RHEUMATISM

EVERETT MINGUS, M.D.

MARSHFIELD, ORE.

If we were able to abandon the word "rheumatism" for more specific interpretation of the actual causes which give rise to a group of symptoms that go to make up the picture of this affection, material advancement would be made in the conception and treatment of this type of human ailments. The terms "neuralgia," "anemia," "dyspepsia," etc., were applied in the early days of medicine, to a certain group of symptoms; many of these vague terms have been replaced by names indicating direct causes of these conditions, and we hope that before long rheumatism will be given a more scientific place in medicine.

In the consideration of rheumatism too much attention has been given to secondary symptoms, as arthritis, endocarditis, pericarditis, etc. There the *materies morbi* has been sought and treatment directed for relief. To make confusion worse, every ache, pain and swelling of the articular structures has been called rheumatism until experience has proved the contrary; some affections of the joints that were not rheumatic underwent resolution, but the diagnosis was never changed. A short time ago I read a very able article by a foreign writer on tuberculous rheumatism. Why should not tuberculous arthritis be called by its real name rather than tuberculous rheumatism? The general use of the word "rheumatism" precludes it being synonymous with arthritis, for we have muscular, cerebral and peritoneal rheumatism. The word "rheumatism" has been badly overworked, and charges mountain-high have piled up against this obscure affection; it has served the interest of doubtful physicians; it has assumed the responsibility of malingering and played the rôle of fraud; it has been a financial pillar for the patent-medicine manufacturer and has upheld the quack; it has been a haven for stupidity and has contributed to the mockery of science.

Rheumatism has always been described as a disease or an affection characterized by certain symptoms. Much work has been done to fix the responsibility on some specific agent, but so far efforts in this particular have not been conclusive, though it would seem that opinion is now firmly established that a microbial infection is the cause. The preponderance of evidence, although lacking in positive proof, supports the belief that the group of symptoms called rheumatic fever is caused by infection; and in view of all the present facts in connection with the disease, no other theory is capable of explaining the phenomena associated with this common affliction. Much valuable labor has been lost in not giving sufficient scope of interpretation to the clinical picture of these cases; too often it has been taken for granted that all articular symptoms of a painful character arise from a common source, and forthwith the case is classified as rheumatic.

The symptoms of articular rheumatism are so constant that a strong belief grew up that there was a single cause; but when the symptoms are examined none of them is found to be pathognomonic. Tuberculous arthritis is often mistaken for rheumatic arthritis; the local picture is practically identical in the beginning and medical history is replete with cases of tuberculous arthritis that have been treated for rheumatism a long time before their true nature was recognized. Gonorrhea, syphilis, osteomyelitis, periostitis from streptococcus or staphylococcus and other infections cause symp-

toms not easily distinguished from rheumatism. The sour odor of the perspiration in rheumatism has nothing characteristic about it; the sweating is produced by low blood-pressure caused by the absorption of toxins. I think more than a single cause can produce the classical symptoms of rheumatic fever. Some infections no doubt have the power to set up an inflammation more severe in one kind of tissue than in another, and the same infection may on different occasions show itself in a mild and anomalous manner. I have seen typical cases of rheumatism follow infectious tonsillitis; I have seen equally typical cases associated with an enterocolitis. Recently I have treated two cases and seen another in consultation that presented the classical picture of rheumatic fever, and one of the patients developed endocarditis. In all of them the picture was the same; the rheumatic manifestations were secondary to an enterocolitis. The enterocolitis was characterized by considerable abdominal distention without tenderness, the passage of a large amount of intestinal mucus, a tendency to constipation, temperature variable but reaching a maximum of 104, soft pulse and sweating.

INVOLVEMENT OF THE INTESTINAL TRACT

The most noticeable symptom in all these cases was the passage of large amounts of intestinal mucus; the articular symptoms kept pace with it and did not disappear until the mucus had left the stools. During the course of these cases there occurred exacerbations and remissions of mucous discharge, which was associated with an increase and diminution of the rheumatic symptoms, clearly indicating that the intoxication producing the rheumatic manifestations was traceable to the morbid processes going on in the intestinal tract. I regret that it was not possible to make a systematic study of the intestinal dejections during the progress of these cases for the purpose of isolating the nature of the bacteria causing the enterocolitis. One of these cases has remained under my observation; it has been interesting to note that any disturbance of intestinal digestion is associated with arthritic symptoms, and that it is only by a close adherence to a suitable dietary that a painful condition of the joints is avoided. I think that the intestinal involvement in this case would go unnoticed by the patient if she had not been instructed as to the source of her rheumatic symptoms.

A short time ago I saw an elderly man about 80 who had suffered from rheumatism for thirty years. He had been compelled to use crutches and canes to go about for twenty years, and this period of his life had been made miserable by painful and stiff joints. My service in his case was called for the purpose of bolstering up a failing heart, but I obtained a history in his case which afforded material for reflection. He cautioned me not to give him anything that would act as a strong physic, for the reason that it would set up a troublesome diarrhea that would be hard to check; he further said that he had been subject to looseness of the bowels for a long time and that food would frequently pass through him undigested and associated with much mucus and rectal tenesmus. His mind was not clear on the question as to the relationship between the rheumatic symptoms and the intestinal trouble except as to their coexistence.

In looking over the literature on rheumatism one is impressed with the little space devoted to the discussion of any direct relationship existing between intestinal disturbances and rheumatic fever. The former is generally treated as a complication of the latter, though by implication much importance is attached to their relationship

In the treatment of rheumatism a proper diet is held as essential by almost all authors; in prophylaxis they hold that hygienic and dietary measures should receive first place; specific articles of diet are mentioned as being repugnant to the best interest of these patients and a general admonition is given to avoid any article which is liable to disturb the digestive system. In my experience the subjective symptoms associated with intestinal involvement in cases of rheumatic fever are rarely severe enough to call for much comment on the part of the patient, and unless special inquiry is made into the significance and relative importance of such manifestations, they will be attributed to complications.

In laying so much stress on the primary involvement of the intestinal tract in certain cases of rheumatic fever and the importance of directing the principal treatment to this tube, it would seem that I am dealing with a few isolated cases which should have no weight or influence in the determination of a well-recognized cause. It does not seem possible that the importance of primary intestinal infection in a common disease like rheumatic fever would have escaped the attention of many acute and careful observers, and for this reason I have much timidity on offering it as a sound suggestion; but the infection enters the body at some place and having a tendency to recur it is rational to conclude that a *locus minoris resistentie* must afford the seat of invasion; it may be the tonsils, pharynx or some other part of the alimentary canal. The point which I want to bring out most is the importance of examining the entire alimentary canal to ascertain the seat of invasion, for the purpose of more intelligent management of these cases. I feel that a more systematic study directed toward locating the initial source of the infection will lead to a better understanding of rheumatic manifestations, simplify treatment and reduce complications.

THE ACTION OF PREDISPOSING CAUSES

Heredity is mentioned as one of the predisposing causes of rheumatism. On the theory of the infectious character of the disease, predisposition is explainable on the grounds that certain families without question possess vulnerability that is not seen in other families, and no doubt this predisposition is not limited to one kind of bacterial life. It is impossible in our present light of organic construction and metabolic activity to give a qualitative or quantitative definition to that peculiarity which we group under the term predisposition to certain diseases; but general observation teaches us that some individuals do not attain, in the process of their development, a normal grade of tissue construction which enables them to offer substantial resistance to a hostile environment.

Other predisposing causes are cold and dampness. The manner in which these act is in depressing the resistance of the individual. Both cold and dampness favor heat radiation from the body and bring the temperature below normal with a consequent reduction in antagonism to bacterial life. The truth of this is so well exemplified in the catching of an ordinary cold that it seems hardly necessary to dwell at length on the part played in the reduction of temperature in the provocation of some diseases. For an individual to maintain his best resistance the temperature must be constant and normal; reduction of temperature decreases physiologic activities and the standard of resistance, under which circumstances bacteria gain a foothold. It does not follow that every time one suffers a reduction

in temperature, disease of some sort will follow. The presence of bacteria in sufficient numbers possessing a certain virulence is necessary. In reviewing the clinical picture of chronic cases of rheumatic fever, that is, those cases which show recurring symptoms after an acute attack, I am led to believe that the patients still harbor bacteria that caused the acute attack. Errors in diet, exposure to cold or dampness, fatigue, etc., provoke these attacks; under these unfavorable circumstances the resistance of the patient is diminished and lurking bacteria are offered less opposition. Latent tuberculosis and other dormant infections manifest themselves in certain conditions; in a like manner the bacteria causing rheumatic fever may remain dormant an indefinite time and show their presence only during perverted metabolic processes of the patient.

Recurring aches and stiffness of the muscles and joints generally spoken of as rheumatic can often be traced to various causes that have no relation whatever with rheumatic infection. I have in mind a patient who has always lived a sedentary life and who has been a sufferer from supposed rheumatism for twenty years. Examination of this case disclosed that the patient had persistent low temperature ranging from 97 to 98.2 F., and when his temperature was brought up to normal by stimulation or supplying artificial heat his symptoms would disappear. He had been fed on remedies for rheumatism without relief until the whole gamut of the Pharmacopeia had been exhausted. This patient obtained almost complete relief by spending a few months in a warm climate, meanwhile taking much physical exercise, which increased the efficiency of his heat mechanism and established a higher temperature range.

METHOD OF RESEARCH

In the interpretation of rheumatic symptoms two general divisions of the subject should be made. First, are the symptoms caused wholly by local morbid processes? Second, do they arise from metastasis? Before any intelligent study of the phenomena can be undertaken these two questions must be settled. Very clearly work of this character will, at times, involve much time, patience, observation and laboratory investigation; but the grave importance of a clear understanding as to all the facts demands that no physician should be contented with empiric treatment when handling an infection causing rheumatic fever. No mild and harmless infection is bringing about such manifestations, and it is the duty of a physician to locate accurately the source of absorption and if possible the kind of infection. If a careful inquiry is made into all the symptoms presented in cases of rheumatic fever I do not think one will fail to find some source of infection from which absorption is taking place; and having entered the circulation it makes its presence more pronounced by affecting sensitive and susceptible tissues and perhaps creating secondary foci. There is not sufficient evidence at hand to justify a theory that rheumatic infection like malarial infection gains entrance to the circulation and in that medium finds conditions suitable for its growth and liberation of toxins; but there is substantial reason for believing that the mucous surfaces are the seat of infection from which absorption occurs, and I am reasonably sure that further observations will show that the intestinal mucosa furnishes a large list of these infections. The arthritic, endocardial and pericardial involvements should be viewed as secondary results or the local manifestations of bacteria, their toxins or both acting on susceptible tissues.

REPORT OF CASES

While I was preparing this paper two more cases have come to my attention confirming the theory of primary intestinal infection in rheumatic fever:

CASE 1.—The patient was a girl, aged 17, whom I saw in consultation with Dr. Walter Culin, of Coquille, Ore. At first she had prodromal symptoms lasting two months which were characterized by general lassitude, indefinite mild chills and constipation. When the acute symptoms were precipitated the intestinal involvement was quite pronounced. Her attending physician thought at first he was dealing with a case of ptomain poisoning but as the case progressed arthritic symptoms developed and since that time it has presented the appearance of typical polyarthritis of rheumatic fever. The temperature in this case has been as high as 106 but when I saw the patient about two weeks after being confined to bed, there was a temperature of 101, respiration twenty-four, meteorism, constipation, stools showing considerable mucus, polyarthritis and sweating, with no enlargement of the spleen or cardiac involvement.

CASE 2.—The patient, a man aged 36, has chronic rheumatism. This patient at the age of 6 years had a very severe attack of inflammatory rheumatism and he informs me that he has had light recurring spells ever since and they are preceded by what he terms bilious attacks. He has a tendency to constipation and requires the continual use of physic to regulate his bowels. Two years ago this patient had an attack of rheumatic purpura which covered a considerable portion of the body; this condition was finally cleared up by the use of active purgatives continued over several days.

CONCLUSIONS

In the absence of any personal information to the contrary, I believe that I am presenting two original ideas in this report:—

1. In many cases of rheumatic fever the initial seat of the infection is in the intestinal tract, from which absorption of bacteria and their toxins occurs; on entering the circulation these cause peripheral symptoms in susceptible tissues.

2. Chronic or recurring attacks are or may be due to the continuance of the bacteria of rheumatic fever in the intestinal tract in an attenuated condition and are aroused to activity by dietetic, hygienic environmental errors of the patient which cause a reduction in metabolic activity and natural resistance.

TRANSPLANTABILITY OF MALIGNANT TUMORS TO THE EMBRYOS OF A FOREIGN SPECIES*

JAMES B. MURPHY, M.D.

NEW YORK

It appeared early in the development of modern surgery that tissues of lower animals could not be grafted into human beings. The extent of this barrier between species was not fully appreciated until the discovery of the transplantability of tumors. It was soon demonstrated by experiment that tumors of lower animals not only fail to grow when inoculated into another species, but often fail or give only slight growth, when grafted into a different variety of the same species. For example, the tumors of the white mice usually fail to "take" when inoculated into the gray or brown mouse. Recently Rous¹ has reported a tumor of a pedigreed chicken, from the first inoculations of which tumors resulted in none

other than blood-related individuals; and only after the malignancy had become greatly increased by repeated transfer did growth take place in other varieties of chickens.

The idea of the specificity of transplanted tumors has become so firmly established among students of cancer research that the fact of a new growth of any kind proving transferable to another species is considered evidence against the growth being a true neoplasm. The views entertained of genital tumor of the dog transplanted to the fox, and a tumor of the hare successfully inoculated into the rabbit, serve as examples of this.²

Ehrlich³ was the first to demonstrate that while tumors of one species cannot be transferred, in the true sense of the word, to a foreign species, yet such tissue when introduced into a closely related species may survive for a short time (from eight to ten days) and the cells actually multiply. If the tissue during this period is returned to the original species, it seems unaffected by its sojourn in the foreign host and is capable of producing an actively growing tumor. If, however, the graft is allowed to remain, or is transferred to another host of foreign species, it soon dies and is absorbed. These observations are accounted for by Ehrlich on the theory that tumor cells lack proper receptors to combine with the food elements of the foreign species and die from lack of nourishment. He considers that enough specific food is carried along with the graft from the original host to account for the temporary survival and growth. When this supply is exhausted the cells quickly die.

We reported last year⁴ the successful inoculation of the Rous chicken sarcoma into the developing chick embryo. In the course of this study the important observation was made that the tumor grew well in the developing pigeon or duck embryo, whereas in the adults of these species it quickly died and was absorbed. This fact suggested a wide difference between the embryo and the adult in their reaction to foreign tissues. The embryo, we might say, either provides a food substance utilizable by these tissues, which is lacking in the adult, or else lacks a defensive mechanism against such an invasion, which is possessed by the adult. The following results, obtained with tissues of a more distantly related species, constitute another and much more remarkable instance of similar kind.

Following the technic described in former papers,⁴ I inoculated a fine hash of the Jensen rat sarcoma into the outer membrane (fused chorion and allantois) of five-day to seven-day chick embryos; these were then incubated from ten to twelve days, that is, to within two days of hatching. When the shell was removed and the membrane cut and turned back, in a high percentage of instances the egg was found to have, at the point of inoculation, a rounded globular mass, suspended from the membrane by a broad flat pedicle. The masses varied in size from 0.2 to over 2 cm. in diameter. The consistency was that of a firm jelly, varying in color from pinkish-gray to red. The surface was smooth and glistening, with numerous large dilated vessels coursing over it, and smaller vessels were visible in the semitranslucent substance of the tumor itself. On section the masses were found to be solid and composed throughout of this pinkish-gray, somewhat translucent tissue, with small

* From the Laboratories of the Rockefeller Institute for Medical Research.

1. Rous: Jour. Exper. Med., 1910, xli, 690.

2. Von Dungern and Coca: Ztschr. f. Immunitätsforsch., 1909, li, 391. Von Dungern: München. Med. Wehnschr., 1912, lix, 238.

3. Ehrlich, P.: Arb. a. d. k. Inst. f. exper. Therapie, 1906, No. 1, p. 84.

4. Murphy, J. B., and Rous, P.: Tumor Implantations in the Developing Embryo; Experiments with a Transmissible Sarcoma of the Fowl, THE JOURNAL A. M. A., March 11, 1911, p. 741; Jour. Exper. Med., 1912, xv, 119.