken notably by Kahlmeter of Sweden (1932), by de Zimmer of Germany (1932), and by Danishevsky of Russia (1930). These studies confirmed the importance of the rheumatic diseases as a cause of disability in Northern Europe. In 1930, in a study in Aachen, it was estimated that no less than 75% of industrial workers over 40 years of age suffered from some form of rheumatism. From the Swedish study it transpired that 0.6% of the insured population were disabled by arthritis involving an annual charge to the state of 6 million krone (about £330,000). Arthritis was the most frequent cause of disability, being responsible for about 11% of all invalidity in males and 13% in females. Similar findings were reported from other European countries.

The initiation of the National Health Service in Britain in 1948 enabled statistics to be collected on a national scale since the service included all who were gainfully employed whether self-employed or employed by others. Thus, apart from housewives, there was complete coverage of all occupational groups in the population. A study revealed that some 28 million days were lost each year because of rheumatic complaints in England and Wales, a proportion of 141 days per 100 individuals at risk. This could be compared with other

causes of incapacity—133 days from tuberculosis, 128 from bronchitis and 118 from neurotic disorders. The remaining causes of loss of work—accidents, digestive troubles and disorders of the circulatory system were relatively unimportant being each responsible for less than 87 days of incapacity per 100 individuals. With the discovery of effective methods for the control of tuberculosis this has ceased to be a major cause of incapacity and rheumatic complaints have assumed a more important role. Statistics from other countries in Northern Europe have confirmed the importance of the rheumatic diseases.

Such statistics however ignore the large number of persons in the population who have rheumatic complaints but do not stay away from work or even consult a doctor. To obtain information about this group field surveys, conducted by house-to-house interviews with questionnaires, were devised (Stocks, 1949; Brooke, 1953) and to obtain more precise information on diagnosis questionnaires were supplemented by clinical examination of individuals with complaints (Edström, 1944; Ehrström, 1951; Kellgren *et al*, 1953; de Blécourt, 1953, 1954). These have involved the random sampling of the population and have resulted in a completely new concept of disease. Sidney Cobb (1970) who was one of the pioneers of this type of study of rheumatism in populations, has described the “rheumatic range”, the most severe cases at the apex of the mountains and least severe mingled in the base of the massif. This he pictures as producing peaks of diagnostic clarity and valleys of indecision. Unfortunately, in any population sample of feasible dimensions, the peaks of diagnostic clarity are sharp and the valleys of indecision wide. There has thus been a temptation, to include amongst the diagnostic groups some who were too close to the base of the massif or even bogged down in the valleys of indecision. As a result, attempts to classify rheumatic complaints into diagnostic categories gave widely divergent results. Estimates of the prevalence of rheumatoid arthritis varied from 0·4 to 2·3% and of osteo-arthritis from 0·04 to 6·2%, the lowest rates being for self diagnosis in reply to questionnaires, the highest for clinical examination in the field.

To obtain more precision in diagnosis x-rays and serological tests were introduced into population surveys as confirmatory data by Miall and his colleagues in 1953 and routine x-rays of population samples were first used by Kellgren and Lawrence in 1956. In the same year diagnostic criteria incorporating clinical, radiographic and serological parameters were devised by Ropes and her colleagues. Radiological criteria for erosive arthritis and degenerative joint disease appeared soon after (Kellgren and Lawrence, 1957a and b) and were summarized in the Atlas of Standard Radiographs of Arthritis (1963).

In 1956 the Arthritis and Rheumatism Council began a series of radiological surveys of rheumatic disease in the United Kingdom

designed primarily to discover the size of the problem. The first survey was undertaken in the town of Leigh in the North West of England, and was based on a 1 in 30 sample of the adult population, a total of 1,565 persons, of whom 1,343 were examined and had x-rays or serological tests. Between the years 1958–60 a similar sample was examined in a rural population in Wensleydale some 70 miles further north. Meanwhile in 1958 a survey had been undertaken in South Wales by the Pneumoconiosis Research Unit and in the same year, radiological surveys were started in Finland by Laine, in the Netherlands by de Graaf and in West Germany by Behrend. These surveys were all designed specifically to investigate rheumatic disease and included routine x-rays and serological tests. In 1961 and 1962 surveys were started in the United States by Burch in American Indians, and by Engel in a general sample of the population. An Indian survey was also made in Canada by Gofton and his colleagues. Surveys have since included Negro populations in the Caribbean and in Central and South Africa, Maoris and various Polynesian races in New Zealand and the Pacific Islands, further European populations in Switzerland, Bulgaria and Czechoslovakia. In addition radiographic and serological studies of rheumatism have been included in a number of more general surveys in various parts of the United States notably in Tecumseh, Sudbury and New Haven.

The first international symposium on Population Studies in Relation to Chronic Rheumatism took place in Bethesda in 1957 and was followed by a second in Rome in 1961 and a third in New York in 1966. The large number of papers presented on the last occasion indicates the increasing interest in this aspect of epidemiology.

Chapter 2

EPIDEMIOLOGICAL METHODS IN RELATION TO THE RHEUMATIC DISEASES

In addition to surveys based on hospital admission and sickness absence certificates a wide variety of techniques have been used in population surveys of chronic rheumatism, varying from household morbidity surveys based on postal or interview questionnaires to complete surveys based on a clinical, radiographic and serological examination of all respondents.

Hospital and other statistics. Since only a proportion of individuals with any one disease attend hospital and the population at risk is seldom known, hospital statistics have a limited value. They have however the advantage that they are based on more accurate diagnosis since adequate facilities are generally available for investigation of the patient. Since the hospital covers a wide population such statistics are particularly useful for the supply of data on rare diseases such as systemic lupus erythematosus and polymyositis and have been used successfully even in studies on diseases as common, for example, as gout.

Apart from incomplete ascertainment, which gives a low prevalence, sometimes less than a tenth of the true value, the attendance of patients at more than one hospital for the same complaint has the opposite effect. Record linkage studies by Acheson (1967) have overcome this difficulty in Oxford and the surrounding area but such methods require a permanent organization which is not generally available.

Family doctors' records. Hospital statistics have also been used for the investigation of climate in relation to rheumatic fever and rheumatic heart disease (Hench, 1948). The relationship to latitude was later confirmed by studies in school children (Saslow *et al*, 1959). Hospital statistics have also been used to assess the prevalence of systemic lupus erythematosus and possible racial differences in prevalence between Negroes and Caucasians (Siegel *et al*, 1962).

If only hospital patients are included in statistical studies of arthritis many arthritics, often with quite serious disease, are omitted as some rheumatoid cripples never attend hospital. Even if all patients attending the family doctor are included, many patients with symptomatic rheumatoid arthritis may be missed (Kellgren *et al*, 1953). During a survey in Leigh by the Rheumatism Research Centre of the University of Manchester a question was introduced to find out the extent to which persons with rheumatic complaints obtained medical care. The results are shown in fig 3.5 and indicate that 38%



Fig. 2.1 X-ray trailer (left) and clinical and laboratory trailer (right).

of females with inflammatory polyarthritis and 50% with osteoarthritis failed to consult a doctor. In males the consultation rate was in general higher than in females and this applied particularly to disorders of the intervertebral discs. Although in some cases the failure to consult was due to the relatively trivial nature of the symptoms, the belief that rheumatism is incurable and treatment of no avail was widespread and was responsible for much of the low consultation rate.

It follows that estimates of the prevalence of these conditions based on consultations with the family doctor are likely to be low. The

population at risk must of course be known and this is possible in small communities served by a single doctor or partnership. In larger communities it may be assumed that the doctors "list" represents the population at risk though this must of necessity exclude a few healthy individuals who have not bothered to register with any doctor. The chief limitation of the method is that each population is examined by a different observer so that observer differences may play a major part. Where results from a large number of practices are summated as in Newman's (1924) survey, or the study by Logan and Cushion (1958) the method may have some value as indicating the economic importance to the community of rheumatic diseases and their relative importance in relation to other diseases.

To illustrate these points data are given in table I. Four hundred and seventeen persons aged 55–64 chosen at random from population samples in Leigh and the Vale of Glamorgan had a detailed clinical examination of the skeletal system, radiographs of the hands, feet, cervical and lumbar spine and hips and a sheep cell agglutination test. Of these 417 persons, 38 were considered by the examining physician to have clinical evidence of inflammatory polyarthritis though in only 10 was it of moderate or severe degree. Of these 38, 36

Table I Prevalence of rheumatoid arthritis in screened sample and in total population samples

Ascertainment	Clinical inflammatory polyarthritis		Radiological erosive arthritis						Confirmed RA clinical and radiological SCAT
			Hands and feet		Cervical spine		Lumbar spine		
Grade	2-4	3-4	2-4	3-4	2-4	3-4	2-4	3-4	2-4
Hospital in-patients	5	3	4	2	1	1	1	0	3
Hospital in-patients or out-patients	9	6	7	3	2	1	5	0	5
Consulted family doctor	25	10	16	5	13	1	12	1	11
History of pain and swelling of hands or feet	28	9	14	5	14	2	5	1	14
Rheumatic complaints	36	10	24	5	27	2	14	1	14
Total population sample 417	38	10	26	5	28	2	17	1	14

had symptoms and would thus have been picked up if all persons with rheumatic complaints had been examined. A history of pain and swelling of the hands or feet was obtained in 28 and the family doctor had seen 25 so that nearly 70% would be picked up by these two methods of screening. In fact there would inevitably have been differences in diagnosis between the family doctor and the survey physician so that some persons with rheumatoid arthritis would be missed and patients with other diseases included. When these had been abstracted the numbers diagnosed as rheumatoid arthritis

would be very much less. From hospital records only 9 of the 38 patients with inflammatory polyarthritis in table I would have come to light, only 5 from the in-patient records. If only those with moderate or severe arthritis (grade 3–4) are considered, ascertainment is more likely to be complete. All ten patients in this category had consulted the family doctor but only 6 of them had attended the hospital and three had been admitted.

Erosions were encountered in the hands or feet in 26 of the 417 persons. If all those with rheumatic complaints had been x-rayed, 24 of those with erosions would have been discovered but it would have meant taking x-rays of almost the entire population since in this age group 80% gave a history of rheumatic complaints. If only those with a history of pain and swelling of the hands or feet had been x-rayed, only 14 of those with x-ray changes in the hands or feet would have been included, but all of the five with grade 3–4 erosions. If all those consulting their family doctor for rheumatic complaints had been x-rayed 62% would have been discovered but again all those with grade 3–4 erosions. As we shall see later many of the grade 2 erosions are probably not rheumatoid.

Rheumatoid arthritis of the spine is even more likely to be missed. Of the 28 persons with cervical rheumatoid arthritis, 14 gave a history of pain and swelling of the hands or feet and 13 had consulted their family doctor. Confirmed rheumatoid arthritis i.e. clinical evidence of inflammatory polyarthritis confirmed either radiologically or serologically was picked up satisfactorily by the questions on pain and swelling of hands or feet. Most of the cases had consulted their doctor but less than half of them had attended the hospital.

It may be concluded that a questionnaire on pain and swelling of the hands or feet is a useful preliminary screening procedure if only moderate or severe cases are sought but it is of little value in picking up the mild forms of arthritis. Similarly the family doctor's register is likely to come up with practically all the moderate or severe disease but little that is minimal. The availability and cost of medical services is an important factor in deciding whether the family doctor is consulted and this varies greatly in different regions. For these reasons a general practice register cannot be used in comparing populations or socio-economic groups.

Incapacity certificates. Issued by a family doctor in connection with national or other sickness insurance schemes, constitute a more limited form of general practitioner survey but one for which data are more readily available. The accuracy of this type of study is limited to the accuracy of the certification on which it is based and this may be a very serious limitation. As a means of indicating where more detailed surveys may most usefully be undertaken, it has obvious value, and it is a useful guide to the relative importance of rheumatic and other diseases as a cause of incapacity.

Data derived from sickness certification also serve as a pointer to segments of the population in which investigation of occupational influences is most urgently needed. Bricklayers for example have been reported as losing 420 days per 100 at risk per annum and considerable loss of work from rheumatic complaints has also been reported in cultivators, blacksmiths, painters, coppersmiths and general labourers (Telefsen, 1949; Anderson and Duthie, 1963). In Scotland coalminers in 1956 lost 266 days per 100 at risk, unskilled labourers 203, clerks and insurance workers 59 (Duthie and Anderson, 1962). A more detailed discussion of the relationship of occupation to rheumatism will be found in chapter 13. Industrial surveys based on such information, have been used to elucidate the role of occupational factors in the causation of rheumatic diseases. They are discussed in detail in chapter 13.

Questionnaires

A postal questionnaire has generally proved of very limited value because of the low completion rate attained. Questionnaires filled in by interviewers give adequate completion rates up to 99%, but the questions must be carefully chosen. This aspect has been studied in detail by Cobb and his colleagues (1956). A question such as "Does anyone in this household have arthritis or rheumatism or any other ailment of that type?" has proved of little value in eliciting information on the prevalence of arthritis. In a later survey, in which a sample of those interviewed in this way were later invited to a health centre for a medical history, examination and x-ray study, Cobb and his colleagues found that from only a third of those with classical arthritis was a positive response elicited to this household question. When the question was asked in an individual interview something over half gave a positive response to the question but positive answers were also obtained in many with questionable complaints or with absolutely no arthritis.

Later a series of three questions was introduced (Cobb, 1965). The questions asked were:

- (1) Have you ever at any time had arthritis or rheumatism?
- (2) Do you wake up with stiffness or aching in your joints or muscles?
- (3) Have you ever had swelling in any joints?

On a positive answer to all of these questions was based the Index of Rheumatoid Arthritis (IRA). Cobb has found that the sensitivity of this index for probable or definite arthritis by the ARA Criteria is 66–77% and the specificity 95–98%. Adler and Abramson (1968) found the sensitivity somewhat lower (41%) though their figure for specificity was similar (93%). This however was based on 4 questions. Using Cobb's 3 questions the specificity was 86%. In estimating specificity the formula of Blumberg (1957) was used (p 522). An

alternative formula, which gives a more satisfactory separation between different degrees of specificity is discussed on p 524. Using this formula the specificity of the IRA is 56%.

One of the chief difficulties arising from the use of a questionnaire is that the response of the individual is affected by variables which it may be desired to study in relation to causation. Adler and Abramson found that the validity of the Index of Rheumatoid Arthritis varied markedly with sex, age, educational level and response to the Cornell Medical Index which is a measure of emotional ill health. Among persons free of active rheumatoid arthritis (probable or definite) the proportion giving 3 or 4 "yes" replies was higher when the CMI score was high than when it was low. This would make the score unsuitable for a study of the influence of emotional factors in aetiology.

Initial screening. Although questionnaires thus have a rather limited place in the diagnosis of arthritis, they may be used as an initial screening procedure.

For example in a survey of rheumatoid arthritis the sample may be screened by a question on pain and swelling of the hands or feet. If only those answering "yes" to this question are seen by the physician and if considered by him to have possible arthritis, subjected to x-rays and serological tests, the cost of the survey is greatly reduced. In a study on these lines by Miall and his colleagues in 1958 of a population of 19,722 in the Rhondda Fach, a Welsh mining valley, 282 persons were considered possible cases by the physician. The number requiring a detailed investigation was reduced to a seventieth of the total. The diagnosis of rheumatoid arthritis was confirmed radiologically or serologically in 272, giving again a prevalence of 1.4%. Five years later a sample of 179 males and 174 females aged 55–64 was taken at random and unscreened from the same population and all were examined clinically, radiologically and serologically. The prevalence of suspected clinical disease in this age group had been 4.6% in females and 1.6% in males in the original survey (table II). In the unscreened sample the prevalence of clinical arthritis was 5.2% in females and 4.5% in males but was confirmed by x-ray or serology in 4.0% of females and 3.4% of males. Thus unless the prevalence had risen in the interim, some 40% of cases were missed by the screening procedure but they were mainly mild cases unassociated with positive radiology or serology.

Unfortunately the results in screened samples are influenced by the attitude of both the respondent and the interviewer. This was shown when the results in a screened sample in the Vale of Glamorgan by the same team were compared with those in the earlier survey in the Rhondda. In the Vale of Glamorgan 339 females aged 55–64 were questioned and the screening was deliberately made at a lower threshold, all persons with pain and swelling of the hands or feet being included, so that 11.2% of the sample were included as

Table II Prevalence of rheumatoid arthritis in the Rhondda and Vale of Glamorgan using screened sample and random sample aged 55–64

Population	Sex	Screened sample			Unscreened sample			Radiological	
		Total questioned	Suspected	Confirmed	Total examined	Clinical	Confirmed	Hands	Feet
Rhondda	Female	1,301	68 (4·6%)	67 (4·5%)*	174	9 (5·2%)	7 (4·0%) NS	3·5%	5·0%
	Male	1,477	21 (1·6%)	21 (1·6%)	179	8 (4·5%)	6 (3·4%) NS		
Vale of Glamorgan	Female	339	38 (11·2%)	36 (10·6%)*	87	6 (6·9%)	1 (1·2%) NS	1·6%	2·2%

*** $P \simeq .001$
NS = Not Significant

suspects. The diagnosis was confirmed in 10·6%. The following year a sample of 87 females in the 55–64 age group were examined clinically, radiologically and serologically. In this sample the prevalence of clinical arthritis was 6·9% and the diagnosis was confirmed by x-rays or serology in 1·2%. The x-rays of the hands and feet from both unscreened samples were subsequently read blind by two observers. Both observers found no significant difference between the two populations but such differences as there were, indicated a higher prevalence in the Rhondda population. Thus, by using a screened sample, a very significant, but apparently spurious clinical difference was demonstrated between two populations. The difference was exaggerated in this instance by a deliberate change in screening threshold but threshold differences could well arise unintentionally and could not be excluded as a cause of any differences in prevalence which might emerge.

Complaints surveys. These criticisms could apply similarly to a wider screening procedure in which all those with rheumatic complaints are submitted to clinical, radiological and serological testing. The members of some population may recall their complaints more readily than others so that a larger proportion of the populations is examined and more disease found. In a survey of rheumatic complaints in coal-miners (Lawrence and Aitken-Swan, 1952) it was found that, whereas the miners had more rheumatism than the general population, their families had less. Routine x-rays of the lumbar spine and knees, which were the principal sites of pain in the miners, showed that there was more disc degeneration and osteo-arthritis in the miners but the miners' families had much the same prevalence as non-mining families. It was concluded that the difference noted between mining and non-mining families was chiefly a base-line effect and was unlikely to be due to any differences in the prevalence of rheumatic disease as such. Because the miners had more lumbar disc degeneration and had lost work from back, hip and sciatic pain, members of their families did not regard pain at these sites as abnormal.

Unscreened samples. When a disease is of frequent occurrence, having a prevalence greater than one per thousand of the population, it is possible to investigate it by studying unscreened population samples. Fortunately, at least for the epidemiologist, most of the rheumatic diseases fall into this category. In surveys of unscreened samples objective information is collected on all respondents whether or not they admit to symptoms or incapacity.

Surveys of unscreened samples, in addition to providing objective evidence of disease which is independent of complaint thresholds, make it possible to study the whole spectrum of each disease.

Sampling techniques. A wide variety of sampling techniques has been used in population surveys of the rheumatic diseases. *Random samples* of individuals taken from a local register or from the electoral

roll have been examined by Laine (1962) in Finland, by Valkenburg (1968) in Holland and by Prior and his colleagues (1966) in New Zealand. In some surveys samples of individuals have been stratified by age an equal number being taken at random from each of the age groups it was desired to study as in surveys in South Wales, Jamaica, the United States and Japan (de Graaf *et al*, 1963; Lawrence, Bremner *et al*, 1966; O'Sullivan and McDonald, 1966; Bennett and Wood, 1968b). The survey in South Wales was also stratified by occupation, an equal number of miners and non-miners being included in each age group. In a survey in Sofia an age stratified sample was first taken from the electoral register and was subjected to a clinical examination. A sample of these including all with rheumatic complaints were then re-examined and had x-rays and serological tests (Tzonchev, 1968). Initial screening by questionnaire of a 1 in 16 population sample was adopted by Allander (1970) in Stockholm. Two age groups were subsequently selected for further study, those fulfilling 3 or more ARA criteria (see p 518) being subjected to clinical, x-ray and serological investigation. Screening by the ARA criteria was also used by Adler and his colleagues in Israel in 1967.

Surveys based on random samples of individuals are unsuitable for the study of diseases related to family size since the sample is biased in favour of individuals from large families. Rheumatoid arthritis and rheumatoid factor formation for example are more frequent in large sibships (Bennett and Burch, 1968a and f). Random household samples overcome this difficulty since large and small families have an equal chance of being selected. They have been used in some population samples for example in a survey of rheumatic complaints in the town of Leigh in Lancashire in which every tenth household was included (Kellgren *et al*, 1953). In such surveys random sampling numbers are generally used to select households from the local register. Where no local register is kept the electoral roll has been used in some surveys but has the disadvantage that those not on the roll are omitted from the sample. As these are more likely to be young families an age bias is thereby introduced.

Where these sources are not available it may be necessary to carry out a private census of the local inhabitants as a preliminary to picking the sample but this is not very practicable in a town.

The main disadvantage of the *random sample* whether of *persons* or *households* is that the respondents are scattered throughout the town and the cost of home visiting and of transportation is thereby increased. This has been mitigated in some surveys of rheumatic diseases by the method of clustering (Lawrence and Bennett, 1960). A smaller number of households was initially chosen and to these were added the households living 5 doors along in either direction. However with all household samples there is the difficulty of explaining to the healthy respondent why he has been chosen for a survey of say arthritis rather than the next-door neighbour who may be crippled by it.

This difficulty was overcome in a survey in Watford by taking a random sample of streets (Ansell and Lawrence, 1966). This is probably less random than a sample of households since a smaller number of units is taken and one street which is in any way unusual, e.g. all the inhabitants in Social class I, or in the older age groups may introduce bias in the sample. It does however enable the survey to be performed at less cost and co-operation is more easily obtained. In rural populations *area samples* have been used, either by marking a map into appropriate subdivisions by a grid or by taking a sample of villages with the surrounding postal districts as in a population survey in Wensleydale (Bremner, 1961). In this survey information obtained from the electoral roll was supplemented by a private census made during an initial house to house survey of rheumatic complaints in the area. From this information the sample of villages was chosen and was checked for age and sex distribution against census data for the district. All those aged 15 and over at the time of the first interview were included no matter how short their residence. Persons normally resident but away from home for less than six months in the previous year were also included.

Village samples were also used by Sitaj and his colleagues (1964) in the area around Pieštany in Czechoslovakia. Area samples were taken by de Blécourt in 1954 and by Steiner *et al* in 1968 in Holland, by Burch in two American Indian reservations one in Montana in 1961, the other in Arizona in 1962 (Bunim *et al*, 1964) and by Gofton in two communities of Haida Indians in the Queen Charlotte Islands in British Columbia (Robinson *et al*, 1963). Area samples have also been studied in New Zealand and various Pacific Islands by Prior and his colleagues (1966) and in Japan by Shichikawa (1968). In New Haven area samples stratified by social class were taken by Acheson *et al* (1965) and in Tecumseh, Michigan by age, social class, housing and occupation (Epstein 1960, 1964).

Two *national surveys* have so far been undertaken; the survey by de Graaf (1960) in the Netherlands in which 68 municipalities were chosen, based on regional economic conformity and degree of urbanization. The inhabitants in the chosen municipalities were screened by a questionnaire and only those with rheumatic complaints were seen. The second, the U.S. Health Examination Survey was based on *cluster sampling*, a 1 in 2 sample of clusters of four households derived by probability selection and stratified to take account of geographical region and population density (National Center for Health Statistics 1966). To determine this sample the country was first divided into strata based on geographic location and population density in such a way that each contained roughly the same number of persons. In this way the country was divided into 1,900 areas or primary sampling units. These in turn were divided into segments. From a listing of households within the segment a random sampling procedure created a subsegment of approximately four households each of which was interviewed.

The surveys so far considered have been designed mainly to determine *point prevalence*, i.e. the number with a disease at a point in time but a number have been used as a base for longitudinal studies, both in the United States and in Europe. Population samples in Leigh and Wensleydale surveyed by the Arthritis and Rheumatism Council have been re-examined at five year intervals with particular reference to rheumatoid serum factors and arthritis (Ball and Lawrence, 1963) and population samples in Tecumseh, Framingham and Sudbury have been re-examined to determine the incidence of both rheumatoid arthritis and gout and their relationship to rheumatoid factors and serum uric acid (Mikkelsen and Dodge, 1969; Hall *et al*, 1967; O'Sullivan, 1968a). A five year follow-up of the survey in Oberhörten was concerned mainly with the incidence of rheumatoid arthritis (Behrend *et al*, 1972).

Two surveys, designed primarily as longitudinal surveys are noteworthy (Beall and Cobb, 1961; Valkenburg, 1968). These were based on small population samples followed up intensively over a period of one year. Since the manifestations of the rheumatic diseases tend to be episodic this type of survey is very important since it distinguishes between chronic and episodic disease.

For a detailed description of these and other surveys undertaken up to 1966 the description by Bennett and Wood (1968c) should be consulted.

Industrial samples. The influence of occupation may be assessed in random and area samples but it is possible to study only those occupations which are predominant in the area. However for occupations not subject to close geographical grouping such as farmers or housewives this is the method of choice. For the remainder an industrial sample must be taken. The Arthritis and Rheumatism Council has undertaken a number of surveys of this type and others have been made at the request of the Miners' Welfare Commission or by industrial medical officers. The methods of sampling have varied. In some surveys all the workers for example in a factory or a coal mine have been included, in others only those in certain occupations, for example the spinners in a textile mill or those working at the coal face in a mine. The first has been termed an industrial, the second an occupational sample.

Industrial and occupational samples are subject to bias more often than population samples since workers who become unfitted, because of rheumatic or other illness, to follow their occupation are transferred to another job or leave the factory and thus are not included in the sample. Those who are suffering from a temporary disability may be examined at home but where the worker has had to leave his employment no record may be available of his existence or it may be impossible to trace him.

In choosing an industrial sample a general review of working conditions in the industry is first desirable. Some industries operate