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Radiological cervical arthritis in populations

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Lawrence, J. S. (1976). *Annals of the Rheumatic Diseases*, **35**, 365–371. **Radiological cervical arthritis in populations.** The prevalence of cervical rheumatoid arthritis and its relationship to rheumatoid serum factors and erosive arthritis in peripheral joints has been studied in radiographs of the cervical spine and of the hands and feet drawn from 12 population samples. The changes were graded in accordance with the *Atlas of Standard Radiographs of Arthritis.*

Rheumatoid arthritis of the cervical spine (grades 2–4) was observed in 4·1% of males and 4·7% of females aged 15 and over. Prevalence was greatest in those born before 1900, 15% of whom were affected. There was a significant association with the sheep cell agglutination test but not with the bentonite flocculation test, though the latter correlated well with erosive arthritis in the joints of the hands and feet. Arthritis of the cervical spine showed a significant correlation with both seropositive and seronegative erosive arthritis in the peripheral joints.

A significantly higher prevalence of cervical arthritis than expected was noted in two population samples, one in Germany and the other in West Africa, though in neither was there a high prevalence of peripheral arthritis. The German population had relatively high antistreptolysin titres. A low prevalence of cervical arthritis was noted in populations in Czechoslovakia and in Arizona. 'Congenital' block vertebra had a prevalence of 0·9% in persons born before 1935, but none was observed in those born since. The figures suggest that environmental influences predisposing to cervical arthritis and block vertebra have changed in the last 40 years.

Involvement of the spine in rheumatoid arthritis has been recognized for some considerable time. Garrod in 1890 noted that the cervical spine was affected in 178 (35%) of his 500 patients with this disease. Sharp (1957) found the cervical spine affected clinically in 40% of rheumatoid patients attending the Rheumatism Research Centre in Manchester. It is generally recognized as a common feature of juvenile polyarthritis (Still, 1897; Coss and Boots, 1946; Potter, Barkin, and Stillman, 1954; Ziff, Contreras, and McEwen, 1956). Bland and others (1962) have found radiological evidence of cervical spine involvement in 86% of cases of classical or definite rheumatoid arthritis and Martel and others (1964) noted subluxation of the atlantoaxial joint in 34% of unselected patients with rheumatoid arthritis attending an arthritis centre. Odontoid erosion was present in 12%, cervical malalignment at other levels in 9%, apophyseal erosion in 9%, and ankylosis in 3%. An abnormal craniovertebral relationship was noted in 19%, neurological symptoms were present in 16%, but only 7% had neurological signs.

The prevalence of rheumatoid arthritis of the cervical spine has been investigated in population samples in the United Kingdom, the United States, West Germany, and Jamaica, and in most has shown much the same prevalence as erosive arthritis of the hands and feet (Lawrence, 1961; Ansell and Lawrence, 1966; Behrend and others, 1972). A significant relationship of spinal arthritis to erosive arthritis in peripheral joints has so far been established only for seropositive arthritis in the 55–64 age group in populations in the UK (Sharp, Purser, and Lawrence, 1958). In the present study the prevalence of rheumatoid arthritis of the spine and its relationship to rheumatoid factors and to arthritis in other joints has been assessed in all age groups from 15

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Table I *Population samples in which routine radiographs of the cervical spine were taken, and prevalence of*

Population samples	*Date of survey*	*Method of sampling*	*Age range (year)*	*No. in sample*	*Completion rate (%)*	*Grade of cervical*		
						Aged 25+		
						Total x-rayed	*Per cent*	
							2–4	*3–4*
Pieštany	1962–64	Area sample	15+	1508	94			
Oberhörlen	1963	Area sample	15+	443	95	340	7·1§	0·8
Watford	1961–62	1:110 streets	15+	496	85	323	1·4	0
Nigeria & Liberia	1965–66	Random sample of households	5+	831 seen	Indeterminate	590	5·8	1·5
Wensleydale	1958–60	1:2 villages	15+	1062	91	779	4·3	0·5
Leigh	1954–58	1:30 households	15+	1610	86	1290	3·6	0·4
Rhondda	1958	Age stratified	35–64	832	88			
Jamaica	1962	Age stratified	35–64	600	89			
Tecumseh	1962–65	Community survey	all ages	9819†	88			
Montana (Blackfeet Indians)	1961–62	Tribal sample	30+	1101	86	849	2·8	0·4
Arizona (Pima Indians)	1963	Tribal sample	30+	1127	86	816	1·8	0
British Columbia (Haida Indians)	1962	Tribal sample	15+	492	89	281	3·9	0·5
Total						5268	3·8§	

* 1964–1969 readings by one observer; prevalence estimates are based on unweighted means of 5, 4, and 3 age groups respectively.
† Samples of 100 cervical spine *x*-rays were taken at random from each of the three age groups 35–44, 45–54, and 55–64 for this study.
‡ $P<0.01$ § $P<0.001$

years onwards and in 12 population samples. The genetic relationship of spinal rheumatoid arthritis to peripheral rheumatoid arthritis and to spondylitis and Still's disease has also been investigated and will be described separately.

Method

The population surveys in Northern Europe and America on which this study is based have already been described (Lawrence and Bennett, 1960; Bremner, 1961; Ball and Lawrence, 1961; Lawrence and Ball, 1958; Ansell and Lawrence, 1966; Behrend and others, 1972). They are summarized in Table I. The *x*-rays of the cervical spine from these surveys totalled 8022, which represents 78·9% of those in the samples.

The *x*-rays were read blind, the changes being graded 0–4 according to the *Atlas of Standard Radiographs of Arthritis* (1963). Those from the population samples of Leigh and Wensleydale were read by two persons independently of one another and of the hand and foot *x*-rays. Those from the remaining surveys were read only by one (J. S. L.) who reread the Leigh and Wensleydale samples mixed with those from the other samples. Where two persons read the *x*-rays, conflicts were resolved by taking a mean of the two readings. Grade 4 was given when severe narrowing without bony proliferation was present in three or more discs and subluxation of at least two vertebrae. Grade 3 was indicated by narrowing in at least one disc without bony proliferation but with subluxation of at least two vertebrae. Grade 2 was given when at least one disc was narrowed without obvious bony proliferation but with subluxation at the affected or an adjacent disc, or when subluxation was present at the atlantoaxial joint.

The sheep cell agglutination test (SCAT) was performed by Dr. J. Ball, Rheumatism Research Centre, Manchester, or by Prof. T. Behrend; the latex fixation test by Dr. H. A. Valkenburg, Department of Rheumatology, University Hospital, Leiden; and the bentonite flocculation test by Dr. T. A. Burch, National Institute of Arthritis and Metabolic Diseases, Bethesda. Antistreptolysin titre was estimated by Prof. T. Behrend in Oberhölen using the method of Scheiffarth and Legler (1951), and in Leigh and Wensleydale by Dr. H. A. Valkenburg using the method of Todd (1934).

Results

PREVALENCE

If minimal changes (grade 2) are included the prevalence of cervical rheumatoid arthritis was 4% in males and 4·7% in females, but only a fifth of the cases were associated with arthritis in the hands or feet (Table II). The prevalence increased with age, most of the moderate or severe cases being found

*x-ray changes**

rheumatoid arthritis									
						Cervical disc degeneration: Per cent grades 3–4	*Per cent with grade 2–4 erosive arthritis in hand joints*		
Age 35+			*Age 35–64*						
Total x-rayed	*Per cent*		*Total x-rayed*	*Per cent*					
	2–4	*3–4*		*2–4*	*3–4*	*Age 25+*	*Age 25+*	*35+*	*35–64*
303	1·4§	0·2	196	0·5	0	14		2·1	1·1
257	8·8§	1·0	208	4·9	0	12	4·7	5·8	2·9
272	1·5	0	192	1·5	0	22	1·1	1·1	0·9
572	6·5	1·8	406	6·8‡§	0·6	14	6·6	7·9	3·2
644	5·2	1·4	463	3·0	0·5	16	3·5	4·2	2·7
1073	4·4	0·4	868	2·2	0·3	19	2·6	3·0	1·8
			686	5·2	0·5				
			526	3·1‡	0	26			4·9
			300	5·8	0·7	20		4·8	1·7
734	3·5	0·4	587	2·1	0·1	12	3·4	4·0	3·1
700	1·8	0	547	1·2	0	8	5·4	6·5	4·4
211	4·9	0·6	172	2·2	0	15	7·7	8·2	3·4
4766	4·3§		5151	3·2§		16			

Table II *Age and sex distribution of 'cervical rheumatoid arthritis' (1958–1965 readings) with and without peripheral joint involvement (erosive arthritis hands or feet grade 2–4) in various population samples**

	Males						*Females*					
		Grade of cervical RA						*Grade of cervical RA*				
Age (years)	*Total x-rayed*				*Per cent*		*Total x-rayed*				*Per cent*	
		2	*3*	*4*	*2–4*	*3–4*		*2*	*3*	*4*	*2–4*	*3–4*
15–24	324	1			0·3	0	308	3			1·0	0
–34	408	2			0·5	0	405	1			0·2	0
–44	744	8(1)	1		1·2(0·1)	0·1	658	7(1)	1(1)	1	1·4(0·3)	0·3(0·2)
–54	751	23(3)			3·1(0·4)	0	562	14(2)	1		2·7(0·4)	0·2
–64	755	43(7)	4(3)		6·2(1·3)	0·5(0·4)	855	45(6)	6(3)		6·0(1·1)	0·7(0·4)
65 +	398	41(8)	11(3)		13·1(2·8)	2·8(0·8)	423	61(12)	11(4)		17·0(3·8)	2·6(0·9)
15 +	3380	Unweighted mean			4·1(0·8)	0·6(0·2)	3211	Unweighted mean			4·7(0·9)	0·6(0·2)

*Based on radiograph readings by one observer; Piestany, Nigeria, & Tecumseh were not included.
Erosive arthritis of hands or feet shown in parentheses.

in those aged 65 and over. The more severe grades were more often associated with erosions in the hands or feet.

RELATIONSHIP BETWEEN RHEUMATOID ARTHRITIS OF THE CERVICAL SPINE AND THE SCAT

None of the 30 seropositive individuals below the age of 35 had radiological evidence in the cervical spine, but only 0·4% of the seronegative persons in these age groups had cervical arthritis and the numbers were too small for this to have any significance (Table III). From the age of 35 the prevalence of cervical arthritis rose, generally more sharply in the seropositive than in the seronegative individuals. The titre distribution using the SCAT indicated that there was little difference between those with and without arthritis up to a titre of 64. Titres of 128 or more, however, were commoner in persons with cervical arthritis than in those without. Seropositivity was related to the severity of the *x*-ray changes, being significantly greater in those with grade 3 than in those with grade 2 arthritis.

Table III *Relationship of cervical rheumatoid arthritis to the sheep cell agglutination test (1958–68 readings) in various population samples*

Age (years)	*SCAT titre (IU)*	*Total tested*	*Grade of cervical RA* 2	3		*Per cent* 2–3
15–24	32+	5	—	—		0
	<32	618	4	—		0·6
–34	32+	25	—	—		0
	<32	759	2	—		0·3
–44	32+	47	1	—		2·1
	<32	1328	12	2		1·1
–54	32+	50	3	—		6·0 NS
	<32	1259	33	1		2·7 NS
–64	32+	91	8	5		14·3 *
	<32	1478	78	5		5·6 *
65+	32+	57	9	2		19·3 NS
	<32	744	92	12		14·0 NS
15+	32+	275	21	7	UM	7·0†
	<32	6186	221	20	UM	4·0†

* $P \leqslant 0{\cdot}001$; † $P < 0{\cdot}01$. NS = $P > 0{\cdot}05$. UM = unweighted mean.

Rheumatoid factors reacting with altered human gammaglobulin were estimated on four of the population samples, those in Montana, Arizona, Jamaica, and Wensleydale. The bentonite flocculation test was used in all except the Wensleydale survey, in which the latex fixation test was used routinely and the bentonite test only in the first half. There was no obvious relationship between seropositivity by the bentonite flocculation test and cervical arthritis. This is in striking contrast to the fact that erosions in the hands and feet were three times as common in persons with a positive bentonite flocculation test or latex fixation test as in those in whom the test was negative.

ASSOCIATION BETWEEN CERVICAL AND PERIPHERAL ARTHRITIS IN SEROPOSITIVE AND SERONEGATIVE INDIVIDUALS

To study this association the population was divided into three groups (Table IV). Erosive arthritis (grades 2–4) was found in the hands or feet in 54% of those in group I, 15% of those in group II, and 16% of group III. In all instances it was significantly more than expected but, whereas in group I it was present at five times the expected frequency, in groups II and III it occurred at only about twice the expected frequency. When the more severe grades of peripheral erosive arthritis were considered the differences between the three groups were even more striking; 29 times more in group I and of the order of three times more in groups II and III. The 4 persons in group II with grade 4 erosions of the hands and feet are of special interest.

None had psoriasis. A female aged 60 had severe polyarthritis of 40 years' duration with tendon sheath swellings, grade 2 cervical arthritis, and a SCAT<4. A male aged 40 with Still's disease had a 30-year history with prolonged incapacity, tendon sheath swellings, subcutaneous nodes, and grade 3 cervical

Table IV *Erosive arthritis hands or feet in persons with cervical rheumatoid arthritis (RA) in various population samples*

	No.	*Grade of erosive arthritis hands or feet* *Observed* 0	1	2	3	4	*Expected* 2–4	3–4
(a) Grade 2–3 cervical RA								
I SCAT positive	28	10	3	3	4	8	2·74†	0·41†
II SCAT negative	241	149	55	29	4	4	15·0†	3·9
(b) Grade 0 cervical RA								
III SCAT positive	196	137	28	17	12	2	15·1*	2·8†

* Expected rates are based on 6011 persons and are corrected for age and geographical zone; Piestany, Nigeria, and Tecumseh not included.
† Difference between observed and expected significance ($P < 0{\cdot}01$).

arthritis; his SCAT was <4 and the latex fixation test negative.

A male aged 56 at the time of examination had a history of arthritis starting at age 25, spreading from ankle to knee and then to hands, feet, shoulders, and elbows, with resort to a wheelchair frequently since the age of 42. On examination he had symmetrical swelling of his wrists, thickening of the lateral metatarsophalangeal joints, and flexion deformities in his fingers. There was limitation of his knees, hips, and several other joints, and a questionable nodule at the elbow. Cervical arthritis was grade 2. There is little doubt that he had a severe erosive but seronegative arthritis. He was examined the following year, and at that time had a bentonite flocculation test of 1:128 but the SCAT was still negative.

The fourth, a male aged 40, had negative bentonite flocculation test and SCAT but had grade 4 rheumatoid arthritis in the hands and feet and grade 2 in the cervical spine. The history dated back to the age of 3, and so the diagnosis was probably Still's disease. However, when examined in 1961 he had morning stiffness, pain on movement of his joints, symmetrically swollen joints, but no subcutaneous nodules. His hands were said to have 'opera glass' deformities, which indicates his general status. His bentonite flocculation test and SCAT were again repeated in 1962, and were both negative.

GEOGRAPHY

The prevalence of rheumatoid arthritis of the cervical spine varied between 1 and 7% in different population samples (Table I). The greatest prevalence was observed in the rural population of Oberhörlen, West Germany, and the lowest in the urban population in Watford, but there was no general urban-rural difference. This is in accord with our experience of rheumatoid arthritis in other joints. A high prevalence was also observed in population samples in Nigeria and Liberia, but another Negro population in Jamaica failed to show an excessive prevalence. Unusually low prevalences were noted in a rural population in Piestany, Czechoslovakia, and in the Pima Indians in Arizona.

We have reviewed the Oberhörlen *x*-rays, both those taken at the time of the original survey and those made 5 years later, and have fully confirmed the diagnosis in 10 of the 11 males and 4 of the 9 females. Other evidence of rheumatoid arthritis was present in 8 of the 10 males and 3 of the 4 females. One new case had arisen in this period, giving a 5-year incidence of 0·3% in the group as a whole and of 1% in those aged 55 and over.

From a comparison in Table I it is evident that the greater prevalence of cervical arthritis in certain populations does not depend on factors influencing degenerative changes in the disc. A comparison with the geographical distribution of erosive arthritis in the hands indicates that the relative prevalences are not identical. The population in Arizona, for example, had a relatively high prevalence of erosions in the hands, whereas the cervical spine was rarely involved.

For the interest of other changes, the frequency of 'congenital' block vertebra is shown in Table V. It appears to be rare under the age of 25 years.

Discussion

Though an association between cervical and peripheral arthritis is found mainly in seropositive individuals, there is a significant association also in seronegative persons. This is to be expected since seronegative polyarthritis can on occasion cause erosion of cartilage, particularly in the juvenile form or in psoriatic arthritis. It is possible that some of the seronegative cases in the present series had Still's disease, though in none were the radiological

Table V *Age and sex distribution of congenital block vertebra in 10 population samples in Europe and America*

	Males			*Females*			*Both sexes*
		Congenital block vertebra			*Congenital block vertebra*		*Congenital block vertebra*
Age (years)	*Total x-rayed*	*No.*	%	*Total x-rayed*	*No.*	%	%
5–14	17	0	0	35	0	0	0
–24	335	0	0	284	0	0	0*
–34	419	2	0·5	388	6	1·5	1·0*
–44	808	9	1·1	705	3	0·4	0·8
–54	824	13	1·6	611	5	0·8	1·3
–64	805	9	1·1	805	4	0·5	0·8
65+	446	4	0·9	442	1	0·2	0·6
5+	3654		0·6 NS	3270		0·6 NS	0·6
15+	3637		0·9 NS	3235		0·6 NS	0·7
25+	3302		1·0			0·7	0·9

Data from the Tecumseh survey are included in this Table. * $P \simeq 0{\cdot}01$. NS = $P > 0{\cdot}05$.

changes characteristic of this disease. The onset of Still's disease in adults has been reported by Bywaters (1971).

Since cervical rheumatoid arthritis may occur with or without erosions in the peripheral joints it must be considered whether this represents two different diseases. We have compared the *x*-ray appearances in those with and without peripheral joint involvement, both seropositive and seronegative, and have been unable to find any qualitative difference.

The geographical findings are of interest in view of the very marked differences in prevalence observed, particularly the high prevalence of cervical arthritis in Oberhörlen and Liberia and the low prevalence in Piešťany and Arizona. It is unlikely that these are due to misinterpretation of degenerative changes in the intervertebral discs since they do not reflect the relative prevalence of cervical disc degeneration in these populations. Moreover, we have found no correlation between disc degeneration and rheumatoid factor titres. The geographical differences observed make it evident that environmental influences play a part, though it is difficult to say at what age they are operative.

It is perhaps of interest that 'congenital' block vertebra is rare in persons under the age of 25, i.e. in cohorts born since 1934 (Table V). Though the condition is described as congenital it could well arise, as judged from the growth defects, at or soon after weaning or at any time up to the third year, when the arch and body are united. The possibility that cervical rheumatoid arthritis may be declining must also be considered, in view of the very high prevalence in the older cohorts. The cervical arthritis in Oberhörlen was mainly in those born before 1899, when 20% were affected compared with 8% in those born between 1899 and 1908. The 5-year follow-up of those in the latter cohort indicated that the present rate of increase does not explain the age distribution, which must depend mainly on environment influences no longer operative. It seems reasonable to suppose that, as in the case of rheumatic fever, this may depend on a reduction in the incidence of certain infections in the population, though these need not necessarily have been streptococcal.

The cervical 'arthritis' in the Liberian population differed from that found in the other populations in that the atlantoaxial joint was mainly affected, the degree of subluxation being at times extreme. In 73% the subluxation was limited to this joint. Though streptococcus C and G were common, antistreptolysin titres were low in this population, reflecting the low group A pharyngeal isolations. The mean titre was 98 for Liberian and 108 for Nigerian adults (Valkenburg, 1974) and it is possible that joint laxity rather than erosion was mainly responsible. Muller (1970) found hypermobility to be of frequent occurrence in Liberians. An association with erosions in the hands or feet was, however, found in 5 (17%) of the 30 with grade 2–4 cervical arthritis in Liberia and Nigeria compared with 20% in those with cervical arthritis in the other population samples.

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