New Haven survey of joint diseases

XVII. Relationship between some systemic characteristics and osteoarthrosis in a general population

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Acheson, R. M., and Collart, A. B. (1975). *Annals of the Rheumatic Diseases,* **34,** 379-387. **New Haven survey of joint diseases. XVII. Relationship between some systemic characteristics and osteoarthrosis in a general population.** In a survey of the general population the presence or absence of osteoarthrosis of the hand was determined radiologically in 685 adults (300 males and 385 females). Of these, 261 (124 males and 137 females), chosen randomly, were given a complete clinical examination of the musculoskeletal system which included x-ray of joints elsewhere in the body. Osteoarthrosis (OA) scores for the hand and for all body sites were computed for each subject by summing the number of affected joints. For all subjects social class, height, weight, total serum protein, serum uric acid, haemoglobin, antistreptolysin O, (ASO), C-reactive protein (CRP), and rheumatoid factor were also measured. Analyses were carried out by simple comparison of means and by calculating multiple regressions and correlations.

The results showed the following. (a) The factor most closely associated with OA score is age. (b) Multiple coefficients of correlation between all the factors and OA were consistently higher in women than in men. For instance, for the hand R^2 was 0·32 in men and 0·49 in women. All the factors significantly associated with OA contributed to this sex difference. (c) In the hands and in all body sites OA scores were significantly higher in males than females under the age of 34 years, the opposite being true for those over 35, but the differences were not significant. (d) Other factors significantly associated with OA score both in weight-bearing and in nonweight-bearing joints in both sexes were CRP, weight/height ratio, serum uric acid, and ASO. In females such an association was also found with rheumatoid factor. With the possible exception of ASO, relationships between all these factors and OA have been found in at least one other epidemiological study.

It is concluded that systemic factors underly the development of degenerative joint disease, and that this systemic component is more important in women than in men. It is also suggested that transient episodes of inflammatory arthritis earlier in life may predispose to osteoarthrosis. Further studies may help to identify those persons at risk for the traumatic or wear and tear component in the causation of the disease.

A cross-sectional survey of the epidemiological and sociomedical aspects of joint disease in the general population of New Haven, Connecticut, was started in December 1963. The data have been useful in describing the epidemiology of osteoarthrosis (OA), the commonest joint disease, and of the characteristics which are related to arthritis and are continuously distributed in the population, such as uric acid. This paper presents a multivariate analysis in which osteoarthrosis as seen in x-rays is treated as the

dependent variable, and various demographic, symptomatic, and biological data are treated as independent variables, with a view to learning something of the aetiology of the disease.

Material and methods

STUDY POPULATION

The study population of persons aged 21 years and over (described previously, Acheson, 1966) was taken from several different socioeconomic areas of New Haven. Estimates from the 1960 census gave a population of about 2500; in fact 2389 were counted. Only persons for whom data were complete for the 11 items in the analysis were considered in this study. The age and sex distribution of the total survey population and of the two subgroups (1) index finger OA, and (2) body site OA, are given in Table I. The subgroups included 685 people about whom the necessary information was available for OA in the hand, and 261, of a subsample of 500, for whom it was available for the whole body.

DIAGNOSIS OF OSTEOARTHROSIS OF INDEX FINGER

X-rays of both hands and both feet of all the respondents were taken and the films read on a joint-by-joint basis for the presence or absence of arthritis (by Dr. Arthur R. Clemett) using the standards of Kellgren and Lawrence (1957, 1963). The scale devised by Kellgren and Lawrence is ordinal and has 5 stages ranging from 0 for an entirely normal joint to 4 for one considered to show severe OA. As a result of our own studies of reliability in the reading of *x*-rays we decided to reduce the number of stages from 5 to 4 by combining stage 0 with stage 1 (described by Kellgren and Lawrence as 'doubtful') and classing both as 0 (Wright and Acheson, 1970). Because we found that in the hands of both sexes the three joints of the index finger are the most severely and the most frequently affected by OA (Acheson, Chan, and Clemett, 1970) and the summed score for OA in the index finger correlates highly with the summed score for OA in all the other joints of the hand ($r = 0.95$), we concluded that OA in the index finger can be taken as a good indicator of OA elsewhere in the hand. Thus, as far as disease of the hand is concerned we simplified computation in this study by concentrating on the two index fingers. Therefore, a person having no OA in either will have a score of zero and, because six joints are considered, each with a range of 0–3, the most severely diseased person will have a score of 18.

DIAGNOSIS OF OSTEOARTHROSIS OF BODY SITES

A subsample of the entire study population selected at random attended a special clinic for detailed examination of the musculoskeletal system. It was thought likely that some members of this group would have joint disease in sites other than the hands or wrists. These sites were cervical spine, thoracic spine, lumbar spine, shoulders, elbows, hips, knees, and feet and ankles. A diagnosis of OA was established by taking *x*-rays of these other body sites.

COMPUTATION OF WHOLE-BODY OSTEOARTHROSIS SCORES

For analyses concerned with OA of multiple sites a site was scored 1 if OA was diagnosed on either side of the body and 0 if it was not diagnosed on either side; in these analyses *all* joints of the hand and wrist were combined as a single site scoring 0 or 1 only, and the same procedure was used for all joints of the feet and ankle. Thus bilateral disease for these groups of joints, or of the other joints, scored 2. The spine was subdivided into the three component parts listed above, each of which could score 0 or 1. The maximum total score for the whole body was therefore 15.

HEIGHT AND WEIGHT

Subjects attending the special clinic were measured by the survey staff. Height (cm) and weight (lb) were measured without shoes and with only light clothing. Subjects not attending clinic reported their weight and height to an interviewer. Weight divided by height was chosen as the variable most suitable as our index of body bulk (Florey, 1970).

Table I *Target population of the survey, and number in 2 subgroups by age and sex*

| | Age (years) | | | | |
	34 or less	*35–54*	*55+*	*Unknown*	*Total*
Total defined population					
Male	190	447	321	96	1054
Female	309	545	395	86	1335
Total	499	992	716	182	2389
Index finger OA subgroup					
Male	53	153	94	0	300
Female	77	190	118	0	385
Total	130	343	212	0	685
*Body site OA subgroup**					
Male	25	64	35	0	124
Female	20	61	56	0	137
Total	45	125	91	0	261

* Those members of a stratified probability sample of the total survey population who co-operated fully.

BLOOD ANALYSIS
All co-operative respondents who attended a special mobile unit had blood drawn (by venepuncture from the antecubital fossa) in a 20 ml aliquot into a dry sterile vacuum tube and in a 2 ml aliquot into a heparinized tube. (For further details see Acheson, Clemett, George, Kolakowski, Payne, and Vicinus, 1965.) In most cases the sample was frozen and centrifuged within 4 hours.

Haemoglobin values were obtained from the 2-ml aliquots by the cyanomethaemoglobin method with a haemo-photometer (Hainline, 1958).

Serum uric acid and serum total protein were measured by AutoAnalyser. A modification of the Folin method (Oser, 1965) was used for the assay of uric acid and the biuret reaction (Weichselbaum, 1946) for serum protein.

Antistreptolysin O (ASO) was measured by diluting graded titres of streptolysin O buffer. The highest dilution showing no haemolysis was recorded in Todd units (Hodge and Swift, 1933).

Rheumatoid factor. The presence of rheumatoid factor in the serum was determined according to the Latex method of Eldon, Jarlov, and Strandberg (1959). Sera were classified according to whether rheumatoid factor was 'present' or 'absent', with an industrially prepared glycine–saline reagent and subsequent mixing with Latex globulin reagent prepared by the same firm. Preparations were then studied under the microscope to determine whether there was any agglutination.

C-reactive protein (CRP) was measured in terms of the amount of precipitate formed in a capillary tube after incubation at 37°C and subsequent refrigeration of a mixture of serum and the appropriate antiserum (Tillet and Francis, 1930).

AGE AND SOCIAL CLASS
Age and social class were determined by questioning. Age was calculated from stated date of birth, and social class categorized by Hollingshead's (1957) technique which classifies the population into five groups on the basis of the present occupation and extent of education by the chief wage earner in each family. Class I represents the most prosperous and best educated and class V the least prosperous members of the community.

STATISTICAL ANALYSIS
Multivariate analysis has been used to estimate the relative importance of the various environmental and personal factors which lead to the development of coronary heart disease by research workers who have had access to sequential data describing a population observed over several years.

No such data are available for osteoarthrosis; and those presented here are strictly cross-sectional. Since it was not possible to observe the sequence of events in the study subjects it has been necessary arbitrarily to omit from the analysis those phenomena about which systematically collected information was available but which clinical experience indicates have probably arisen as a result of the disease—such as pain or stiffness of the joints. This latter group includes some, such as age and sex, which cannot be

considered to have been caused by disease. However, overweight and increased serum uric acid, etc. could be manifestations of processes which lead to or are caused by degeneration of articular cartilage.* These limitations apply equally to the less powerful statistical technique of using the t-test for examining the difference between means which is shown in Table III.

The assumption underlying the multiple regression analysis is that several variables, known as the independent variables, are related to the severity of osteoarthrosis in a rectilinear manner, and therefore a knowledge of them in any individual will be of value in predicting how severe is his osteoarthrosis. Should this assumption be correct for, say, two variables, and their inter-relationship with osteoarthrosis be to some extent independent of each other, then the accuracy of predicting who in a population has the disease will be improved if values for both are known for that population. In the tables the coefficient of multiple correlation (R) is given as a measure of the effectiveness of prediction. Analysis has been done in such a way that the highest correlate, which is by definition the best predictor, has been chosen first, and then the remaining data are re-examined and the second best chosen, and so on. The differences between the squares of the multiple correlations (R^2) are a measure of the effectiveness of each variable as a predictor of the severity of osteoarthrosis in an individual within the mathematical assumptions of the analysis. Thus, the more closely the value of the multiple correlation approximates its upper maximum limit of 1·00, the more effective is the prediction. Indeed if the multiple correlation proved to be 1·00 it would be possible to calculate how severe OA is in a person by measuring the 10 variables considered in this study.

Analysis and results

The mean values and standard deviations for OA in the index finger are given in Table II for each sex for ages 34 years or less, 35–54 years, and 55 years and over. It is clear that the mean scores for both OA of the index finger and of the body as a whole rise steadily with increasing age in both sexes. The females, however, have significantly lower scores than the males at the younger ages but over age 55 years they have higher scores though the differences in this older group are not significant. Mean values for the 8 independent variables were calculated by sex and age and it was found that, while the means for serum acid rise steadily with age in both sexes, those for ASO fall in both sexes. In men mean CRP increases with age and mean haemoglobin decreases. Among females haemoglobin increases with age and latex means tend to decrease. Latex values for men and CRP values for women showed no consistent pattern with increasing age, and trends for weight/height are slight.

* It was arbitrarily decided that the following could not be assumed to have preceded the development of osteoarthrosis: joint swelling, joint pain, and joint stiffness. Since no such assumptions could be made about the other variables, namely age, social class, height, weight, total serum protein, serum uric acid, haemoglobin, ASO, CRP, and rheumatoid factor, they were included in the analysis. This does not of course mean that any deviations from normal in them did precede the development of osteoarthrosis.

Table II *Means and standard deviations of osteoarthrosis scores for index finger and all body sites by age and sex*

Age (years)	Index finger OA score			Body site OA score		
	Mean	SD	n	Mean	SD	n
Males						
34 or less	0·30	0·64	53	1·04	0·89	25
35–54	1·42	1·67	153	2·94	1·30	64
55+	3·13	2·52	94	4·34	1·71	35
Females						
34 or less	0·13	0·41	77	0·40	0·60	20
35–54	1·15	1·55	190	2·98	1·51	61
55+	4·87	3·40	118	4·45	1·93	56
Probabilities for differences between sexes*						
34 or less	<0·01			<0·01		
35–54	>0·1			>0·1		
55+	<0·1			>0·1		

* Calculated by Mann-Whitney modified t-test.

Although the number of people in the group with OA of the index finger is about three times bigger than the group with body site OA the age and sex specific means for the 8 variables are with few exceptions similar to each other. Thus, at least as far as these variables are concerned, it can be concluded that the smaller group is representative of the larger.

Table III gives a simple approach to determining the relationship between the two OA scores and the other variables. Males and females alike were separated according to whether their OA scores for the index finger and/or the whole body were indicative of disease in more than an isolated joint (a score in each case of 2 or more); t-tests were carried out comparing the means for this case group with a disease-free control group, that is to say subjects whose score was 1 or 0. This was done by sex for index finger and all body sites. Only one variable, age, showed a consistently significant difference at the 1% level in all four groups, indicating that the prevalence of OA increases with increasing age. That there is an association between the score for the index finger and for all body sites is shown by the fact that for both sexes the total body score was higher in those who were classed as 'cases' of OA of the index finger than in those who were not so classified. The only other variable showing a significant difference among males was height. The results among females were not the same, however. Whereas the means for height did not differ significantly between the case and control groups, the means for weight and the weight/height index both did. Other means significantly different at the 1% level in females were those for serum uric acid, ASO, and haemoglobin. Trends for uric acid and ASO in males were similar but not significant.

In similar comparisons for total body OA scores, in which again a score of 2 or more was classified as a 'case', the weight/height index and age were the only variables showing differences significant at the 1% level in both males and females. Among males, weight and total protein both showed differences significant at the 5% level. Again the pattern among females was not the same, the means for weight, serum uric acid, and haemoglobin differing significantly at the 1% level, differences for height, ASO, and latex at the 5% level.

Some of the findings in women can be ascribed to the fact that the level of several biological quanta, such as haemoglobin, serum uric acid, and to a lesser extent body weight, tends to increase after menopause. Since the prevalence of OA increases sharply with increasing age, the association between the other variables and OA could be indirect, and simply be a consequence of the relationship of each with age. The number of subjects in the study was not large enough to permit multiple comparison of means of the many variables on an age-specific basis. Instead, step-wise linear multiple regression analyses were undertaken in which index finger or total body site OA scores were treated as dependent variables, and age, weight/height ratio, ASO, CRP, haemoglobin, rheumatoid factor, and total serum protein as independent variables. The assumptions underlying this analysis together with its general suitability are briefly considered in the Methods section above.

Results are shown by sex for index finger and all body sites in Table IV, and indicate that the most important single correlate of osteoarthrosis is age. Therefore, analyses for each sex were carried out for three age groups, <35 years, 35–54 years, and >55 years of age. Table V shows the multiple regressions when OA of the index fingers is the dependent variable. The independent variables account for only 15–18% of the variance of OA in each age group

Table III *Comparison between means of various factors in 'cases' of osteoarthrosis and in controls by sex*

Demographic and lab data means	Males						Females					
	Index finger			All body sites including hands and wrists			Index finger			All body sites including hands and wrists		
	Case group	Control group	P	Case group	Control group	P	Case group	Control group	P	Case group	Control group	P
Age	53·83	39·18	‡‡	51·17	32·84	†	54·43	37·23	†	54·23	33·82	†
Social class	3·17	3·17		2·99	3·23		3·34	3·21		3·03	2·92	
Height (cm)	171·85	174·94	‡‡	172·07	174·12	*	159·98	160·63	‡‡	158·70	160·88	*
Weight (lb)	172·13	171·58		175·17	164·90		143·96	134·48	‡‡	141·96	131·18	‡‡
Wt/ht	1·00	0·98		1·01	0·94†	†*	0·90	0·83	‡‡	0·89	0·81	‡‡
Total protein (g/100ml)	7·52	7·59		7·40	7·71		7·40	7·45		7·39	7·52	
Serum uric acid (mg/100 ml)	6·38	6·35	‡	6·27	6·15	‡	4·98	4·46	‡‡	4·92	4·36	‡‡
Haemoglobin (g/dl)	15·38	15·43		15·39	15·41		13·82	13·35	†	13·75	13·10	†
ASO	2·87	3·12		2·76	3·42		2·74	3·25	†	2·52	3·28	†
CRP	0·22	0·14	‡	0·20	0·07	‡	0·20	0·14	‡	0·18	0·23	‡
Latex	1·11	1·14	†	1·09	1·14		1·15	1·10	‡	1·15	1·05	*‡
OA elsewhere in body	2·63	1·46	†			—	2·98	1·18	‡‡			—
Number§	153	147		94	30		189	196		101	26	

* t value significant at 5% level; † t value significant at 1% level; ‡ t variances assumed not equal according to Bartlett's test; § persons for whom data were available for analysis do not represent a random sample of the population so prevalence cannot be estimated from these numbers.
For definition of a 'case' of osteoarthrosis see Methods section of text.

Table IV *Variables shown by multiple regression analysis to be associated with severity of osteoarthrosis in index finger and in all body sites, by sex, all ages*

Index finger			All body sites		
Variable	R^2 (cumulative)	% of variance of OA accounted for by each variable	Variable	R^2 (cumulative)	% of variance of OA accounted for by each variable
Males			*Males*		
Age	0·3010	30·1‡	Age	0·4191	41·9‡
CRP	0·3130	1·2*	CRP	0·4398	2·1*
Wt/ht	0·3218	0·9	Wt/ht	0·4587	1·9*
			Serum uric acid	0·4804	2·2*
				0·4834	0·3
Females			*Females*		
Age	0·4780	47·8‡	Age	0·4508	45·1‡
CRP	0·4853	0·7*	Wt/ht	0·4732	2·2*
Serum uric acid	0·4903	0·5	Haemoglobin	0·4970	2·4*
			Latex	0·5020	0·5

Probability of variable on entry to the analysis significant at *5%, †1%, and ‡0·1%.
Analysis of R^2 is discussed in the Methods section.

Table V *Index finger only. Variables shown by multiple regression analysis to be associated with severity of osteoarthrosis, by age and sex*

Age (years)	Males			Females		
	Variable	R^2 (cumulative)	% of variance of OA accounted for by each variable	Variable	R^2 (cumulative)	% of variance OA accounted for by each variable
34 or less	Wt/ht	0·0925	9·2*	ASO	0·1296	13·0†
	Total protein	0·1269	3·4	Wt/ht	0·2238	9·4†
				Total protein	0·2364	1·3
35–54	Age	0·1344	13·4‡	Age	0·1201	12·0‡
	CRP	0·1429	0·8	Serum uric acid	0·1274	0·7
55+	Age	0·0994	9·9†	Age	0·2204	22·0‡
	CRP	0·1196	2·0	CRP	0·2532	3·3*
				Serum uric acid	0·2795	2·6*
				Wt/ht	0·3044	2·5*
				Latex	0·3176	1·3*

For probability values see footnote to Table IV.

among males. In the two oldest age groups, age is the most important predictor and CRP is the second most important. In the youngest age group the weight/height factor alone accounts for nearly 10% of the variance. Age is the single most important independent variable in the two oldest groups while serum uric acid is second at 35–54 years and CRP is second at 55 years and over. In the youngest age group age contributes very little to the prediction of index finger OA, while ASO and the weight/height factor are the first and second most effective predictors.

Multiple regressions with the body site OA score as the dependent variable are shown in Table VI. In contrast to the results for the index finger (Table V), within each age group age is never the most effective predictor in males and only ranks second for subjects aged 35–54 years. ASO, serum uric acid, and total protein were the most effective predictors in the youngest, middle, and oldest age groups, respectively, while in the youngest group the weight/height factor and in the oldest group serum uric acid were the second most effective predictors. In the youngest and middle age groups, age alone contributed the most to the variance with 20% and 17% in the two groups. Total protein was the second most effective predictor at the youngest ages and latex was second for the 35–54 age group. In females aged 55 and over the most effective predictor was haemoglobin and next was the weight/height factor, but the contribution of neither was significant.

Table VI *All body sites. Variables shown by multiple regression to be associated with severity of osteoarthrosis by age and sex*

Age (years)	Males			Females		
	Variable	R^2 (cumulative)	% of variance of OA accounted for by each variable	Variable	R^2 (cumulative)	% of variance OA accounted for by each variable
34 or less	ASO	0·1855	18·6*	Age	0·1972	19·7*
	Wt/ht	0·2910	10·6	Total protein	0·3195	12·2
35–54	Serum uric acid	0·1217	12·2†	Age	0·1712	17·1†
	Age	0·1590	3·7	Latex	0·2155	4·4
55+	No significant contribution from any independent variable; R^2 for all variables was 0·2787			No significant contribution from any individual independent variable; R^2 for all variables was 0·1818		

For note on probability values see footnote to Table IV.

Discussion

These data bear out the importance of age in the development of a disease. The data also confirm earlier analyses of this and of other surveys (Kellgren and Lawrence, 1958; Engel and Burch, 1966; Bennett and Henry, 1971) that there are differences in the *pattern* of osteoarthrosis as it relates to the sexes. The relative magnitude of the multiple correlations in the two sexes supports a sex difference in aetiology. When the age groups are taken together (Table IV), and in almost every instance in which the data are treated on an age-specific basis (Tables V and VI), the multiple correlations are higher for women than for men. This means that those factors considered in the survey which are shown in the tables are more effective predictors of the severity of osteoarthrosis in women than in men. As Table II shows, the mean score for severity of osteoarthrosis age-for-age tends to be higher in women aged 35 or over than in men. Although tests of probability do not show the difference to be significant, the finding is such a consistent characteristic of most prevalence surveys that it must be accepted as general. A clear exception, however, is in those aged 34 or less in whom the means for index finger only and for all body sites are clearly and significantly higher in males than in females. This excess in younger males has been found in many studies, such as those in Leigh (Kellgren, 1961), Wensleydale (Lawrence, Bremner, and Bier, 1966), and in two tribes of North American Indians (Bennett and Burch, 1966), but it has attracted little comment. In Tecumseh (Mikkelsen, Duff, and Dodge, 1970), and in a recent study of Pima Indians (Bennett and Henry, 1971), prevalence in males was also observed through middle age. In general, however, women *with* osteoarthrosis of the hands and wrists have *more* osteoarthrosis elsewhere in the body than do men with lesions; whereas women *without* hand and wrist disease have *less* disease of other body sites

than men without hand and wrist disease. This agrees with a recent study by Benn and Wood (1974), and bears out earlier analyses of symptoms in this population (Acheson, Chan, and Payne 1969). It agrees also with a previous analysis of disease in the hand (Acheson and others, 1970) and with the view that a general systemic component may be more important in the aetiology of osteoarthrosis in women than in men. Further evidence of differing aetiology between the sexes is to be found in the work of Benn and Wood (1974), who show a correlation between age of onset and extent of disease in men but not in women.

The study would have been more complete and more useful if it had been possible to include among the putative aetiological factors data which quantified the amount of wear and tear on a joint, because data from clinical studies which suggest that wear and tear play a causal role in osteoarthrosis are most persuasive. Epidemiological studies in general, however, have not clearly shown an association between OA and wear and tear in joints. This may be due in part to the problem of quantifying wear and tear. The only attempt to do this in the New Haven survey was a study of the patterns of OA in the joints of the two hands, and this did show the disease to be more extensive and severe in the right than in the left hands of right-handed people. Had it been possible to include a wear factor for each joint, in the present analysis, the coefficients of multiple correlation which are all low could have been expected to be much higher.

For some factors which were included, such as social class, no relationship whatsoever with OA was found. For others an association which had been reported by earlier workers was confirmed. These included weight/height, which is an index of obesity (Florey, 1970), serum uric acid (Lawrence, 1969; Benn and Wood, 1974), and rheumatoid factor (Benn and Wood, 1974). For others again, the association found in the present data has not to the authors'

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knowledge been previously reported. This group includes ASO and haemoglobin. The relationship between osteoarthrosis and haemoglobin is only found in women, and could be due to the fact that they are strongly correlated with age in women.

The present analysis can be interpreted as suggesting, in addition to sex, age, and wear and tear (which of course are inter-related), that there may be at least two other general factors which are associated with a liability to develop osteoarthrosis. One is the general metabolic status that is concerned with overweight and obesity, a status which tends to be associated with a rise in such indicators of general metabolism as serum uric acid, serum cholesterol, and blood sugar. Of these, only weight/height index and serum uric acid could be considered in the present analysis, but inter-relationships exist between these and hypercholesterolaemia and hyperglycaemia, and are considered in more detail elsewhere (Fowler, Butterfield, and Acheson, 1970; Acheson, 1973; Acheson and Baird, 1973). Overweight almost certainly increases the probability of developing OA in certain weight-bearing joints, for instance the hip and knee, by adding to wear and tear, but this cannot explain its association with disease in the finger, which has been found here and is described by others (Kellgren and Lawrence, 1958; Engel, 1968).

A second hypothesis drawn from these findings is that previous inflammatory conditions of the joints may *predispose* to the subsequent development of OA. ASO is high during the course of rheumatic fever, and may take years to return to normal values (Tillet and Francis, 1930; Hodge and Swift, 1933). Although CRP was originally identified in association with pneumococcal pneumonia, it was subsequently shown to be a good indicator of activity in acute rheumatic fever (Anderson and McCarthy, 1950).

As far as rheumatoid factor is concerned none of the present sample had overt rheumatoid arthritis, but the remittent nature of this disease, together with its incomplete correlation with rheumatoid factor, are both well-known facts. Unfortunately, systematic information was not collected in the New Haven survey about past history of rheumatic fever, of transient polyarthritis, or of rheumatoid arthritis, but support for the hypothesis is to be found in the work of Lawrence (1969) who found a relationship between non-nodal generalized osteoarthrosis and previous polyarthritis in general populations in Leigh and Wensleydale. Similar associations were found in the family studies of Kellgren, Lawrence, and Bier (1963).

It is more difficult to argue that serum uric acid may indicate previous subclinical gout; as has been suggested, it is more likely that this is related to overweight and the 'metabolism of surfeit'.

The possibility that OA is more likely to develop after transient acute arthritic episodes would, however, explain various associations. For instance, why do cysts, which have long been looked upon as a sign of rheumatoid arthritis (Fletcher and Rowley, 1952; Cathcart, Bolzan, and O'Sullivan, 1968) also appear in x-rays in OA (Bennett and Henry, 1971)? Perhaps it also explains why in certain cases OA is associated with what can only be looked upon as acute inflammatory episodes. Kellgren and others (1963) have, among others, shown that there are also genetic factors in the development of generalized osteoarthrosis, and Engel and Burch (1966), in a national survey, made the intriguing finding that osteoarthrosis is more prevalent in the widowed and separated of both sexes than in the married and the single.

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