POPULATION STUDIES OF RHEUMATIC DISEASES ON A COASTAL ISLAND

PART I. CLINICAL AND SEROLOGICAL STUDY

BY

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In 1951 the first population study of the incidence of rheumatism in the Netherlands was conducted on Schiermonnikoog, a small coastal island in the Waddensee with some 600 inhabitants. Similar studies were also made on another coastal island, Terschelling, and in a community in the province of Groningen. The results of this combined study involving some 4,000 persons have already been published in this Journal (de Blécourt, 1954). During the first population study at Schiermonnikoog, a rheumatologist interviewed all persons over 15 years of age, and if it was ascertained that, at the time of the investigation or less than a year before, the subject was suffering or had suffered from a disorder that might possibly be "rheumatic",

a physical examination was made by the same rheumatologist, the erythrocyte sedimentation rate was estimated, and an analysis of the urine performed. Radiological and serological investigations were not carried out at that time. The population of Schiermonnikoog mainly comprises small farmers, sailors, and middle-class people. The composition of the population is influenced by the absence of certain men in the age groups 20 to 60 years (sailors) and of some adolescents (training elsewhere). Thus there are rather more women than men and more old than young people, in comparison with a normal population. The results of the 1951 study are summarized in Table I.

TABLE I
FINDINGS IN POPULATION STUDY IN 1951 AND 1961

Year of Study		1951	1961
Population Over 15 yrs of Age	Male	232	227
	Female	335	316
	Total	567	543
Persons Investigated	Male	199	187
	Female	270	254
	Total	469	441
	Completion Rate (per cent.)	87.5	81.2
Persons Found to have Rheumatic Disease	Male	40	43
	Female	86	78
	Total	126 (24 per cent.)	121 (27.4 per cent.)
Rheumatic Diseases Diagnosed (per cent.)	Rheumatic Fever	2.5	0
	Rheumatoid Arthritis	4.0	6.6
	Osteo-arthritis	47.4	55.4
	Fibrositis	46.1	38.0
		100	100

This study was repeated 10 years later in 1961, when all those above 15 years of age had a physical examination by a rheumatologist, and extensive laboratory tests were made, including examination of the urine, erythrocyte sedimentation rate, serological tests for abnormal plasma proteins and the presence of antithyroid and antinuclear factors, haemoglobin, blood group, and Rhesus factor.

The results of the 1961 study are also shown in Table I. There were no great differences between the results of the first and second studies, but the results of the second study are more valuable as every subject had a physical examination and the American Rheumatism Association criteria (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959) were used for diagnosis.

Clinical Findings

A comparison of the patients with rheumatoid arthritis in 1951 and 1961 is shown in Table II.

TABLE II
NUMBERS OF CASES OF RHEUMATOID ARTHRITIS,
BY SEX

Year of Study ..		1951	1961
Sex ..	Male ..	2	3
	Female ..	3	5
	Total ..	5*	8 (5† definite, including 2‡ sero-positive) (3§ probable)

* In 1961 2 had died, 2 had definite R.A., and one probable R.A.
† In 1951 2 of these had had R.A., 1 had had fibrositis, and 2 had been normal.
‡ Waaler-Rose test above 1:16 and latex-fixation test above 1:156.
§ In 1951 1 had had R.A., 1 osteo-arthritis, and 1 normal.

The distribution of the different forms of rheumatism in 1961 is shown by sex in Table III.

TABLE III
PERCENTAGE TYPES OF RHEUMATISM DIAGNOSED
IN 1961, BY SEX

Diagnosis	Percentage of Total Population			Percentage of Rheumatic Cases		
	Male	Female	Total	Male	Female	Total
Rheumatoid Arthritis ..	1.6	1.9	1.8	7.0	6.4	6.6
Osteo-Arthritis ..	11.2	18.1	15.2	48.9	58.6	55.4
Fibrositis ..	10.0	10.6	10.4	44.1	35.0	38.0
Total ..	22.8	30.6	27.4	100.0	100.0	100.0

If the 1961 series is divided into two main groups, above and below 50 years of age, it is clearly seen

that below age 50 rheumatic complaints are mainly due to "fibrositis", whereas above age 50 osteo-arthritis is the chief source of trouble (Table IV).

TABLE IV
PERCENTAGE TYPES OF RHEUMATISM IN 1961,
BY SEX AND AGE

Diagnosis	223 Below 50 yrs			218 Above 50 yrs		
	Male	Female	Total	Male	Female	Total
Rheumatoid Arthritis ..	2.2	0.0	0.9	1.0	4.0	2.7
Osteo-Arthritis ..	1.0	3.0	2.3	23.1	34.1	27.1
Fibrositis ..	8.9	13.5	11.4	10.0	7.3	9.0
Total ..	14.6	16.5	21.1	34.1	45.4	39.4

Serological Studies

The main interest in the 1961 study, however, was the search for the "rheumatoid factor" and other plasma macroglobulins associated with "connective tissue" and/or "auto-immune" diseases (see Part II). Of sixteen subjects in whom the Waaler-Rose test was positive (1:16 or more), only two had definite rheumatoid arthritis and in them the latex-fixation test was also positive. These both remained positive in 1962. There were thus fourteen false-positive Waaler-Rose tests and also one false-positive latex-fixation test; the latter and three of the former were negative when re-tested in 1962.

The details are set out in Table V (opposite).

Of these sixteen persons eleven were over 50 years of age.

Consanguinity.—The so-called "false-positives" were not closely related (when traced back for three generations) to the patients with sero-positive or sero-negative rheumatoid arthritis or to each other. 32.5 per cent. of the population over 50 years, and 17.4 per cent. under 50 years had been born on the island and formed the autochthonous section of the population. No differences were found in the incidence of rheumatoid arthritis or positive serological tests between those considered as autochthonous (with a fair chance of consanguinity) and those who were not.

Follow-up

Sero-positive.—In 1962, after one year's interval, all those who gave "false-positive" results were re-examined physically and serologically. The findings are shown in the footnotes to Table V (opposite).

TABLE V
POSITIVE WAALER-ROSE AND LATEX-FIXATION TESTS, BY SEX AND DIAGNOSIS, 1961

Test			With Rheumatoid Arthritis			False Positive			Total		
			Male	Female	Total	Male	Female	Total	Male	Female	Total
Waalser-Rose	Over 1 : 16	.. ..	0	2	2§	8	0	8† (1·8%)	8	2	10 (2·27%)
	1 : 16	.. ..	0	0	0	2	4	6‡	2	4	6
	Total	.. ..	0	2	2	10	4	14	10	6	16*
Latex-Fixation	Over 1 : 156	.. ..	0	2	2§	1	0	1 (0·22%)	1	2	3

Follow-up in 1962:
* 11 of these were above 50 years of age, and 5 below.
† 2 were negative in 1962.
‡ 1 was negative and 1 increased to 1 : 32 in 1962.
§ Remained positive in 1962. These are the same 2 subjects.
|| Was negative in 1962.

Sero-negative.—The sero-negative patients with probable or definite rheumatoid arthritis in 1961 remained sero-negative and the two sero-positive remained sero-positive. During this interval, one man aged 43, who had complained only of mild shoulder pain, then described as “fibrositis”, with negative serological tests and a normal erythrocyte sedimentation rate, developed definite sero-positive rheumatoid arthritis.

It is our intention to re-examine those with definite sero-positive rheumatoid arthritis, the false-positives, and those with plasma protein abnormalities each year, and the whole population every 5 years.

Conclusion

Our results are somewhat contradictory and do not confirm the findings of many previous workers, including Ziff, Schmid, Lewis, and Tanner (1958), McKusick (1959), Lawrence and Ball (1958), Lawrence (1961), and Scotch and Geiger (1962).

They are also at variance with some of our own earlier findings (de Blécourt, Polman, and de Blécourt-Meindersma, 1961; de Blécourt, Westendorp Boerma, and Vorenkamp, 1962). The numbers involved are too small to draw any definite conclusions, but regular examination will show the further progress of those with abnormal plasma proteins, and also which members of the population developed into new cases of rheumatoid arthritis.

The detection of “rheumatoid factor” or other abnormal plasma proteins does not lead to the detection of disease, which suggests that screening of populations or of patients’ relatives by examining the plasma proteins is of little value unless combined with a physical and, if possible, radiological examination. Our results also failed to show any correlation between the erythrocyte sedimentation rate, blood groups, and rhesus factor with the presence of rheumatic disease.

PART II. ANTINUCLEAR FACTORS AND ANTITHYROID ANTIBODIES

BY

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Tests for antinuclear factor and antithyroid antibodies were also carried out in the population described above.

Methods

The presence of the antinuclear factor (ANF) was demonstrated by Coons’ indirect fluorescent antibody technique (Coons and Kaplan, 1950) by the method of Mandema, Pollak, Kark, and Rezaian (1961). Smears of human buccal mucosal epithelial cells were used as a

substrate. The globulin fraction of rabbit anti-human gamma globulin conjugated with fluorescein isothiocyanate (commercially produced by Sylvana Chemical Co.) was used as an antiserum.

Before use the conjugated antiserum was absorbed twice with acetone-dried rat-liver powder. The smears were incubated with the test serum for 90 min. and with the fluorescein-conjugated globulin fraction of rabbit anti-human gamma globulin serum for 30 min.

All sera were tested undiluted in duplicate, and if they were positive titrations were made as described above.