EPIDEMIOLOGY OF RHEUMATIC FEVER IN A RURAL DISTRICT IN ITALY
WITH PARTICULAR REFERENCE TO SOME ENVIRONMENTAL FACTORS

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Scope of Inquiry
The purpose of this research was to ascertain the prevalence of rheumatic fever and rheumatic heart disease in a region of Italy, where the high incidence of both complaints is well known to practising physicians, and to evaluate the weight of some factors generally admitted as important in the pathogenesis of the disease.

Material
The research was carried out in a sample of the population living in a well delimited area of the lower Po valley. The sample was also homogeneous with respect to two other factors: all the subjects were women, and all of them were working as manual labourers. The reason for this selection was to confine the investigation to the incidence of rheumatic fever in a special group of manual labourers, the workers in the rice fields; in Italy these workers are almost exclusively women. A comparable number of women from the same district, but not engaged in the rice fields, were used as controls.

The inquiry (which took 5 months of team-work, from October to February) concerned 930 women, aged 14 to 70 years. The mean age was 34, and the percentage distribution of the cases according to age is shown in the figure. At the time of the investigation, all the subjects were actively pursuing their occupations. The incidence of rheumatic heart disease in this group is therefore referable only to the whole of the active or apparently fit and well population.

The 930 women represented 2.3 per cent. of the total population, and 4.4 per cent. of the female population of the districts where the inquiry took place. The 607 rice workers represented 15.5 per cent. of all the women employed in this way in the districts investigated. The distribution of subjects according to age was almost the same with the rice workers as with the other peasant women (see Figure).

Methods
Investigation.—In each subject this comprised:
1. Medical History and Family History.—Particular attention was paid to rheumatic fever and rheumatic conditions. As definite evidence of rheumatic fever in the past history, we accepted only one or more episodes either of acute migrating polyarthritis, confining the patient to bed for many days, with fever subsiding after salicylates, or of Sydenham's chorea. We considered "atypical rheumatic history" to be that referring only to vague muscular or joint pains, sciatica, stiff-neck, lumbago, etc., without any definite sign of rheumatic activity.
2. Clinical Examination.—Special attention was given to the condition of the heart.
3. Screening of Chest, with orthodiag ramm of the heart.
4. Electrocardiogram, with Einthoven and unipolar limb leads, and unipolar chest leads V1, V6.

Classification of Cases.—In addition to the classification according to occupation (workers in the rice fields and other labourers), the subjects were classified according to:
(a) Medical History.
1. Past history of typical acute rheumatic fever or rheumatic chorea.
2. No such history.
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(b) Results of Clinical Investigation.
(1) Proved rheumatic heart disease.
(2) Probable rheumatic heart disease.
(3) Possible rheumatic heart disease.
(4) No rheumatic heart disease.

Results

History.—14.9 per cent. of the cases had a history of acute rheumatic fever or rheumatic chorea; and 3.4 per cent. proved to have rheumatic heart disease, without any preceding episode of this kind being recorded. We are unable to give a mean value for the age of onset of the disease, since it was difficult or impossible to get a definite date from the past history in most of the cases. We do, however, consider the observation that the disease began before the age of 35 in 88.4 per cent. of the cases, as reliable. We should like to point out also that, among the cases in which rheumatic fever apparently began later, there were some in which there was little doubt that the onset had occurred at an unusually advanced age (55, 62, and 64 years).

Diagnosis.—Unequivocal evidence of rheumatic heart disease was found in 8.7 per cent. of the 930 cases; it was diagnosed as “probable” in a further 3.3 per cent., and as “doubtful” in a further 6.7 per cent. It was, of course, much more frequently present in subjects with a past history of acute rheumatic fever (35.5 as against 2.3 per cent.).

We were unable to confirm the diagnosis of rheumatic heart disease in more than a quarter of the cases previously so diagnosed (according to the history), and the condition appeared to have been overlooked in 40.7 per cent. of the cases in which we found definite evidence of it. This indicates how commonly a diagnosis of rheumatic heart disease is made which cannot be confirmed by a thorough cardiological examination, and, on the other hand, how often a valvular lesion can remain unnoticed, sometimes, for many years.

Our diagnoses in the 81 cases with valvular lesions are shown in Table I.

<table>
<thead>
<tr>
<th>Cardiac Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral insufficiency</td>
<td>49.4%</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>24.7%</td>
</tr>
<tr>
<td>Mitral disease (stenosis and insufficiency)</td>
<td>24.7%</td>
</tr>
<tr>
<td>Mitral disease and aortic lesions</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

The orthoangiogram was of considerable use in the diagnosis of rheumatic heart disease, the heart shadow being completely normal in only 2.4 per cent. of the cases in which the other findings were consistent with this diagnosis.

The electrocardiogram was abnormal in 21.0 per cent. of all the cases studied. Abnormal records were obtained in 79.8 per cent. of cases with a rheumatic history, in 13.4 per cent. of cases with an atypical rheumatic history (history of joint pains, stiff-neck, lumbago, sciatica, etc., without any definite evidence of rheumatic activity), and in 6.9 per cent. of cases without rheumatic history.

The most frequent changes were those indicative of left atrial strain (26.5 per cent. of the pathological electrocardiograms), or of left ventricular strain (25.0 per cent.).

Relation of Incidence of Rheumatic Fever to Other Diseases

(1) Other Rheumatic Manifestations.—History of mild arthralgia or myalgia, stiff-neck, lumbago, sciatica, etc., was found in 44.7 per cent. of all cases. The frequency of these manifestations was slightly greater in association with a history of acute rheumatic fever (53.6 per cent.) than in the remaining cases (43.2 per cent.); the difference was not statistically significant at the 5 per cent. probability level (0.1 > P > 0.05). Signs of osteo-arthritis were seldom observed and occurred almost entirely in the older subjects.

(2) Other Cardiac Findings.—A systolic murmur at the apex, apparently classifiable as an “innocent murmur”, was found in 4.8 per cent. of all the cases studied. The incidence of this finding was higher (9.9 per cent.) among the subjects who had no history of rheumatic fever, and this supports the view that the finding has no pathological significance.

Hypertensive heart disease was diagnosed clinically in 5 per cent. of the whole series; the average age of the cases with hypertension was 52 years, considerably higher than the average age of the remainder. It must be emphasized that among the subjects over 40 years of age, hypertensive heart disease was significantly more frequent among subjects with a “typical” (5.8 per cent.) or an “atypical” (6.2 per cent.) rheumatic history, than among subjects without any previous rheumatic complaint (2.3 per cent.).

(3) Correlations with Incidence of Other Disorders. By the \( \chi^2 \) test the correlations shown in Table II
were found to be statistically significant, the probability \( P \) being less than 0.001 in each case.

In addition, significant differences in the frequencies of various other disorders were found when cases with a rheumatic history were compared with the remainder. The disorders in question are shown in Table III.

<table>
<thead>
<tr>
<th>Other Disorders</th>
<th>History of Rheumatic Fever</th>
<th>No previous Rheumatic Complaint</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of Pleurisy</td>
<td>35.5</td>
<td>13.6</td>
</tr>
<tr>
<td>Alveolar Pyorrhea</td>
<td>13.8</td>
<td>2.7</td>
</tr>
<tr>
<td>Diagnosis of Erythema Nodosum in the History*</td>
<td>4.1</td>
<td>0.8</td>
</tr>
</tbody>
</table>

* It is possible that a number of the cases which were said to have had erythema nodosum had, in fact, been suffering from rheumatic fever.

Relation to Family History of Rheumatism

Of all subjects studied 16.6 per cent. had some history of rheumatic fever in a blood-relations. When the subjects had been classified into groups, it was found that there was a rheumatic family history in 20.3 per cent. of subjects with a personal history of acute rheumatic fever or rheumatic chorea, in 16.7 per cent. of subjects with an "atypical" rheumatic history, and in 14.0 per cent. of subjects with no personal rheumatic history. There was thus a highly significant correlation between personal history of rheumatic fever and family history of the disease \( \chi^2 = 26.7; P = <0.005 \).

It was also found that 21.3 per cent. of subjects with rheumatic heart disease had a rheumatic family history, while the corresponding figure for subjects with no heart disease was 15.1 per cent.

Of the women studied, 662 had been married. The incidence of rheumatic fever among their husbands was 6.5 per cent. The incidence of the disease among husbands of women who had had rheumatic fever was 10.4 per cent., while that among husbands of women with no rheumatic history was 5.1 per cent. These data confirm the abnormal prevalence of rheumatic fever in the country where the inquiry was performed. The frequent coincidence of rheumatic history in husband and wife demonstrates the importance of common living conditions; the possible role of an infective agent cannot be eliminated.

Effect of Environmental Conditions

1. Geography, Climate, and Housing.—The inquiry was carried out in a region consisting largely of a reclaimed land, very little above sea-level, and rich in water-courses and rice fields. The climate was characterized by long periods of rainy and foggy weather. Housing was generally poor and about one-third of the houses were damp and unhealthy. Subjects with a past history of rheumatic fever were frequently found to be living in damp houses, and a highly significant correlation was obtained between "history of rheumatic fever" and "damp house" \( \chi^2 = 26.4; P = <0.005 \). There was no significant correlation between crowded living accommodation and the incidence of rheumatic fever.

2. Diet.—An accurate study of the present diet of the subjects of our inquiry would have been too difficult, owing to the large size of the sample, and owing to its not sufficiently reliable composition. Poor and ignorant country women could not provide data adequate for appraisal of the diet in terms of its caloric value or of its content of individual nutritional factors. Besides, we thought that the knowledge of the total intake of calories, proteins, and vitamins of each subject at the moment of the inquiry was less relevant to the scope of our inquiry than an outline of what had been her alimentary habits during her whole lifetime.

Therefore, the inquiry was necessarily carried out using very elementary questions, as, for instance:

- How often do you eat meat each week?
- Which kind of fat (butter, oil, lard, margarine) is usually employed in your cooking?
- Do you eat fresh vegetables and fruits, throughout the year? and so on.

This part of the inquiry was entirely conducted by a single researcher, in order to secure uniform evaluation of the information obtained. Taking into account the general dietary habits of the Italian people, it was possible to judge, for each subject questioned, whether the dietary intake of carbohydrates (bread, macaroni, rice, potatoes, sugar, etc.), proteins (meat, fish, poultry, etc.), fat (butter, oil, lard), and fresh fruits and vegetables had been "poor", "normal", or "rich". For the purpose of statistical evaluation, these adjectives were translated into arbitrary degrees (1, 2, 3). We may add, incidentally, that the intake of eggs, cheese, and milk (too expensive to be afforded by most of our subjects) had been so scanty, with very few exceptions, as to provide no information useful for our evaluation.

The main observations we were able to make by considering the mean values were that the diet of the studied group was characterized by a considerable excess of carbohydrates and an evident deficiency of proteins, fats, and especially of vitamin-rich foods. Dark adaptation measurements, which suggested that the majority of the subjects were deficient in vitamin A, provided support for the latter finding.

A scanty and unbalanced diet was more frequent
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among subjects with a history of rheumatic fever than among those with no such history. In particular there was a highly significant correlation between history of rheumatic fever and an inadequate dietary protein intake ($\chi^2 = 45.4; P < 0.005$).

(3) Working Conditions.—The importance of factors related to occupation in the aetiology of rheumatic fever and their bearing on the high incidence of the disease in the district investigated is emphasized by a comparison between the workers in the rice fields and the other labourers (Table IV).

| Table IV
| PERCENTAGE INCIDENCE OF RHEUMATIC CONDITIONS IN RICE WORKERS AND OTHER LABOURERS |
|-----------------------------------|----------------|----------------|
| History of Rheumatic Fever        | Rice Workers  | Other Rural Workers |
| History of Rheumatic Fever        | 24.3          | 6.8             |
| Rheumatic Heart Disease           | 11.3          | 2.8             |
| "Atypical" Rheumatic History      | 17.1          | 10.8            |

In addition, it was found that among the rice workers, the incidence of rheumatic fever varied directly with the number of years the subjects had been working in the rice fields. 90.5 per cent of the rice workers who had suffered from rheumatic fever experienced the first attack after they had started working in the rice fields, and in one-third of them the onset of the disease occurred during their first three years in this occupation.

Discussion

The above results allow us to draw certain conclusions with regard to the epidemiology of rheumatic fever.

It is evident that in the district where our inquiry was performed, the incidence of rheumatic fever is extremely high, being comparable only with those reported some years ago in northern countries, as, for instance, in Britain or in New England (Paul, 1943). No enquiries conducted in large Italian towns and strictly comparable with ours are at present available. Nevertheless, the incidence of rheumatic heart disease among school children in Milan (1.7 per cent.; Guglielmini, 1940), and in Rome (1.35-1.7 per cent.; Spolverini, 1939), is very much less than the frequency of rheumatic disease found by us (history of acute rheumatic fever or rheumatic chorea 14.9 per cent.; proved rheumatic heart disease 8.7 per cent.).

These findings agree with the opinion of Puntoni and Tizzano (1948) that rheumatic fever is prevalent in the rural districts of Italy; and with statistics collected in such countries as Hungary (Barath, 1953) and Rumania (Sapira, 1949), where the economic standards of the peasants and their environmental conditions resemble those of the area of our inquiry.

The frequency of a preceding episode of rheumatic polyarthritis in the history of the husbands of the 662 of the investigated women (6.49 per cent.) provides further evidence of the surprisingly high prevalence of rheumatic fever in this region. Poppi, Martinelli, and Abbati (1952) found that acute rheumatic fever was one of the main causes of hospitalization in four general hospitals in the same area, accounting for 1.79, 1.97, 2.4, and 10.8 per cent. respectively of the total number of adults admitted to the medical wards in a period of 5 years.

One possibility to be considered is the genetic factor. The inquiry took place in small villages where the immigration is quite negligible, and where through the centuries, inter-marriage has resulted in some degree of relationship between the majority of the inhabitants.

Several points brought out by our inquiry cast light on the importance of environmental factors.

(1) The geographical and meteorological peculiarities of the area (reclaimed land, very little above the sea-level, rich in water courses, and rice fields, climate characterized by long periods of rainy and foggy weather).

(2) Poverty, the principal reason for unhygienic living conditions (poor housing, overcrowding, scanty and poorly-balanced diet, etc.).

The explanation of the extremely high correlation of “past history of acute rheumatic fever” with “dental caries” or “liver disorders” is probably to be found in common factors favourable to all these conditions: low standards of diet and hygiene.

The whole population in these districts suffer to some degree from the poor living conditions; and the women working in the rice fields are the most exposed. Their economic standard is considerably lower than that of the other labourers in the region; until 20 or 25 years ago they usually started working at the age of 10 or 11 years. They stand long hours in water under a considerable physical strain; most of them migrate seasonally into the rice area and live in badly ventilated and overcrowded barracks, on a poorly-balanced diet.

These unhealthy conditions must have some bearing on the surprisingly high incidence of “rheumatic fever history” (24.3 per cent.) and rheumatic heart disease (11.3 per cent.) among the rice workers. This study, therefore, gives confirmation of the importance of poor living conditions in the epidemiology of rheumatic fever. Many of these adverse environmental factors may be improved or elimi-
nated, and we are glad to say that the publication of the results of the present inquiry caused the Italian Government (1949) to introduce legislation aimed at reducing the risk of rheumatic fever, through a better medical selection in recruiting labourers for the rice fields, and through an improvement in the living conditions of the workers.

Summary

A sample of the population of the rice growing area of the lower Po valley was examined. Of 930 women, aged 14-70, 607 were rice field workers and the other 323 were manual workers otherwise employed.

The incidence of rheumatic fever, rheumatic heart disease, and atypical rheumatic manifestations was found to be 24·3, 11·3, and 17·1 per cent. amongst the rice field workers, as against 6·8, 2·8, and 10·8 per cent. amongst the other workers. There is thus a close connection with the type of employment as well as with poor conditions of life.

REFERENCES

Barath, E. (Budapest) (1953). Personal communication.


