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ON THE PROGNOSIS OF RHEUMATOID ARTHRITIS

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Of all internal diseases rheumatoid arthritis certainly is one of the most difficult from the therapeutical point of view. Also the diagnosis can be rather intricate, especially in early cases where the clinical picture varies considerably.

What can be said concerning the prognosis?

More and more we have become aware of the fact that we know very little of the natural course of the disease and of the factors which influence it. "By the very nature of the material dealt with, human subjects, the course of the disease has rarely been studied in its natural state because aspirin can be obtained without prescription and is commonly used by patients long before they consult the physician" (Ragan). Further, studies of the course of rheumatoid arthritis are usually restricted to patients who come to a particular physician, clinic or hospital. Thus, such groups of patients are to be considered as ill-defined selections from the total number of individuals with rheumatoid arthritis in the general population (Reynolds, Short and Bauer).

It would appear, says Duthie, that about 50 per cent of the patients fare "reasonably well" regardless of the form of treatment used. In 15–25 per cent, the prognosis is said to be "excellent". In the 50 per cent, who do badly, about 15 per cent become inactive with considerable residual disability and 10 per cent become "severely crippled". Of course Duthie's figures are to be considered approximate. Only a few long-term studies have been conducted.

The choice of criteria for assessing the course of the disease has been much discussed. Clinical and laboratory observations are usually divided into two categories: a. those which are thought to reflect the degree of activity of the disease, e.g. signs of joint inflammation, sedi-

mentation rate etc., and b. those which indicate the functional capacity of the patient, e.g. range of joint motion, strength of grip and so forth. Although changes in these two categories are often related, it seems desirable to maintain the distinction (Reynolds, Short and Bauer). Data from one or both categories have been used to measure remission or exacerbation in the course of the disease but too little is known about the reproducibility of such measurements in term of "observer errors".

As for laboratory findings we know that the sedimentation rate, the acute phase protein etc. often run parallel with the activity of the disease. Determination of serum glycoproteins has also been widely used in evaluating activity changes. Previously the sialic acid content of serum (measured by very unspecific colorimetric methods!) has been the usual test, Shetlar and coworkers have recommended determination of "seromucoid" according to Winzler (= perchloric acid soluble glycoprotein fraction). This heterogenous fraction has been specially studied at the South Hospital by Nettelbladt and Sundblad.—We do not know much about the relationship between the activity of the rheumatoid process and titer of the rheumatoid factor.—In all clinical studies outside the laboratory we should not forget 2 important factors which are often overlooked: the patients' psychic reactions and the examiner's personality!

In order to obtain a suitable material for our prognostic studies we first of all should decide what is meant by "rheumatoid arthritis". Unfortunately there is a wide difference of opinion as regards this matter even if we exclude all cases of juvenile arthritis, psoriatic arthropathy, arthritis in ulcerative colitis, rheumatoid cases with L.E. cells, agamma-globulinemia cases and—of course!—ankylosing spondylitis.

If too rigid diagnostic criteria are employed whereby only typical, far-advanced cases are included we will get another impression of the course and prognosis of the disease than if we adopt more liberal criteria whereby atypical, early and less severe cases are included in the material to be examined (Ragan). Unfortunately we have not had as yet so much benefit from the sheep cell agglutination and other such tests for practical diagnostic purposes in early cases.

Kellgren et al., Cobb et al. and Lawrence and Bennet point out that, although rheumatoid arthritis is commonly thought of as a severe and crippling disease, many individuals suffer from minor forms of the rheumatoid process, which give rise to only minor degrees of disability.

Even the best diagnostic criteria therefore are insufficient. Cobb, having given a survey of the work of the "Criteria Committee" of the American Rheumatism Association, exclaims: "It came as a bit of a shock to the Committee to discover that 30 per cent of cases that might be called definite rheumatoid arthritis by one or another physician did not meet the set of criteria that the Committee was able to establish". There remained cases that most physicians would consider definite rheumatoid arthritis which did not meet the criteria, and similarly, there were cases that met the criteria "but which would not be considered to be definite rheumatoid arthritis by most astute clinicians".

One and the same doctor should follow the cases all the time, i.e. for a *very* long time. A material where one doctor has examined the cases at their onset and another doctor five or ten years later, is of very limited value.

Data obtained in whole or in part from retrospective searches of clinical records are especially suspect; yet much of our present knowledge of the course of rheumatoid arthritis depends upon information obtained in this way (Reynolds, Short and Bauer).

Another difficulty ought to be touched upon: The onset of *articular* symptoms does not mark the onset of the disease process in a case of rheumatoid arthritis. Prodromal symptoms are often observed (general weakness, low grade fever, emotional symptoms, loss of weight etc.). But can we be sure that even these prodromal symptoms denote the beginning of the disease process? Certainly not, because the rheumatoid panmesenchymal process may have been going on for a long time without giving any clinical symptoms at all. Thus we find that in fact it is impossible to establish at what time the disease process really started in a case of rheumatoid arthritis.

Often the patient has had a period with atypical joint symptoms long before the appearance of a manifest rheumatoid arthritis. (The patients should be thoroughly interrogated about this as they cannot very well remember slight symptoms years ago and seemingly without any connection with their actual disease!) If such cases are included in a clinical material the result of prognosis studies will be quite different according to which phase of the disease the examination and the evaluation is made.

Thus, in studies of the prognosis of rheumatoid arthritis one must arrive at different conclusions depending upon which material one is working with: easy cases, severe cases, cases with a long or a short duration and so forth. Indeed it seems rather debatable if such a vari-

able condition as rheumatoid arthritis, really constitutes one single and unitary disease! Anyhow it seems advisable in prognostic studies to separate the patients into groups "with features that have a clearly established and strong relationship to the course of the disease" and which "should be very likely to react to a markedly different degree from each other" (Calkins et al.).

We had better refrain from intricate and subtle statistical methods, the primary material, i.e. the clinical data often being very diffuse. The basis for subdivision of the cases should be as simple and unsophisticated as possible: age, sex, type of onset and the like. In this way a few types can be discerned:

1. *Cases with insidious onset* are thought to have a more unfavorable prognosis—just as cases with a persistently high sedimentation rate, marked muscular atrophy, abundant subcutaneous nodules etc.

Symmetry of the joint symptoms may also involve an unfavorable prognosis. The present author observed a type of rheumatoid arthritis that displayed pronounced asymmetrical articular symptoms and seemingly had a very slight tendency to progress. However, after having followed these cases for a long time I am no longer inclined to believe the prognosis so favorable as I had anticipated, a fact which clearly illustrates the importance of a very long time of observation in rheumatoid arthritis cases.

2. Probably the prognosis is *better in males* than it is in females. An illustrative example:

♂ born in 1904. 2191/55. Rheumatoid arthritis with symptoms first in one wrist, later in most joints. Sedimentation rate 55 mm. Temperature normal. Gold treatment. After 2 months much better post or propter. Sedimentation rate 1 mm. A slight exudate persisted in the left knee for some time but disappeared after 6 months. The patient was later free from symptoms and now feels perfectly well. A slight atrophy of the left quadriceps muscle persists. The sedimentation rate is still normal.

In this case the prognosis may be favorable. But in all prognostic studies in rheumatoid arthritis it is important to remember that remissions are often seen especially in early cases and that they can be of a long duration (See below Fig. 2).

3. *Cases with an acute onset* may subside rapidly and may have a better outlook than those with an insidious onset:

♀ born in 1927. 13451/57.—Very acute onset in August 1957 with high fever (40°), severe joint symptoms especially in her shoulder

joints and sedimentation rate 160 mm. Electrophoresis very pathological: Albumin 38, $\alpha_1$5, $\alpha_2$16, β15, γ26 % = decreased albumin value and increased α_2 and γ. Neisseria complement tests negative.

After a few months the articular symptoms subsided and disappeared. The sedimentation rate and the electrophoresis curve became normal.

The patient is still in excellent health.

♂ born in 1905. 20380/58. Very acute onset 1958 with joint effusions and high fever (39.5°). Sedimentation reaction 156 mm. Electrophoresis: $\alpha_1$10, $\alpha_2$18, β17, γ20. Total protein 3.5.—Electrophoresis curve of a type which is encountered in nephrosis! Neisser complement tests were negative.

In this case too the symptoms subsided post or propter gold treatment. The patient is still in excellent health and his sedimentation reaction is normal.

Certainly these two cases must be supervised for many years, as the ultimate prognosis is still uncertain and an exacerbation may supervene. Unfortunately we are quite unable to establish if the disease process in a case of rheumatoid arthritis is healed or not. The expression "burnt out case" is very unsuitable and should not be used!

4. Evidently the prognosis in juvenile arthritis is better than in adult rheumatoid arthritis (Ansell and Bywaters, Edström et al.). As for adults Duthie et al., think that age at onset of the disease is of no great significance and apparently Short, Bauer and Reynolds are of the same opinion.

However, a correlation between age at onset of the disease and prognosis seems to exist for adult cases too. At the South Hospital and over a long period several cases have been observed (E. Jonsson and A. Wesslau) who started in the early youth and have done remarkably well:

♀ born in 1913. 2655/44. Rheumatoid arthritis since 1931 when she was 18 years old. Very long remissions. X-ray: small but distinct articular erosions. Sedimentation rate always elevated, at present 80 mm. The patient's subjective symptoms are mostly slight and her exacerbations as a rule of short duration. No anemia.

In some of these cases the radiological changes are very severe although the subjective symptoms are very slight. Fig. 1 shows the x-ray picure from such a case. The patient, born in 1918, has had rheumatoid arthritis since she was about 15 years. In spite of the extensive destructions in her right foot she can walk very well and she has

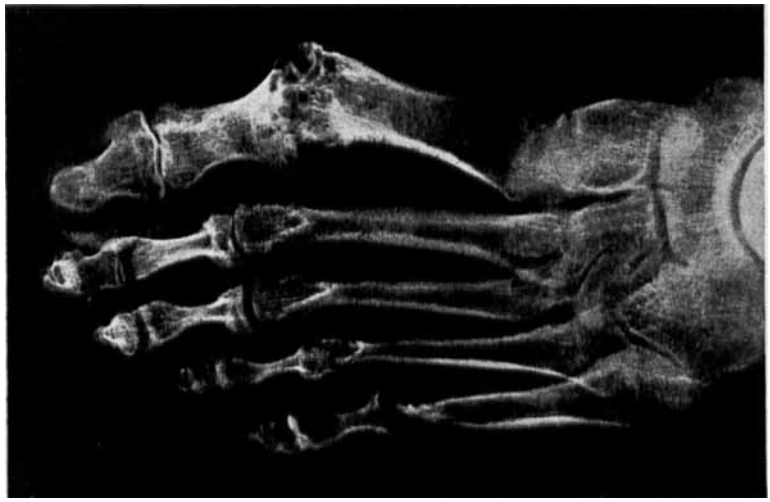

Fig. 1.

♀ born in 1918. "Adolescent case". Extensive radiological changes. Severe destruction in the basal interphalangeal joint I and extreme atrophic changes in the V metacarpal bone (arthropathia mutilans). Only slight subjective symtoms.

worked as a head waitress at a restaurant. Sedimentation reaction 36 mm. No anemia.

Apparently the inflammatory reaction is milder in these "adolescent cases".

The rheumatoid arthritis thus runs a long course often with erratic exacerbations and remissions. Can we by means of *therapeutic measures* influence the prognosis?

Without more exact information on the natural history of the disease it will be impossible to answer this question and to assess the value of our therapeutic methods. And here we are touching on the same problems as before, i.e. the imprecision in our present day diagnostic methods, the difficulty in recording the course of the disease, in measuring the disease activity and so on. And unfortunately it is impossible to obtain an adequate control material for therapeutical research.

As Ragan points out, it is also difficult to make an adequate assessment of the end result. The intensity of the disease waxes and wanes and every evaluation must be classed by the day the evaluation was made.

Ragan suggests the use of the term "management" rather than "cure" or "treatment". We have come to realize that we cure very few!

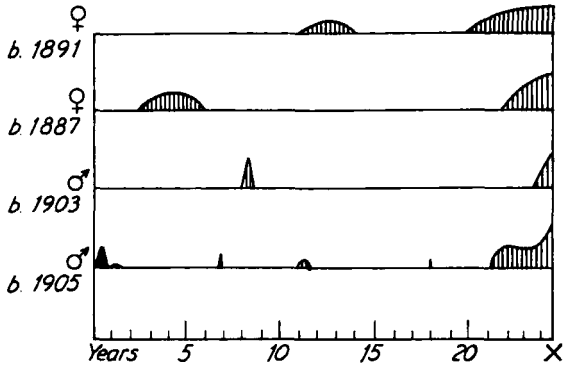

Fig. 2.

The course in 4 cases of rheumatoid arthritis.

▲ = acute episodes. |||||||| = chronic symptoms. Diagnosis settled at ×.

Discoveries of potent and wondrous remedies for rheumatoid arthritis are not made as frequently nowadays as formerly, and healing is not claimed as in older times. More criticism but also more pessimism has succeeded the former naive optimistic attitude when enthusiastic therapeuts achieved good results in the "inevitable 75 %" of all cases of rheumatoid arthritis without suspecting that they were only watching the natural course of the disease. In Fig. 2 the course of 4 cases is accounted for graphically. It appears from the figure that without acquaintance with the tendency for remissions of this annoying disease wrong conclusions could easily be drawn about the efficacy of a remedy given in one of these cases shortly before such a remission.

Certainly we had better fairly admit that we—as in most other internal diseases!—do not dispose of any potent therapeutical method in rheumatoid arthritis (possibly with the exception of gold treatment in early cases?) and that "optimal methods of therapeutical evaluation must await further knowledge concerning the nature, epidemiology, course and pathogenesis of the disease" (Calkins et al.). The surgery of rheumatoid arthritis presents a "peculiar problem" because of the "difficulty of foretelling with any accuracy the subsequent course of the disease" (Bastow).

SUMMARY

The prognosis in some types of rheumatoid arthritis is discussed and therapeutical questions are touched upon.

In fact we know very little of the natural course of this disease and

only a few long-term studies have been made.—Present-day diagnostic methods are imprecise and the diagnostic criteria are insufficient. Because of this and because of the difficulty in recording the course of the disease, research work on its prognosis constitutes a very delicate problem.

RESUME

Le pronostic des différents types d'arthrite rhumatoïde est discuté et les questions thérapeutiques sont abordées.

En fait, nous savons très peu de chose sur le cours normal de ces maladies et très peu d'études à long terme ont été effectuées. Les méthodes actuelles de diagnostic sont imprécises et les critères du diagnostic insuffisants. Pour cette raison et à cause de la difficulté qu'il y a à enregistrer le cours de ces maladies, les travaux de recherche sur leur pronostic constituent un problème très délicat.

ZUSAMMENFASSUNG

Die Prognose einiger Arten von chronischem Gelenksrheumatismus wird besprochen und Fragen der Behandlung werden berührt.

Wir wissen tatsächlich sehr wenig über den Verlauf der Krankheit und nur wenige Untersuchungen über einen langen Zeitraum sind ausgeführt worden. – Die heutigen diagnostischen Methoden sind ungenau und die diagnostischen Richtlinien sind ungenügend. Deshalb und auch wegen der Schwierigkeit den Verlauf der Erkrankung aufzuzeichnen, stellt die Forschungsarbeit hinsichtlich der Prognose ein sehr schwieriges Problem dar.

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