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Anti-malarial and Anti-protozoal Drugs in the Treatment of Rheumatoid Disease

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In 1975 Dr. Roger Wyburn-Mason astounded the medical world with his announcement that he had found two genus of protozoa, Naegleria and Acanthamoeba, as the cause of rheumatoid arthritis and some other diseases[1]. New and profitable fields for medical and laboratory research have been opened as a result of his discoveries. Although full confirmation of his original premise has as yet not been confirmed by clinical pathologists, a new study is now in progress to determine the nature and roles of these amoebae. This is funded by the Rheumatoid Disease Foundation of the United States of America[2]. At the present time no less than 161 physicians and medical centers in 9 countries are engaged in treating patients with the anti-protozoal drugs and are accumulating useful clinical data for the management of the rheumatoid diseases, following a standard protocol[3].

While the "ideal drug" has not been found there are several antiprotozoal agents which are so effective as to deserve formal clinical trials. A comparison of the preliminary results with some of these substances is the subject of this paper. Therapeutic information and recommendations are being kept current and are exchanged through the Medical and Scientific Advisory Board of the Foundation. This data is available to any physician who may obtain it by writing to the international headquarters[4].

The acceptance of the probable protozoal etiology of collagen and "auto immune diseases" should not be difficult for the critical rheumatologist.

Every medical practitioner who treats these conditions recognizes that a choice of medicines is necessary and will produce improvement and a high percentage of remissions, without serious side effects or complications. A second research project is under way to select such a drug by *in vitro* studies[5] and *in vivo* studies[6], both sponsered by the Rheumatoid Disease Foundation.

Many investigators have long believed that the rheumatoid diseases were infectious in origin. This was reviewed in 1960 in the textbook edited by Hollander[7]. Fortunately, it is no longer necessary to quote the frequent saying, "There is no known cause and no known cure for rheumatoid arthritis".

Dr. Wyburn-Mason, as a result of his many years of well documented clinical studies concluded that all of the clinical criteria of an infectious disease are manifested in some stage and form in the acute or chronic forms of rheumatoid disease.

In his 480 page monograph, published only in Japan, he makes the following conclusions:

1. Collagen and auto-immune diseases (the rheumatoid diseases) are all various manifestations of one systemic disease.
2. Successful treatment causes the RF and ANF and various tissue antibodies to disappear.
3. The rheumatoid diseases appear to be infections.
4. Free living (limax) amoebae have been isolated from all causes of these diseases examined.

5. Many substances, known to be amoebaestatic or amoebaecidal to limax amoebae, may rapidly and completely relieve all manifestations or local or generalized rheumatoid disease.
6. And, to fulfill all of Koch's postulates as to the causation of collagen-auto-immune disease, injections of free living amoebae into the tissues of animals result in tissue lesions closely resembling those of rheumatoid disease — even though the same organisms cannot be distinguished in the tissues.
7. The causative organisms must differ antigenically with strain or species and must contain antigens specific to certain body tissues to produce such a wide range of antibodies, or none at all in certain instances.
8. Most significant is the finding that while a wide range of anti-protozoal drugs are effective in rapidly relieving most cases of rheumatoid disease, in a small proportion of patients there will be a recurrence or no beneficial effect. This would indicate differences in susceptibility and resistance of various strains and manifestations of the amoebae[8].

Because no virus or bacterial sources have been identified as the etiological agents, and even because these illnesses produce profound disturbances in the immune systems, this is sparse evidence for the "auto-immune" theory. The "infection theory" of rheumatoid diseases has a much broader base of pathological findings and an almost inexhaustible number of protozoa, mycoplasmas and other microscopic agents for investigation and possible identification with these illnesses[9].

The therapeutic use of anti-protozoal drugs is a natural forward step for physicians treating arthritis. The antimalarial agents — which have some anti-protozoal activity — have been accepted by many physicians and medical centers as a new but successful method of treating rheumatoid disease. The reasons for the effectiveness of these widely differing chemical substances cannot be explained without accepting that some types of infections, probably with protozoa or biologically related organisms, are the cause of this family of illnesses.

The inflammatory natures of rheumatoid diseases have been medically accepted for more than 90 years. But since no single infectious agent has been positively identified, various other etiologies have been accused, including allergies, lack of certain hormones, viruses, bacteria, metabolic defects and the equally unproven "auto-immune" theory.

Evidence on the therapeutic aspect is more tangible. Quinine and quinacrine, long known for their anti-malarial effect, were used in the 1930's and 1940's with some success. Chloroquine phosphate, which inhibits protozoal activity and acts similar to gold salts, is still a standard therapeutic agent with many physicians[10]. Looking for a heavy metal similar to gold, copper sulphate and Cuprimyl, a synthetic organic compound including the hydroxyquinoline radical, have produced beneficial results in some patients[8]. Bile salts, which may be the body's natural protection from pathogenic amoebae in the intestinal tract, have been administered with clinical benefit to persons with rheumatoid diseases by Hench, the Nobel Prize winner for his discovery of cortisone. All of these substances have been demonstrated to be anti-protozoal in laboratory tests.

Seeking drugs which have a stronger and more rapid action, and at the same time may have fewer side effects and toxicity, Dr. Wyburn-Mason continued his treatments with the 4-aminoquinolines and the medicines containing the imidazole complex.

This brief report covers nine years experience and the treatment of 842 patients with various rheumatoid diseases using drugs of known anti-protozoal action. The clinical improvement and numbers of remissions from the active forms of these illnesses not only confirms their usefulness as therapeutic agents but lends further support to the protozoal source of these syndromes.

The further clinical signs of a Jarisch-Herxheimer reaction in many cases soon after administration of the anti-protozoal drug is most probably brought on by the killed organisms in the patient's body[11].

Why isn't every patient "cured" by these treatments? Studies in progress, and accumulated knowledge about the types of protozoans linked with the rheumatoid diseases indicate that in the body some of the organisms are resistant, some may become resistant, others may encyst for a time to become "immune" to that particular therapeutic agent. For this reason drug therapy may be prolonged, or a change from one form to another of the substances which have proved to be antiprotozoal may be required.

Conclusions

The discovery of some species of amoebae in many patients with the rheumatoid diseases by the late Dr. Roger Wyburn-Mason has been a giant forward step in our knowledge of the etiology and treatment of these conditions.

The traditional use of the anti-malarial drugs now has a biological basis for their mode of action.

The anti-protozoal drugs are even more successful in the treatment of rheumatoid arthritis. This is therapeutic evidence of the protozoal origin of many of these disease syndromes.

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A Comparison of the Effectiveness of Anti-malarials and the Anti-protozoal Drugs in the Treatment of Rheumatoid Arthritis

Drugs	Number of Patients	Improved	+	Remissions	=	% Improved plus Remissions*	Not Improved
Controls							
Anti-inflammatory	82	21	+	8	=	34	6
Anti-malarials							
Chloroquine	40	26	+	1	=	67	6
Di-iodohydroxiquin	256	165	+	25	=	74	66
Quinacrine	61	22	+	14	=	59	25
Anti-protozoal							
Clotrimazole	9	2	+	5	=	77	2
Metronidazole	462	312	+	67	=	82	83
Tinidazole	14	8	+	4	=	85	2

*Percentage Totals of "improved" patients plus "remissions."

Data from three clinics now using anti-protozoal medications as of April 15, 1985.

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