

THE RHEUMATOID DISEASE FOUNDATION

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Executive Director/Secretary

Imidazole Compounds for the Treatment of Rheumatoid Arthritis

(The Use of Antiamoebic Compounds in the Treatment of Rheumatic Diseases)

by

Jack M. Blount, Jr., M.D. (*Physician: Mississippi*)

John R.A. Simoons, Ph.D. (*Pharmacologist: North Carolina*)

Introductions: **Gus J. Prosch, Jr., M.D.** (*Physician: Alabama*)

AMERICAN ACADEMY OF MEDICAL PREVENTICS, FRIDAY, NOVEMBER 16, 10:58AM TO 11:28AM
WORKSHOP: 2:00AM 3:00PM AND 3:45PM - 4:45PM

Cooperating physicians of *The Rheumatoid Disease Foundation (The Roger Wyburn-Mason & Jack M. Blount Foundation for the Eradication of Rheumatoid Disease: non-profit, tax-exempt, charitable)*, using the findings of Dr. Roger Wyburn-Mason (deceased) have treated and cured or brought under remission thousands of patients having rheumatoid diseases.

Open studies show an effectiveness ranging from 78% to 98%, depending upon the physician, antiamoebic used, and patient group studied.

The use of antiamoebics for treatment of Rheumatoid Diseases was introduced by Roger Wyburn-Mason at the IXth International Conference of Chemotherapy held in London, England in July 1975. Chief antiamoebics recommended by *The Rheumatoid Disease Foundation* are imidazoles where substitution has been made in the ONE position.

These compounds are amoebicidal *in vitro* against species of *Naegleria* and *Acanthamoeba* (See historical references attached).

Wojtulewski evaluated clotrimazole in a double-blind study, finding this compound "effective in the treatment of Rheumatoid Arthritis and superior to Ketoprofen." *The Rheumatoid Disease Foundation* is funding placebo controlled, double-blind studies at Bowman Gray School of Medicine (Chief Investigator, Robert A. Turner, M.D., Chief, Rheumatology Section).

The Rheumatoid Disease Foundation views Rheumatoid Disease as consisting of perhaps more than 100 different presenting symptoms, depending upon which tissues are affected by which genus, species, or strain of limax amoeba. Key to understanding the treatment protocol is observing the Jarisch-Herxheimer effect (flu-like-symptoms) accompanying the use of antiamoebics.

Jack M. Blount, Jr., M.D. will briefly discuss his personal interest in being treated, and also statistics represented by open studies of Robert Bingham, M.D., Gus J. Prosch, Jr., M.D., and Dr. Paul K. Pybus.

John R.A. Simoons, Ph.D., will describe the nature of imidazoles used in the treatment protocol.

While *The Rheumatoid Disease Foundation* views the limax amoeba theory as being the most probable (and workable) hypothesis in explaining and bringing about cure/remission of Rheumatoid Diseases, it recognizes that a multiplicity of factors are at work, including genetic susceptibility, nutrition and other good health rules; and it does not view free-radical explanations as being inconsistent with the limax amoeba hypothesis.

The Foundation is dedicated to: (1) stopping progress of rheumatoid disease, (2) repairing damage, and (3) maintaining health.

The follow-on workshop will include **Drs. Jack M. Blount, Jr., David A. Darbro, James P. Frackelton, Seldon Nelson, Gus J. Prosch, Jr., Paul K. Pybus, John R.A. Simoons.**

The workshop will be in two sections: (1) discussions related to the treatment and cure/remission of rheumatoid diseases, (2) demonstration of intra-neural injections for the immediate relief of sciatica pain resulting from either (a) Rheumatoid Disease, or (2) Osteoarthritis.

THE RHEUMATOID DISEASE FOUNDATION IS A PROJECT OF
THE ROGER WYBURN-MASON & JACK M. BLOUNT FOUNDATION
FOR THE ERADICATION OF RHEUMATOID DISEASE

TAX EXEMPTION APPROVED BY THE UNITED STATES INTERNAL REVENUE SERVICE
CHARTERED STATE OF TENNESSEE / SOLICITATION PERMIT APPROVED

The tables that follow represent open studies, using various antiamoebics in the treatment of Rheumatoid Diseases by Drs. Robert Bingham, Gus J. Prosch, Jr., Paul K. Pybus. (Dr. Anna Boland's (Korea) figures are less while Dr. Seldon Nelson's (Michigan) are more, but neither available at this printing.)

The final table represents use of the Wyburn-Mason/Pybus intra-neural techniques when treating pains of Rheumatoid Disease and Osteoarthritis by Paul K. Pybus.

**Jarisch-Herxheimer Symptoms Observed by Gus J. Prosch, Jr.
While Treating Rheumatoid Disease Patients With Various Antiamoebics**

(Letter to John R.A. Simoons: July 7, 1984)

Let me make some general statements concerning past observations and studies that I have concluded to be the truth in treating Rheumatoid Disease with antiamoebic drugs.

1. I recently completed a research project concerning the treating of 200 patients with Rheumatoid Disease with antiamoebic medication. The primary antiamoebic used was Metronidazole and when the desired response was not forthcoming I used other antiamoebics such as Allopurinol, Furazolidone or Rimactane. Final analysis demonstrated 78% good to excellent (cured or in remission) results and 22% showing poor to no result. All patients having a favorable response had some Herxheimer reaction and those showing poor to no response demonstrated very mild to no Herxheimer reaction. Incidentally, no serious side effects were observed from the medication.
2. The amoeba (or offending agent) can involve (or infect) *any* body tissue, organ or system.
3. If involved (or infected) that tissue, organ or system can demonstrate some form of a Herxheimer reaction when antiamoebic medication is introduced into the body.
4. With the initial introduction (1st week) of the antiamoebic medication, the Herxheimer reaction can be so severe that patients become fearful that the medication is doing them great harm and may want to stop the treatment. For this reason a single initial injection of 20-40 mg. of Depot Medrol is usually given to lessen the severity of the reaction.
5. After the second week of medication, the reaction gradually begins to subside, as fewer amoebae (or offending germ or agent) are killed and less antigen is released in the body.
6. If a patient has *any* Herxheimer reaction following the sixth week of medication, the patient is still infected and further treatment is indicated.
7. Long standing or chronic Rheumatoid Disease responds slower than acute disease.
8. If a patient being treated with antiamoebics does not have a Herxheimer reaction, the patient simply does not have Rheumatoid Disease or the particular amoebae (or offending agents) are resistant to the particular antiamoebic medication being given.
9. Herxheimer reaction signs and symptoms:
 - a. General and usual: Sweating and especially night sweats, diarrhea, nausea, vomiting, headache, fever, general malaise, flushing of skin, anorexia, aching bones and "flu" symptoms resembling a serum reaction.
 - b. The inflamed and affected tissues become more inflamed and tissues previously unknown to be involved become inflamed.
 - c. If the urinary bladder tissues are infected, patients may develop signs of full blown cystitis.
 - d. If the heart, pericardium or cardiac tissue is infected the patient may develop some paroxysmal auricular tachycardia, premature ventricular contractions or ectopic beats.
 - e. If the brain or meninges are infected the patient may develop severe (temporary) depression, lethargy, generalized weakness, temporary memory loss (personal experience), irritability along with headaches.
 - f. If the mouth tissues are infected, a bitter and/ or metallic taste may be noted along with mild shedding or peeling of the mucosal tissues. This has also been noted in the rectal tissues.
 - g. When the periosteal tissues and skeletal muscle tissues are involved, fairly severe bone pain usually accompanied by severe muscle pains and spasms may be observed, usually at night.
 - h. When the lungs and bronchial tissues are infected the patients may develop bronchitis symptoms and occasionally pneumonitis (resembling viral) has been observed.

From the above, one can easily see that most all of the previously observed side effects of [antiamoebics] may also be simply manifestations of the Herxheimer reaction. Therefore a clinician that is not totally knowledgeable concerning these possible signs and symptoms could easily mistake the Herxheimer reaction for possible side effects of the [antiamoebic]. Should this information not be taken into consideration, a misleading and false evaluation of any adverse experiences by various patients caused by the [antiamoebics] will be inevitable. . . . the medicine could be labeled more dangerous than it actually may be, and the aggravated symptoms could be misconstrued as an intensification of the disease being treated. The information and the above facts *must be considered* in evaluating [antiamoebic] effectiveness and side effects [when treating patients].

Comparative Results of Treatment With Other Drugs

Robert Bingham, M.D.

	Patients Treated	Improved or Remissions	Percent Change
Controls	22	7	30
Conventional Care	30	8	27
Copper Sulfate	12	8	66
Bile Salts	12	9	75
Clotrimazole	9	7	78
Diodoquin	204	189	93
Chloroquine	12	6	50
Flagyl	221	181	82*

* Recent cases have done better on increased dosages.

Conclusions. The discovery of Dr. Roger Wyburn-Mason that many cases of rheumatoid arthritis are infectious in origin with limax amoeba seems confirmed by success with treatment of acute active cases using anti-protozoal drugs. Diodoquin® and Flagyl® have been the most successful. Further clinical and pathological studies are recommended to verify these results and determine the pathological relationships between the protozoa and the rheumatoid diseases.

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SA Medical Journal, Vol. 65, March 24, 1984

Metronidazole in Rheumatoid Arthritis

Paul K. Pybus, *B. Chir., M.R.C.S., L.R.C.P., DRCOG, F.R.C.S.*

To the Editor: Further to my two previous letters,^{1,2} I wish to report that I have been using Metronidazole (Flagyl®) constantly in my practice for the treatment of rheumatoid arthritis, in 2 g doses for two consecutive nights at weekly intervals for 6 weeks.

If a normal person takes this dose there will be no reaction. However, of a total of 156 patients with rheumatoid arthritis, 133 (85%) manifested a Herxheimer reaction (fever, drenching sweats, headache and rigors among other symptoms). In 44 cases this reaction was extremely severe, while in the remainder the reaction was milder but nevertheless easy to recognize (Table I).

The clinical results, although subsidized by intraneural injections, were also most satisfactory and are shown in Table II. It will be observed that one-third of the patients are now almost symptomless, half of these experiencing only an occasional twinge of pain in their joints. Of the remaining two-thirds, only 11 (7%) showed no response whatsoever while the rest showed considerable improvement.

Degree of Herxheimer Reaction in 156 Patients: Table I

Herxheimer Reaction	Number	Percent
Absent	23	15
Mild (blushing only)	40	26
Moderate (fever and other 'flu-like symptoms)	49	31
Severe (rigors and other severe symptoms)	44	28

Clinical Results in 156 Patients: Table II

Clinical results	Number	Percent
Poor (no change)	11	7
Fair (slightly improved)	35	22
Good (one joint still troublesome)	60	38
Excellent (symptomless)	50	32

In view of these figures, I should like to advocate strongly the wider use of this drug and encourage further trials to confirm its effectiveness.

1. Pybus P.K. "Metronidazole in rheumatoid arthritis." *S. Afr. Med. J.* 1982;61:261.
2. Pybus P.K. "Anti-amoebic drugs in rheumatoid arthritis" *S. Afr. Med. J.* 1983; 63: 31.

SA Mediese Tydskrif, Februarie 20, 1982

Metronidazole in Rheumatoid Arthritis

Paul K. Pybus, *B. Chir., M.R.C.S., L.R.C.P., DRCOG, F.R.C.S.*

To the Editor: Encouraged by my initial success in the treatment of osteoarthritis by means of intraneural injections,^{1,3} I have been treating many patients with rheumatoid arthritis in a similar manner.

Several writers have reported success in the treatment of rheumatoid arthritis using various amoebicidal drugs. Levamisole has been used by Schuermans^{4,5} and McGill⁶ and clotrimazole by Wojtulewski *et al.*⁷ with mixed success, but both are toxic substances and require careful monitoring.

In his address at the 15th International Congress of Rheumatology in Paris, Wyburn-Mason⁸ suggested that the condition is caused by a free-living amoeba (*Naegleria fowleri* or *Acanthamoeba*) and reported success using certain imidazole derivatives, metronidazole and tinidazole. He also stated that this treatment is accompanied by a Herxheimer reaction. Both of these drugs have a potent anti-amoebic activity, and since they are fairly harmless I decided to use them to supplement my intraneural injection treatment. I used metronidazole in doses of 2 g on successive nights with a glass of milk.

Since the concurrent intraneural injections produce instant relief of pain and stiffness I was unable accurately to assess any therapeutic benefit from this amoebicidal substance, but it was possible to report on the occurrence of the Herxheimer reaction as follows: metronidazole was given to 35 patients with rheumatoid arthritis, of whom 30 experienced a considerable response. The drug was also given to 15 patients with osteoarthritis, but they showed no reaction whatsoever.

It would seem that the rheumatoid arthritis patients responded in some way to the metronidazole, suggesting an infection by amoebae as postulated by Wyburn-Mason.⁹ The osteoarthritis patients, however, would not react as the condition is a response to trauma and *Naegleria* is not involved.

I would like to advocate further investigations along these lines as the results could be most encouraging and rewarding.

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3. Idem (1981) *Ibid*, 59, 514.
4. Schuermans, Y. (1975): *Lancet*, 1, 111.
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7. Wojtulewski, P.J., Gow, J., Walter, R. et al. (1980): *Ann. Rheum. Dis.*, 39, 469.
8. Wyburn-Mason, R. (1981). Address, *15th International Congress of Rheumatology, Paris*.
9. Idem (1979): *Int. Med.*, 1, 20.

Relief by Means of Intra-neural Injections

Paul K. Pybus, *B. Chir., M.R.C.S., L.R.C.P., DRCOG, F.R.C.S.*

Type of joint	Numbers	of Failures	Months of Relief	Average relief of joint pain (months)
Hips	37	3	385	10.4
Knees	124	7	1421	11.45
Ankles	44	5	491	11.15
Shoulders	44	1	716	16.27
Elbows	19	0	339	7.3
Hands	56	7	549	9.6
Sciatica	49	1	496	10.12
Neck	20	2	283	14.2
Totals	393	25	4740	11.31

This is a survey of one third of Paul Pybus' patients, (A-G), treated by this method over the past 4 years. Only those patients who have been regularly followed up are included. There are many other patients whose results we do not have, as the patients have been lost to follow-up.

The following have been accumulated from many different sources, but chiefly represent articles and/or books that have been sent to *The Rheumatoid Disease Foundation*. They represent, chiefly, review of protozoal literature related to rheumatoid disease, but otherwise there is no intent to present these publications as being more than a collection; *The Rheumatoid Disease Foundation* does not necessarily endorse views presented. Where possible, this *Foundation* will provide copies at retail price or the service of copying at 10 cents a sheet, plus \$1.00 for postage and handling. Mail your requests to *The Rheumatoid Disease Foundation*, Rt. 4, Box 137, Franklin, TN 37064 (615) 6464-3757.

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