Mechanistic Treatment

By eliminating the cause(s) the mechanistic approach can be more effective and less costly in controlling and preventing chronic disease activity. This is unlike the symptomatic treatment approach that temporarily relieves symptoms. Basically there are three therapeutic targets: 1) to search for and eliminate the microbial cause(s) and metabolic defects, 2) to identify and block immune complex formation, and 3) to control and eliminate inflammation, pain, and fatigue. The elimination of the microbial root cause should be the primary target. The less pathogenic or nonvirulent microbes would be less reactive requiring less antibiotic treatment.

Three-Prong Prescription

1. Antibiotics; such as minocyclines, in low pulsed doses should be directed at inhibiting the microbial cause and preventing the disease. The multi-prong tetracyclines can also act as antioxidants, immunosuppressants, and protein synthesis inhibitors.
2. Immunosuppressants; that come in many different forms of alternatives including low dose prednisone that blocks the immune-complex formation and the activation of Complement which promotes tissue destructive inflammation.
3. Antiinflammatory antioxidants; such as dietary supplements and the nonsteroidal antiinflammatory drugs (NSAIDs) to eliminate and prevent the tissue destructive inflammation.

Several other major contributing factors affecting the occurrence and severity of the rheumatoid disorders must also be considered in selecting the most effective treatment. These include variable factors such as: Health, Diet, Exposure, physical & mental Stress. The most effective treatment is Good Health that is individually controlled by ones’ Diet, and exposures to physical and mental Stress. The goal of many alternative therapies is helping to achieve maximum good health with natural dietary supplements and both physical and mental stimulants. In addition fixed factors that include: Age, Gender, and Genetic susceptibility, all of which can help, hinder or predispose the therapeutic success. The treatment, for optimum benefits, should be individually adjusted for ones’ age, body size, and gender. Even though the symptoms on the surface are similar the underlying mechanisms can be different. (From the book: “Why Arthritis? Searching for the Cause and the Cure of Rheumatoid Diseases” Copyright by Harold W. Clark, Ph.D., used by permission, book available through this foundation’s website.)

Dr. Brown’s Antibiotic Treatment Plans

In his medical practice the late Thomas McPherson Brown, M.D. seemed to have a treatment protocol, a plan, for each rheumatoid patient that included some form of anti-mycoplasma antibiotics. Using different medications and dosages made it difficult to statistically compare and evaluate any single therapy. Medications were often changed trying to find both a tolerable and effective therapy. As new drugs became available they were continuously evaluated. For example tetracycline dosages varied from 10 mg. to 1000 mg. or from daily to weekly with oral and intravenous administration including several days of hospitalization. A significant study of 98 hospitalized rheumatoid arthritis patients treated over a five year period found that over 70 were substantially improved using the variable antibiotic treatment plan which was anything but the standard infection plan of 1 gm./day for 10 days.

The protocols weren’t just drugs and antibiotics as Dr. Brown was also interested in the psychosocial aspects of illness
and patient care. With extensive interviews the treatment also focused on both the patient and their family and not simply the disease. He worked extensively with a team of rehabilitation experts in helping to alleviate and solve the underlying patient problems. A good example of comprehensive medicine was the support by John L. Lewis, president of the Miners Union, that provided total care of the West Virginia miners’ medical problems. Although not discussed in his book The Road Back Dr. Brown was also the director of a multi-discipline medical Rehabilitation Center that also pursued the causes and the solutions to the related physical and mental health problems associated with rheumatoid diseases. The Allied Health staff proved essential for the therapeutic effectiveness. Like their diverse rheumatoid patients, doctors after leaving school and with experience developed their own theories and philosophy of patient care that are a little different from their professor’s and others. A consensus of what is the right medicine, a protocol for all patients, is not the question or the issue as medicine is more of an art than a science. There are many skilled artists and also 171 different wide ranging forms of arthritis. Most symptoms have suspected or unknown causes and become chronic or are short lived with periods of spontaneous remission. Because of the many different kinds and severity of symptoms many will require more than antimicrobials for control and eradication. Eventually with control comes prevention of the various forms of arthritis with regulated living and application of improved and alternative therapies. In his treatment plans Dr. Brown promoted a Mechanistic approach in searching for the cause and cure of rheumatoid diseases. Because of the many targets Symptomatic treatment requires multiple medications that further complicate the protocol and the evaluation of safe and effective results. Prescribing a treatment for the primary causes provides a direction for the evaluation of effectiveness. For nearly forty years Dr. Brown was considered a maverick who’s antibiotic treatment plan was criticized as unproven quackery and who’s strong personality convinced patients they were better. Now today after the antibiotic approach has been extensively tested and proven to be safe and effective in rheumatoid diseases both doctors and patients are finding the treatment beneficial.

Dr. Thomas McPherson Brown [was] the chairman of the Arthritis Clinic of Northern Virginia. A world-renowned leader in arthritis research and treatment, Dr. Brown has served as a consultant to the White House and has been a member of the National Research Council and the Food and Drug Administration’s Arthritis Advisory Committee.

He is a graduate of Swarthmore College and Johns Hopkins Medical School. Dr. Brown has served as Chief Resident in Medicine at Johns Hopkins and as a Resident at the Rockefeller Institute Hospital. He has held several prestigious positions, including Director of Arthritis Research at the Veterans Hospital in Washington, D.C., and Chairman of the Department of Medicine at George Washington University School of Medicine for a twenty year period. He founded the Arthritis Institute of the National Hospital for Orthopaedics and Rehabilitation in 1970.

His work on rheumatoid arthritis dates back to the late 1930’s during his tenure at the Rockefeller Institute when a colleague, Dr. Albert Sabin, found a strain of mycoplasma in a mouse while studying the disease, Toxoplasmosis. Dr. Sabin injected another mouse with this mycoplasma strain and the second mouse contracted arthritis. During this same period, Dr. Brown had been researching for an unknown virus in rheumatic tissues. No virus was found but one culture of joint fluid revealed mycoplasma. Subsequently, he found the same agents in the cultures from the genital tracts of men and women.

Dr. Sabin had found that the mouse strain of mycoplasma was susceptible to gold salts and Dr. Brown and his coworkers found this to be true of human strains as well. This prompted the search for a non-toxic antimycoplasma substance to substitute for gold. Such a substance was found with tetracycline antibiotics.

These findings suggested the initial use of antibiotic therapy in rheumatoid arthritis. A clinical finding which encouraged the pursuit of this approach was the Helxheimer reaction common to both gold and tetracycline with the initiation of treatment.

The concept of an infectious agent as a trigger of autoimmune diseases is not new. Indeed cross-reactions between group A streptococcal antigens and human myocardium elicit autoantibodies that have been associated with acute rheumatic fever. Several microorganisms (bacteria, mycoplasmas and viruses) have been proposed as likely etiologic agents for rheumatoid arthritis and animal arthritis. In particular the swine arthritis that mimics the disease in humans is known to be caused by a mycoplasma.

The recent report that Lyme arthritis, (which is known to result from a bacterial infection), can demonstrate rheumatoid arthritis-like symptoms, and can be treated with antibiotics, has once again stimulated interest in the infectious theory.

Dr. Brown and his staff continued to conduct research to confirm his working hypothesis.

His clinical observations throughout the years regarding which classes and combinations of antibiotics, and routes and intervals of administration were more tolerable, while at the same time providing the most effective means of sustained control in patients is summarized below. It is significant that the only antibiotics effective in the long term management of rheumatoid disease are also the only antibiotics effective against mycoplasmas.

Arthritis affected tissues are very reactive, and early cases of arthritis respond to treatment much better than the most severe long standing cases.

Dosage and administration of drugs

Tetracycline: (250 mg. dosages in capsule form) are administered once a day, three times a week at the onset of treatment.

Non-steroidal Anti-inflammatory Drugs (NSAIDs): The concomitant use of NSAIDs varies. Aspirin is often given initially, followed by a variety of substitutes for cortisone.

Cortisone: To reduce the inflammatory barrier and allow penetration of the antibiotics, 7 to 5 mg. of prednisone may be administered to the patient simultaneously with the antibiotic. Preferably, no more than 10 mg. should be administered for flares. Larger doses when required should be given in short interrupted courses. It is of interest that the concomitant use of antibiotics with the steroids makes steroid withdrawal easier. The dosage of the drug must be kept low to avoid interfering with the immune system but high enough to reduce the hypersensitivity or allergic inflammatory reactions of the disease.

The therapeutic outline can be modified by the physician at any time using the following major guideline:

1. Titration of the antibiotic dosage
2. Treatment complex to be given in interrupted fashion
3. Aim to phase out steroids in time

Ampicillin: in the presence of streptococcal infection as determined by the presence of an ASO titer, and/or a strong history of streptococcal infection, 250 mg. of ampicillin to be taken once daily (preferably in the evenings) twice or three times a week is administered.

As treatment progresses, a gradual increase in the tetracycline dose, up to 500 mg. one to three times a day, three times a week, (Monday, Wednesday and Friday) is administered. Care should be taken not to administer the drug at too high a dosage too fast, to avoid an allergic reaction by the patient.

Medical data is for informational purposes only. You should always consult your family physician, or one of our referral physicians prior to treatment.
When remission becomes established, the antibiotics may be gradually phased out. When flare-ups occur, short courses of antibiotics, should be given until no longer needed.

**Intravenous Therapy**

For patients who usually do not tolerate oral antibiotics, or those patients with a history of drug resistance from earlier treatment with a variety of drugs (e.g. gold, penicillamine, etc.), an intravenous regimen is followed.

Cleocin (the least irritating effective antibiotic for intravenous use) is given daily in the course of 5 to 7 days in the following manner: 300 mgm. cleocin in 250 cc. 5% dextrose solution given by intravenous drip for a period of 40 minutes for the first two days. The dose is increased to 600 mgm. and finally 900 mgm. on subsequent days.

Following the courses of intravenous therapy, the oral medication is usually more effective and acceptable. Thus the intravenous therapy serves as a booster.

Some patients are likely to develop a Jarisch-Herxheimer (J-H) reaction. The most likely candidates are those who present at the onset of the disease with high levels of gamma globulin, C-reactive protein, BFT titer, anemia and low white cell count. When this J-H reaction occurs, it is best to discontinue treatment, and to administer cortisone (not to exceed a maximum of 10 mg, to relieve flares) as well as symptomatic remedies.

The J-H reaction is rather brief, and when the symptoms subside, treatment should proceed by using a carefully titrated course of tetracyclines; e.g. starting with doxycycline, 50 mg. three times a day, and gradually increasing the dosage to 100 mg.

When it is determined that the patient’s symptoms have stabilized as may be observed by improvement in laboratory tests, (i.e. ESR, CBC, gammaglobulin, BFT titer (bentonite flocculation test; Rheumatoid Factor determination, etc.) the higher dose of antibiotics, i.e. tetracycline, 250 mg. to 500 mg. three times a week, etc. can be administered.

Anemia may be induced either by a spontaneous or drug related flare. Thus, the hemoglobin or hematocrit serves as a good therapeutic guide. Concurrently with the treatment, the patient’s blood chemistry is monitored. This includes CBC, the platelet count; ESR, BFT, and C-reactive protein. Urinalysis screening is also performed.

Tests for MCF (mycoplasma complement fixing antibodies), BFT and Kunkel Globulin (gamma globulin) determination are available for these analysis.

In his four decades of experience with antibiotics, Dr. Brown notes that significant benefits from this type of treatment require on the average one to two years. Some patients do experience a worsening of the condition during the first few months prior to improvement; however, some patients were able to notice a dramatic improvement in their situation: as early as six weeks. The length of therapy varies widely depending on the extensiveness of the disease. In severe cases, it may take up to thirty months for the patient to gain sustained improvement, and the achievement of remission may take 3 to 5 years.

The primary importance of the antibiotic approach is that once remission is established it is generally permanent unlike the experience with other treatment approaches. It appears that the absence of drug toxicity allows suppression of antigen long enough for the body’s immune system to take over.

Persistence is usually required in seeking the right combination of antibiotic dosage and method of administration in the difficult cases that require reduction of sensitization to the antigen.

Although the antibiotic treatment approach is still considered experimental, Dr. Brown treated hundreds of patients successfully over a 40 year period, bringing many of them back from hopelessness to living healthy and productive lives.

**Note:** For those interested in the specific treatment protocol, go to the internet at [http://www.rheumatic.org](http://www.rheumatic.org).

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**Dr. Brown’s Modified Protocol for Using Antibiotics In the Treatment Of Rheumatic Diseases**

**Presented at the 32nd International Congress of the Great Lakes College of Clinical Medicine**

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**Introduction**

Rheumatoid arthritis affects about 1 percent of our population and at least two million Americans have definite or classical rheumatoid arthritis. It is a much more devastating illness than previously appreciated. Most patients with rheumatoid arthritis have a progressive disability. More than 50% of patients who were working at the start of their disease are disabled after five years of rheumatoid arthritis. The annual cost of this disease in the U.S. is estimated to be over $1 billion.

There is also an increased mortality rate. The five-year survival rate of patients with more than thirty joints involved is approximately 50%. This is similar to severe coronary artery disease or stage IV Hodgkin's disease.

Thirty years ago, one researcher concluded that there was an average loss of eighteen years of life in patients who developed...
rheumatoid arthritis before the age of 50.

Most authorities believe that remissions rarely occur. Some experts feel that the term "remission-inducing" should not be used to describe ANY current rheumatoid arthritis treatment. A review of contemporary treatment methods shows that medical science has not been able to significantly improve the long-term outcome of this disease.

**My Experience with the Dr. Brown’s Protocol**

I first became aware of Doctor Brown’s protocol in 1989 when I saw him on 20/20 on ABC. This was shortly after the introduction of his first edition of *The Road Back*. The newest version is *The New Arthritis Breakthrough* that is written by Henry Scammel. Unfortunately, Dr. Brown died from prostate cancer shortly after the 20/20 program so I never had a chance to meet him. By the year 2000, I will have treated over 1,500 patients with rheumatic illnesses, including SLE, scleroderma, polymyositis and dermatomyositis.

My application of Dr. Brown’s protocol has changed significantly since I first started implementing it. Initially, I followed Dr. Brown’s work rigidly with very little modification other than shifting the tetracycline choice to Minocin. I believe I was one of the first people who recommended the shift to Minocin, which seems to have been widely adopted at this time.

In the early 90s, I started to integrate the nutritional model into the program and noticed a significant improvement in the treatment response. I cannot emphasize strongly enough the importance of this aspect of the program. It is absolutely an essential component of the revised Dr. Brown protocol. One may achieve remission without it, but the chances are much improved with its implementation. The additional benefit of the dietary changes is that they severely reduce the risk of the two to six month worsening of symptoms that Dr. Brown described in his book.

In the late 80s, the common retort from other physicians was that there was "no scientific proof" that this treatment works. Well, that is certainly not true today. If one peeks ahead at the bibliography, one will find over 200 references in the peer-reviewed medical literature that supports the application of Minocin in the use of rheumatic illnesses. The definitive scientific support for minocycline in the treatment of rheumatoid arthritis came with the MIRA trial in the United States. This was a double blind randomized placebo controlled trial done at six university centers involving 200 patients for nearly one year. The dosage they used (100 mg twice daily) was much higher and likely less effective than what most clinicians currently use. They also did not employ any additional antibiotics or nutritional regimens, yet 55% of the patients improved. This study finally provided the "proof" that many traditional clinicians demanded before seriously considering this treatment as an alternative regimen for rheumatoid arthritis.

Dr. Thomas Brown’s effort to treat the chronic mycoplasma infections believed to cause rheumatoid arthritis is the basis for this therapy. Dr. Brown believed that most rheumatic illnesses respond to this treatment. He and others used this therapy for SLE, ankylosing spondylitis, scleroderma, dermatomyositis and polymyositis.

Dr. Osler was also a preeminent figure of his time (1849-1919). Many regard him as the consummate physician of modern times. An excerpt from a commentary on Dr. William Osler provides a useful perspective on application of alternative medical paradigms:

Osler would be receptive to the cautious exploration of non-traditional methods of treatment, particularly in situations in which our present science has little to offer. From his reading of medical history, he would know that many pharmacologic agents were originally derived from folk medicine. He would also remember that in the 19th century physicians no less intelligent than those in our own day initially ridiculed the unconventional practices of Semmelweis and Lister.

Osler would caution us against the arrogance of believing that only our current medical practices can benefit the patient. He would realize that new scientific insights might emerge from as yet unproved beliefs. Although he would fight vigorously to protect the public against frauds and charlatans, he would encourage critical study of whatever therapeutic approaches were reliably reported to be beneficial to patients.

**Nutritional Considerations**

Limiting sugar is a critical element of the treatment program. Sugar has multiple significant negative influences on a person's biochemistry. Its major mode of action is through elevation of insulin levels. However, it has a similarly severe impairment of intestinal microflora. Patients who are unable to decrease their sugar intake are far less likely improve.

One of the major benefits of implementing the dietary changes is that one does not seem to develop worsening of symptoms the first three to six months that is described in Dr. Brown's book. Most of my patients tend to not worsen once they start the antibiotics. I believe this is due to the beneficial effects that the diet has on the immune response. I ask all new patients to read my 6-page handout on the dietary changes. Rather than repeat it here, one could obtain the current version on my web site at www.mercola.com under the tab heading on the left side of the page entitled Read This First.

**Antibiotic Therapy With Minocin**

There are three different tetracyclines available: simple tetracycline, doxycycline, or Minocin (minocycline).

Minocin has a distinct and clear advantage over tetracycline and doxycycline in three important areas.

1. Extended spectrum of activity
2. Greater tissue penetrability
3. Higher and more sustained serum levels

Bacterial cell membranes contain a lipid layer. One mechanism of building up a resistance to an antibiotic is to produce a thicker lipid layer. This layer makes it difficult for an antibiotic to penetrate. Minocin’s chemical structure makes it the most lipid soluble of all the tetracyclines.

This difference can clearly be demonstrated when one compares the drugs in the treatment of two common clinical conditions. Minocin gives consistently superior clinical results in the treatment of chronic prostatitis. In other studies, Minocin was used to improve between 75-85% of patients whose acne had become resistant to tetracycline. Strep is also believed to be a contributing cause to many patients with rheumatoid arthritis. Minocin has shown significant activity against treatment of this organism.

There are several important factors to consider when using Minocin. Unlike the other tetracyclines, it tends not to cause yeast infections. Some infectious disease experts even believe that it even has a mild anti-yeast activity.

Women can be on this medication for several years and not have any vaginal yeast infections. Nevertheless, it would be prudent to have patients on prophylactic oral *Lactobacillus acidophilus* and bifidus preparations. This will help to replace the normal intestinal flora that is killed with the Minocin.

Another advantage of Minocin is that it tends not to sensitize patients to the sun. This minimizes the risk of sunburn and increased risk of skin cancer. However, one must incorporate several precautions with the use of Minocin. Like other tetracyclines, food impairs its absorption. However, the absorption is much less impaired than with other tetracyclines. This is fortunate because some patients cannot tolerate Minocin on an empty stomach.
They must take it with a meal to avoid GI side effects. If they need to take it with a meal, they will still absorb 85% of the medication, whereas tetracycline is only 50% absorbed. In June of 1990, a pelleted version of Minocin became available. This improved absorption when taken with meals. This form is only available in the non-generic Lederle brand and is a more than reasonable justification to not substitute for the generic version. Clinical experience has shown that many patients will relapse when they switch from the brand name to the generic. It is strongly advised that only the non-generic brand name Minocin by Lederle be used.

However, many patients are on NSAID's which contribute to micro-ulcerations of the stomach which cause chronic blood loss. It is certainly possible they can develop a peptic ulceration contributing to their blood loss. In either event, patients frequently receive iron supplements to correct their blood counts. IT IS IMPERATIVE THAT MINOCIN NOT BE GIVEN WITH IRON. Over 85% of the dose will bind to the iron and pass through the colon unab sorbed. If iron is taken, it should be at least one hour before the minocin or two hours after. One recent uncommon complication of Minocin is a cell-mediated hypersensitivity pneumonitis.

Most patients can start on Minocin 100 mg. every Monday, Wednesday, and Friday evening. Doxycycline can be substituted for patients who cannot afford the more expensive Minocin. It is important to not give either medication daily, as this does not seem to provide as great a clinical benefit.

Tetracycline type drugs can cause a permanent yellow-grayish brown discoloration of the teeth. This can occur in the last half of pregnancy and in children up to eight years old. One should not routinely use tetracycline in children. If patients have severe disease, one can consider increasing the dose to as high as 200 mg three times a week. Aside from the cost of this approach, several problems may result from the higher doses. Minocin can cause quite severe nausea and vertigo. Taking the dose at night does tend to decrease this problem considerably.

However, if one takes the dose at bedtime, one must tell the patient to swallow the medication with TWO glasses of water. This is to insure that the capsule doesn't get stuck in the throat. If that occurs, a severe chemical esophagitis can result which can send the patient to the emergency room.

For those physicians who elect to use tetracycline or doxycycline for cost or sensitivity reasons, several methods may help lessen the inevitable secondary yeast overgrowth. Lactobacillus acidophilus will help maintain normal bowel flora and decrease the risk of fungal overgrowth. Aggressive avoidance of all sugars, especially those found in non-diet sodas will also decrease the substrate for the yeast's growth. Macrolide antibiotics like Biaxin or Zithromax may be used if tetracyclines are contraindicated. They would also be used in the three pills a week regimen.

Clindamycin

The other drug used to treat rheumatoid arthritis is clindamycin. Dr. Brown's book discusses the uses of intravenous clindamycin. It is important to use the IV form of treatment if the disease is severe. Nearly all scleroderma patients should take an aggressive stance and use IV treatment. Scleroderma is a particularly dangerous form of rheumatic illness that should receive aggressive intervention.

A major problem with the IV form is the cost. The price ranges from $100 to $300 per dose if administered by a home health care agency. However, if purchased directly from Upjohn, significant savings will be appreciated. A case of two-dozen 900 mg prefilled IV bags can be purchased directly from Upjohn for about $200.

For patients with milder illness, the oral form is preferable. If the patient has a mild rheumatic illness (the minority of cases), it is even possible to exclude this from their regimen. Initial starting doses for an adult would be a 1200 mg dose once a week. Patients do not seem to tolerate this medication as well as Minocin. The major complaint seems to be a bitter metallic type taste, which lasts about 24 hours after the dose. Taking the dose after dinner does seem to help modify this complaint somewhat. If this is a problem, one can lower the dose and gradually increase the dose over a few weeks.

Concern about the development of C. difficile pseudomembranous enterocolitis as a result of the clindamycin is appropriate. This complication is quite rare at this dosage regimen, but it certainly can occur. It is important to warn all patients about the possibility of developing a severe uncontrollable diarrhea. Administration of the acidophilus seems to limit this complication by promoting the growth of the healthy gut flora.

If one encounters a resistant form of rheumatic illness, intravenous administration should be considered. Generally, weekly doses of 900 mg are administered until clinical improvement is observed. This generally occurs within the first ten doses. At that time, the regimen can be decreased to every two weeks with the oral form substituted on the weeks where the IV is not taken.

What To Do If Severe Patients Fail To Respond

The most frequent reason for failure to respond to the protocol is lack of adherence to the dietary guidelines. Most patients will be eating too many grains and sugars, which disturb insulin physiology. It is important that patients adhere as strictly as possible to the guidelines. A small minority, generally under 15%, of patients will fail to respond to the protocol described above despite rigid adherence to the diet. These individuals should already be on the IV Clindamycin.

It appears that the hyaluronic acid, which is a potentiating agent commonly used in the treatment of cancer may be quite useful. It seems that hyaluronic acid has very little to no direct toxicity but works in a highly synergistic fashion when administered directly in the IV bag with the Clindamycin. Hyaluronic acid is also used in orthopedic procedures. The dose is generally from 2 to 10 cc into the IV bag. Hyaluronic acid is not inexpensive as the cost may range up to $10 per cc. One does need to exert some caution with its use as it may precipitate a significant Herxheimer flare reaction.

Patients will frequently have emotional traumas that worsen their illness. Severe emotional traumas can seriously impair the immune response to this treatment. A particularly useful and rapid technique called Neuro Emotional Technique (NET) can be used to resolve this problem. Practitioners using this technique can be found by calling the One Foundation 800-638-1411.

Anti-Inflammatories

The first non-aspirin NSAID (non-steroidal anti-inflammatory drug), indomethacin was introduced in 1963. Now more than 30 are available. Relafen is one of the better alternatives as it seems to cause less of an intestinal dysbiosis. If cost is a concern, generic ibuprofen can be used. Unfortunately, recent studies suggest this drug is more damaging to the kidneys. One must be especially careful to monitor renal function studies periodically. It is important for the patient to understand and accept the risks associated with these more toxic drugs.

Unfortunately, these drugs are not benign. Every year, they do enough damage to the GI tract to kill 2,000 to 4,000 patients with rheumatoid arthritis alone. That is ten patients EVERY DAY. At any given time patients receiving NSAID therapy have gastric ulcers in the range of 10-20%. Duodenal ulcers are lower at 2-5%. Patients on NSAIDs are at approximately three times greater relative risk for developing serious gastrointestinal side effects than are non-users.

Approximately 1.2% of patients taking NSAIDs are hospital-
alyzed for upper GI problems per year of exposure. One study of patients taking NSAIDs showed that a life-threatening complication was the first sign of ulcer in more than half of the subjects.

Celebrex has received much recent press due to its decreased toxicity to the gut. That is certainly a step in the right direction. Celebrex inhibits a specific type of prostaglandin and is called a COX2 inhibitor. A similar new drug introduced in 1999 is Vioxx. There was a report in early 1999 in the Proceedings of the National Academy of Science, which showed that these drugs might increase the risk of heart attack, stroke and blood clotting disorders.

Researchers found that the drugs suppress production of prostacyclin, which is needed to dilate blood vessels and inhibit clotting. Earlier studies had found that mice genetically engineered to be unable to use prostacyclin properly were prone to clotting disorders. Anyone who is at increased risk of cardiovascular disease should steer clear of these two new medications. Ulcer complications are certainly potentially life-threatening, but, heart attacks are a much more common and likely risk, especially in older individuals.

Risk factor analysis helps to discriminate those that are at increased danger of developing these complications.

Those associated with a higher frequency of adverse events are:

1. Old age
2. Peptic ulcer history
3. Alcohol dependency
4. Cigarette smoking
5. Concurrent prednisone or corticosteroid use
6. Disability
7. High dose of the NSAID
8. NSAID known to be more toxic

Studies clearly show that the non-acetylated salicylates are the safest NSAIDs. Celebrex and Vioxx likely cause the least risk for peptic ulcer. But as mentioned, they pose an increased risk for heart disease. Factoring these newer medications out would leave the following less toxic NSAIDs: Relafen, Daypro, Voltaren, Motrin, and Naprosyn. Meclomen, Indocin, Orudis, and Tolectin are among the most toxic or likely to cause complications.

They are much more dangerous than the antibiotics or non-acetylated salicylates. One should run an SMA at least once a year on patients who are on these medications. One must monitor the serum potassium levels if the patient is on an ACE inhibitor as these medications can cause hyperkalemia. One should also monitor their kidney function. The SMA will also show any liver impairment that the drugs might cause.

These medications can also impair prostaglandin metabolism and cause papillary necrosis and chronic interstitial nephritis. The kidney needs vasodilatory prostaglandins (PGE2 and prostacycline) to counterbalance the effects of potent vasoconstrictor hormones such as angiotensin II and catecholamines. NSAIDs decrease prostaglandin synthesis by inhibiting cyclooxygenase, leading to unopposed constriction of the renal arterioles supplying the kidney.

One might consider the use of non-acetylated salicylates such as salsalate, sodium salicylate and magnesium salicylate (i.e., Salflex, Disalcid, or Trilisate). They are the drugs of choice if there is renal insufficiency. They have minimal interference with antiinflammatory effects and other prostaglandins.

Additionally, they will not impair platelet inhibition of those patients who are on every other day aspirin to decrease their risk for stroke or heart disease. Unlike aspirin, they do not increase the formation of products of lipooxygenase-mediated metabolism of arachidonic acid. For this reason, they may be less likely to precipitate hypersensitivity reactions. These drugs have been safely used in patients with reversible obstructive airway disease and a history of aspirin sensitivity.

They also are much gentler on the stomach than the other NSAIDs and are the drug of choice if the patient has problems with peptic ulcer disease. Unfortunately, all these benefits are balanced by the fact they may not be as effective as the other agents and are less convenient to take. One needs to push them to 1.5-2 grams bid and tinnitus is a frequent complication.

One should warn patients of this complication and explain that if tinnitus does develop they need to stop the drugs for a day and restart with a dose that is half a pill per day lower. They repeat this until they find a dose that relieves their pain and doesn’t give them any ringing.

**Prednisone**

One can give patients with severe disease a prescription for prednisone 5 mg. They can take one of them a day if they develop a severe flare-up as a result of going on the antibiotics. They can use an additional tablet at night if they are in really severe flare. Explain to all patients that the prednisone is very dangerous and every dose they take decreases their bone density. However, it is a trade-off. Since they will only be on it for a matter of months, its use may be justifiable. This is the first medicine they should try to stop as soon as their symptoms permit.

Blood levels of cortisol peak between 3 and 9am. It would, therefore, be safest to administer the prednisone in the morning. This will minimize the suppression on the hypothalamic-pituitary-adrenal axis. Patients often ask the dangers of these medications. The most significant one is osteoporosis. Other side effects that usually occur at higher doses include adrenal insufficiency, atherosclerosis acceleration, cataract formation, Cushing’s syndrome, diabetes, ulcers, herpes simplex and tuberculosis reactivation, insomnia, hypertension, myopathy and renal stones.

One also needs to be concerned about the increased risk of peptic ulcer disease when using this medicine with conventional non-steroidal anti-inflammatory. Persons receiving both of these medicines may have a 15 times greater risk of developing an ulcer.

If a patient is already on prednisone, it is helpful to give them a prescription for 1 mg tablets so they can wean themselves off of the prednisone as soon as possible. Usually one lowers the dose by about 1 mg per week. If a relapse of the symptoms occurs, then further reduction of the prednisone is not indicated.

**Remission**

The following criteria can help establish remission:

* A decrease in duration of morning stiffness to no more than 15 minutes
* No pain at rest
* Little or no pain or tenderness on motion
* Absence of joint swelling
* A normal energy level
* A decrease in the ESR to no more than 30
* A normalization of the patient’s CBC. Generally the HGB, HCT, & MCV will increase to normal and their "pseudo"-iron deficiency will disappear

The natural course of rheumatoid arthritis is quite remarkable. Less than 1% of patients who are rheumatoid factor seropositive have a spontaneous remission. Some disability occurs in 50-70% of patients within five years after onset of the disease. Half of the patients will stop working within 10 years. This devastating natural prognosis is what makes the antibiotic therapy so exciting.

Approximately one third of patients have been lost to follow-up for whatever reason and have not continued with treatment. The remaining patients seem to have a 60-90% likelihood of improve-
conventional regimens and results of the NIH trial have finally sci-
because remissions may take up to 3 to 5 years. Dr. Brown's pio-
the patients to gain sustained improvement. One requires patience
and more severe the illness the more difficult it seems to treat.
If patients discontinue their medications before all of the above
criteria are met, there is a greater risk that the disease will recur. If
the patient meets the above criteria, one can have them to try
to stop their anti-inflammatory medication once they start to experi-
ence these improvements. If the improvements are stable for six
months, then discontinue the clindamycin. If the improvements are
maintained for the next six months, one can then discontinue their
Minocin and monitor for recurrences. If symptoms should recur, it
would be wise to restart the previous antibiotic regimen.

Overall, nearly 80% of the patients do remarkably better with
this program. Approximately 5% of the patients continued to worsen
and required conventional agents, like methotrexate, to relieve their
symptoms. Approximately 15% of the patients who started the treatment
dropped out of the program and were lost to follow-up. The longer
and more severe the illness, the longer it takes to cure. Smokers
tend not to do as well with this program. Age and competency of
the person's immune system are also likely important factors.

Dr. Brown successfully treated over 10,000 patients with this
protocol. He found that significant benefits from the treatment re-
quire on the average one to two years. I have treated nearly over
1,500 patients and find that the dietary modification I advocate accelerates the response rate to several months. The length of therapy
can vary widely. In severe cases, it may take up to thirty months for
the patients to gain sustained improvement. One requires patience
because remissions may take up to 3 to 5 years. Dr. Brown's pio-
neering approach represents a safer less toxic alternative to many
conventional regimens and results of the NIH trial have finally scien-
tifically validated this treatment.

Preliminary Laboratory Evaluation
For Non-Rheumatologists

It is important to evaluate patients to determine if indeed they
have rheumatoid arthritis. Most patients will have received evalu-
ations and treatment by one or more board certified rheumatologists.
If this is the case, the diagnosis is rarely in question and one only
needs to establish some baseline laboratory data.
However, patients will frequently come in without having any
appropriate workup done by a physician. Arthritic pain can be an
early manifestation of 20-30 different clinical problems. These in-
clude not only rheumatic disease, but also metabolic, infectious
and malignant disorders. These patients will require a more exten-
sive laboratory analysis.

Rheumatoid arthritis is a clinical diagnosis for which there is
not a single test or group of laboratory tests which can be consid-
ered confirmatory. When a patient hasn't been properly diagnosed,
then one needs to establish the diagnosis with the standard Rheu-
matism Association's criteria found in the table at the end of the
article.

One must also make certain that the first four symptoms listed
in the table are present for six or more weeks.

These criteria have a 91-94% sensitivity and 89% specificity
for the diagnosis of rheumatoid arthritis. However, these criteria
were designed for classification and not for diagnosis. One must
make the diagnosis on clinical grounds. It is important to note that
many patients with negative serologic tests can have a strong clini-
cal picture for rheumatoid arthritis.

The metacarpophalangeal joints, proximal interphalangeal and
wrists joints are the first joints to become symptomatic. In a way,
the hands are the calling card of rheumatoid arthritis. If the patient
completely lacks hand and wrist involvement, even by history, the
diagnosis of rheumatoid arthritis is doubtful. Rheumatoid arthritis
rarely affects the hips and ankles early in its course.

Fatigue may be present before the joint symptoms begin. Morn-
ing stiffness is a sensitive indicator of rheumatoid arthritis. An in-
crease in fluid in and around the joint probably causes the stiffness.
The joints are warm, but the skin is rarely red. When the joints
develop effusions, the patients hold them flexed at 5 to 20 degrees
as it is too painful to extend them fully.

The general initial laboratory evaluation should include a
baseline ESR, CBC, SMA, U/A, and an ASO titer. One can also
draw RF and ANA titers to further objectively document improve-
ment with the therapy. However, they seldom add much to the as-
essment.

Follow-up visits can be every two months for patients who live
within 50 miles, and every three to four months for those who live
farther away. An ESR at every visit is an inexpensive and reli-
able objective parameter of the extent of the disease. However, one
should run this test within several hours of the blood draw. Other-
wise, one cannot obtain reliable and reproducible results. This is
nearly impossible with most clinical labs that pick up your speci-
men at the office.

Inexpensive disposable ESR kits are a practical alternative to
the commercial or hospital labs. One can then run them in the of-
ice, usually within one hour of the blood draw. One must be care-
ful to not run the test on the same countertop as your centrifuge.
This may cause a falsely elevated ESR due to the agitation of the
ESR measuring tube.

Many patients with rheumatoid arthritis have a hypochromic,
microcytic CBC. This is probably due to the inflammation in the
rheumatoid arthritis impairing optimal bone marrow utilization of
iron. This type of anemia does NOT respond to iron. Patients who
take iron can actually worsen if they don't need it as the iron serves
as a potent oxidant stress. Ferritin levels are generally the most
reliable indicator of total iron body stores. Unfortunately it is also
an acute phase reactant protein and will be elevated anytime the
ESR is elevated. This makes ferritin an unreliable test in patients
with rheumatoid arthritis.

Fibromyalgia

One needs to be very sensitive to this clinical problem when
treating patients with rheumatoid arthritis. It is frequently a com-
plicating condition. Many times, patients will confuse the pain from
it with a flare-up of their arthritis. One needs to aggressively treat
this problem. If this problem is ignored, the likelihood of success-
fully treating the arthritis is significantly diminished.

Fibromyalgia is a very common problem. Some experts be-
lieve that 5% of people are affected with it. Over 12% of the pa-
ients at the Mayo Clinic's Department of Physical Medicine and
Rehabilitation have this problem. It is the third most common di-
agnosis by rheumatologists in the outpatient setting. Fibromyalgia
affects women five times as frequently as men.

Signs And Symptoms of Fibromyalgia

One of the main features of fibromyalgia is the morning stiff-
ness, fatigue, and multiple areas of tenderness in typical locations.
Most patients with fibromyalgia complain of pain over many areas
of the body, with an average of six to nine locations. Although the
pain is frequently described as being all over, it is most prominent.
in the neck, shoulders, elbows, hips, knees, and back.

Tender points are generally symmetrical and on both sides of the body. The areas of tenderness are usually small (less than an inch in diameter) and deep within the muscle. They are often located in sites that are slightly tender in normal people. Patients with fibromyalgia, however, differ in having increased tenderness at these sites than normal persons. Firm palpation with the thumb (just past the point where the nail turns white) over the outside elbow will typically cause a vague sensation of discomfort. Patients with fibromyalgia will experience much more pain and will often withdraw the arm involuntarily.

More than 70% of patients describe their pain as profound aching and stiffness of the muscles. Often it is relatively constant from moment to moment, but certain positions or movements may momentarily worsen the pain.

Other terms used to describe the pain are dull and numb. Sharp or intermittent pain is relatively uncommon.

Patients with fibromyalgia often complain that sudden loud noises worsen their pain. The generalized stiffness of fibromyalgia does not diminish with activity, unlike the stiffness of rheumatoid arthritis, which lessens as the day progresses.

Despite the lack of abnormal lab tests, patients can suffer considerable discomfort. The fatigue is often severe enough to impair activities of work and recreation. Patients commonly experience fatigue on arising and complain of being more fatigued when they wake up than when they went to bed. Over 90% of patients believe the pain, stiffness, and fatigue are made worse by cold, damp weather. Overexertion, anxiety and stress are also factors.

Many people find that localized heat, such as hot baths, showers, or heating pads, give them some relief. There is also a tendency for pain to improve in the summer with mild activity or with rest.

Some patients will date the onset of their symptoms to some initiating event. This is often an injury, such as a fall, a motor vehicle accident, or a vocational or sports injury. Others find that their symptoms began with a stressful or emotional event, such as a death in the family, a divorce, a job loss, or similar occurrence.

Pain Location

Patients with fibromyalgia have pain in at least 11 of the following 18 tender point sites (one on each side of the body):

1. Base of the skull where the suboccipital muscle inserts.
2. Back of the low neck (anterior intertransverse spaces of C5-C7).
3. Midpoint of the upper shoulders (trapezius).
4. On the back in the middle of the scapula.
5. On the chest where the second rib attaches to the breastbone (sternum).
6. One inch below the outside of each elbow (lateral epicondyle).
7. Upper outer quadrant of buttocks.
8. Just behind the swelling on the upper leg bone below the joint (trochanteric prominence).
9. The inside of both knees (medial fat pads proximal to the joint line).

Treatment Of Fibromyalgia

There is a persuasive body of emerging evidence that indicates that patients with fibromyalgia are physically unfit in terms of sustained endurance. Some studies show that cardiovascular fitness training programs can decrease fibromyalgia pain by 75%.

Sleep is critical to the improvement. Many times, improved fitness will correct the sleep disturbance. Allergies, especially to mold, seem to be another common cause of fibromyalgia. There are some simple interventions using techniques called Total Body Modification (TBM) 800-243-4826 or Neuro Emotional Technique (NET) 800-638-1411. These may be helpful in rapidly resolving the problem.

Exercise For Rheumatoid Arthritis

It is very important to exercise or increase muscle tone of the non-weight bearing joints. Experts tell us that disuse results in muscle atrophy and weakness. Additionally, immobility may result in joint contractures and loss of range of motion (ROM). Active ROM exercises are preferred to passive. There is some evidence that passive ROM exercises increase the number of WBCs in the joint. If the joints are stiff, one should stretch and apply heat before exercising. If the joints are swollen, application of ten minutes of ice before exercise would be helpful.

The inflamed joint is very vulnerable to damage from improper exercise, so one must be cautious. People with arthritis must strike a delicate balance between rest and activity. They must avoid activities that aggravate joint pain. Patients should avoid any exercise that strains a significantly unstable joint.

Employing a good rule of thumb is that if the pain lasts longer than one hour after stopping exercise, the patient should slow down or choose another form of exercise. Assistive devices are also helpful to decrease the pressure on affected joints. Many patients need to be urged to take advantage of these. The Arthritis Foundation has a book, Guide to Independent Living, which instructs patients about how to obtain them.

Of course, it is important to maintain good cardiovascular fitness. Walking with appropriate supportive shoes is also another important consideration.

The Infectious Cause Of Rheumatoid Arthritis

It is quite clear that autoimmunity plays a major role in the progression of rheumatoid arthritis. Most rheumatology investigators believe that an infectious agent causes rheumatoid arthritis. There is little agreement as to the involved organism. Investigators have proposed the following infectious agents: Human T-cell lymphotropic virus Type I, rubella virus, cytomegalovirus, herpes-virus, and mycoplasma. This review will focus on the evidence supporting the hypothesis that mycoplasma is a common etiologic agent of rheumatoid arthritis.

Mycoplasmas are the smallest self-replicating prokaryotes. They differ from classical bacteria by lacking rigid cell wall structures and are the smallest known organisms capable of extracellular existence. They are considered to be parasites of humans, animals, and plants.

In 1939, Dr. Sabin, the discoverer of the polio vaccine, first reported a chronic arthritis in mice caused by a mycoplasma. He suggested this agent might cause that human rheumatoid arthritis. Dr. Thomas Brown was a rheumatologist who worked with Dr. Sabin at the Rockefeller Institute. Dr. Brown trained at John Hopkins Hospital and then served as chief of medicine at George Washington Medical School before serving as chairman of the Arthritis Institute in Arlington, Virginia. He was a strong advocate of the mycoplasma infectious theory for over fifty years of his life.

Culturing Mycoplasmas From Joints

Mycoplasmas have limited biosynthetic capabilities and are very difficult to culture and grow from synovial tissues.

They require complex growth media or a close parasitic relation with animal cells. This contributed to many investigators failure to isolate them from arthritic tissue. In reactive arthritis immune complexes rather than viable organisms localize in the joints. The infectious agent is actually present at another site. Some investigators believe that the organism binding in the immune complex contributes to the difficulty in obtaining positive mycoplasma cultures.

Despite this difficulty some researchers have successfully iso-
lated mycoplasma from synovial tissues of patients with rheuma-
toid arthritis. A British group used a leucocyte-migration inhibi-
tion test and found two-thirds of their rheumatoid arthritis patients
to be infected with Mycoplasma fermentens. These results are im-
pressive since they did not include more prevalent Mycoplasma
strains like M. salivarium, M. ovale, M. hominis, and M. pneu-
monia.

One Finnish investigator reported a 100% incidence of iso-
tation of mycoplasma from 27 rheumatoid synovia using a modified
culture technique. None of the non- rheumatoid tissue yielded any
mycoplasmas. The same investigator used an indirect hemaggluti-
nation technique and reported mycoplasma antibodies in 53% of
patients with definite rheumatoid arthritis. Using similar techniques
other investigators have cultured mycoplasma in 80-100% of their
rheumatoid arthritis test population.

Rheumatoid arthritis follows some mycoplasma respiratory infec-
tions. One study of over 1000 patients was able to identify
arthritis in nearly 1% of the patients. These infections can be asso-
ciated with a positive rheumatoid factor.

This provides additional support for mycoplasma as an etio-
logic agent for rheumatoid arthritis. Human genital mycoplasma
infections have also caused septic arthritis.

Harvard investigators were able to culture mycoplasma or a
similar organism, ureaplasma urealyticum, from 63% of female
patients with SLE and only 4% of patients with CFS. The research-
ers chose CFS as these patients shared similar symptoms as those
with SLE, such as fatigue, arthralgias, and myalgias.

Animal Evidence For The Protocol

The full spectrum of human rheumatoid arthritis immune re-
sponses (lymphokine production, altered lymphocyte reactivity,
immune complex deposition, cell-mediated immunity and develop-
ment of autoimmune reactions) occurs in mycoplasma induced
animal arthritis. Investigators have implicated at least 31 different
mycoplasma species.

Mycoplasma can produce experimental arthritis in animals from
days to months later. The time seems to depend on the dose
given and the virulence of the organism.

There is a close degree of similarity between these infections
and those of human rheumatoid arthritis.

Mycoplasmas cause arthritis in animals by several mechanisms.
They either directly multiply within the joint or initiate an intense
local immune response. Mycoplasma produces a chronic arthritis
in animals that is remarkably similar to rheumatoid arthritis in hu-
mans. Arthritogenic mycoplasmas cause joint inflammation in ani-
mals by many mechanisms. They induce nonspecific lymphocyte
cytotoxicity and antilymphocyte antibodies as well as rheumatoid
factor. Mycoplasma clearly causes chronic arthritis in mice, rats,
fowl, swine, sheep, goats, cattle and rabbits. The arthritis appears
to be the direct result of joint infection with culturable mycoplasma
organisms.

Gorillas have tissue reactions closer to man than any other
animal. Investigators have shown that mycoplasma can precipitate
a rheumatic illness in gorillas. One study demonstrated mycoplasma
antigens occur in immune complexes in great apes. The human and
gorilla IgG are very similar and express nearly identical rheuma-
toid factors (IgM anti-IgG antibodies). The study showed that when
mycoplasma binds to IgG it can cause a conformational change.
This conformational change results in an anti-IgG antibody, which
can then stimulate an autoimmune response.

The Science of Why Minocycline Is Used

If mycoplasma were a causative factor in rheumatoid arthritis,
one would expect tetracycline type drugs to provide some sort of
improvement in the disease. Collagenase activity increases in rheu-
matoid arthritis and probably has a role in its cause. Investigators
demonstrated that tetracycline and minocycline inhibit leukocyte,
macrophage, and synovial collagenase.

There are several other aspects of tetracyclines that may play a
role in rheumatoid arthritis. Investigators have shown minocycline
and tetracycline to retard excessive connective tissue breakdown
and bone resorption while doxycycline inhibits digestion of hu-
man cartilage. It is also possible that tetracycline treatment improves
rheumatic illness by reducing delayed-type hypersensitivity re-
ponse. Minocycline and doxycycline both inhibit phospholipases
which are considered proinflammatory and capable of inducing
synovitis.

Minocycline is a more potent antibiotic than tetracycline and
penetrates tissues better. These characteristics shifted the treatment
of rheumatic illness away from tetracycline to minocycline.
Minocycline may benefit rheumatoid arthritis patients through its
immunomodulating and immunosuppressive properties. In vitro
studies demonstrated a decreased neutrophil production of reactive
oxygen intermediates along with diminished neutrophil chemot-
axis and phagocytosis. Investigators showed that minocycline re-
duced the incidence of severity of synovitis in animal models of
arthritis. The improvement was independent of minocycline's ef-
fect on collagenase.

Minocycline has also been shown to increase intracellular calcu-
lum concentrations that inhibit T-cells.

Individuals with the Class II major histocompatibility com-
plex (MHC) DR4 allele seem to be predisposed to developing rheu-
matoid arthritis. The infectious agent probably interacts with this
specific antigen in some way to precipitate rheumatoid arthritis.
There is strong support for the role of T cells in this interaction.
Minocycline may suppress rheumatoid arthritis by altering T cell
calcium flux and the expression of T cell derived from collagen
binding protein. Minocycline produced a suppression of the de-
layed hypersensitivity in patients with Reiter's syndrome. Investi-
gators also successfully used minocycline to treat the arthritis and
early morning stiffness of Reiter's syndrome.

Clinical Studies

In 1970 investigators at Boston University conducted a small,
randomized placebo-controlled trial to determine if tetracycline
would treat rheumatoid arthritis. They used 250 mg of tetracycline
a day. Their study showed no improvement after one year of tetra-
cycline treatment. Several factors could explain their inability to
demonstrate any benefits. Their study used only 27 patients for a
one-year trial, and only 12 received tetracycline.

Noncompliance could have been a factor. Additionally, none
of the patients had severe arthritis. Patients were excluded from the
trial if they were on any anti-remittive therapy.

Finnish investigators used lymecycline to treat the reactive ar-
thritis in Chlamydia trachomatis infections. The study compared
the effect of the medication in patients with two other reactive ar-
thritis infections Yersinia and Campylobacter. Lymecycline produced
a shorter course of illness in the Chlamydia induced arthritis pa-
tients, but did not affect the other enteric infections-associated re-
active arthritis. The investigators later published findings that sug-
gested lymecycline achieved its effect through non-antimicrobial
actions. They speculated it worked by preventing the oxidative ac-
tivation of collagenase.

Breedveld published the first trial of minocycline for the treat-
ment of animal and human rheumatoid arthritis. In the first pub-
lished human trial, Breedveld treated ten patients in an open study
for 16 weeks. He used a very high dose of 400 mg per day. Most
patients had vestibular side effects resulting from this dose. How-
ever, all patients showed benefit from the treatment. All variables
of efficacy were significantly improved at the end of the trial. Breedveld concluded an expansion of his initial study and observed similar impressive results. This was a 26-week double-blind placebo-controlled randomized trial with minocycline for 80 patients. They were given 200 mg twice a day. The Ritchie articular index and the number of swollen joints significantly improved (p < 0.05) more in the minocycline group than in the placebo group.

Investigators in Israel studied 18 patients with severe rheumatoid arthritis for 48 weeks. These patients had failed two other DMARD. They were taken off all DMARD agents and given minocycline 100 mg twice a day. Six patients did not complete the study, three withdrew because of lack of improvement, and three had side effects of vertigo or leukopenia. All patients completing the study improved. Three had complete remission, three had substantial improvement of greater than 50% and six had moderate improvement of 25% in the number of active joints and morning stiffness.

Criteria For Classification Of Rheumatoid Arthritis

Morning stiffness in and around joints lasting at least one hour before maximal improvement is noted.

Arthritis of three or more joint areas At least three joint areas have simultaneously had soft-tissue swelling or fluid (not bony overgrowth) observed by a physician. There are 14 possible joints: right or left PIP, MCP, wrist, elbow, knee, ankle, and MTP joints.

Arthritis of hand joints

At least one joint area swollen as above in a wrist, MCP, or PIP joint

Symmetric arthritis

Simultaneous involvement of the same joint areas (as in criteria 2) on both sides of the body (bilateral involvement of PIPs, MCPs, or MTPs) is acceptable without absolute symmetry. Lack of symmetry is not sufficient to rule out the diagnosis of rheumatoid arthritis.

Rheumatoid Nodules

Subcutaneous nodules over bony prominences, or extensor surfaces, or in juxta-articular regions, observed by a physician. Only about 25% of patients with rheumatoid arthritis develop nodules, and usually as a later manifestation.

Serum rheumatoid factor

Demonstration of abnormal amounts of serum rheumatoid factor by any method that has been positive in less than 5% of normal control subjects. This test is positive only 30-40% of the time in the early months of rheumatoid arthritis.

Radiological Changes

Radiological changes typical of rheumatoid arthritis on PA hand and wrist X-rays, which must include erosions or unequivocal bony decalcification localized to or most marked adjacent to the involved joints (osteoarthritic changes alone do not count).

Note: Patients must satisfy at least four of the seven criteria listed. Any of criteria 1-4 must have been present for at least 6 weeks. Patients with two clinical diagnoses are not excluded. Designations as classic, definite, or probable rheumatoid arthritis is not to be made.

Harold W. Clark, Ph.D. adds, “I’m not sure whether the tests (MCF, BFT, and Kunkle) are still available but should be included.”

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Fig. 6. Comparison of acrylamide gel electrophoretic patterns of diffusable protein from M. pharyngis and M. hominis, type II, grown in various tissue broths: HH = human placenta with human serum, HR = human placenta with rabbit serum. The other broths all had rabbit serum enrichment.
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ANTIBIOTIC THERAPY OF RHEUMATOID ARTHRITIS
An Independent Retrospective Analysis of Hospitalized
Patients treated by Dr. Brown Over Five years
(1978-1983)

An independent group of biostatisticians reviewed the risks
and benefits in the treatment of all patients admitted to the
National Hospital by Dr. Brown in the last five years (1978-
1983). The data from all those patients with rheumatoid arthri-
tis, who had begun their first course of antibiotic treatment
during this time frame, was used for the report.

The biostatistical evaluations demonstrate:
1) Eighty four Percent (84%) of the patients report an im-
provement of 50% or more in their joints and in their morning
stiffness. 75% of the patients report symptomatic improvement
with respect to weakness, fatigue, depression and feeling of
well being.

2) Sixty percent (60%) of the patients had previously re-
ceived, and subsequently discontinued, gold therapy for rea-
sons of insufficient response or toxicities prior to beginning
antibiotic therapy; many of the patients had also received other
slow acting anti-rheumatic drugs which had been discontinued
again for lack of effect or toxicity.

3) An unexpectedly positive and statistically significant
correlation between duration of treatment and improvement was
observed. In other words the patients continued to improve over
the five year period of treatment, in contrast to the published
reports on gold and penicillamine and plaquenil, where im-
provement is not sustained. (Figure 1)

4) Patients on antibiotic therapy where able to reduce
and in some cases discontinue their corticosteroid therapy, a
critically important clinical observation.

5) Seventy percent (70%) of patients will remain on
antibiotic therapy with continued control of their rheumatoid
arthritis five years after starting treatment. By contrast other
studies have shown that only 10 to 20 percent of patients treated
with gold will remain on that drug for five years. What this
means is that the chance of achieving a sustained improvement
for five years from Dr. Brown’s antibiotic treatment is as much
as seven times better than with conventional gold therapy, (Fig-
ure 2).

6) No serious toxicities or side effects developed, in
marked contrast to the serious and sometimes life threatening
side effects of gold or d-penicillamine or methotrexate.

SUMMARY:
1) Patients with rheumatoid arthritis definitely improve
with antibiotic therapy.

2) Many of these patients who improved had failed on
gold or other anti-rheumatic agents.

3) Improvement continues to get better with time rather
than fade.

4) Patients were able to reduce their cortico-steroid dos-
ages.

5) Seventy percent (70%) of patients stay on therapy for
five years of treatment with antibiotic.

The risks and benefits from the long term antibiotic treat-
ment are substantially more favorable than the historical expe-
rience reported by other investigators using conventional slow
acting drugs such as gold, pencillamine or plaquenil. To quote
authors: “Data from this retrospective study of 98 patients with
definite or classical RA, who were treated with antibiotic
therapy, suggests better than expected outcomes based on cur-
rent treatment standards.” The authors also state: “Thus, anti-
biotic therapy appears to be associated with the ability to main-
tain a majority of patients with RA in either a stable or an im-
proved clinical state over a longer period of time with a lower
degree of toxicity, with no serious side effects.”
* CALCULATED FROM PUBLISHED DATA. (KEAN & ANASTASSIADES – 1979)
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FIGURE 9: RHEUMATOID ARTHRITIS PATIENTS SUSTAINING 50% IMPROVEMENT ON LONG TERM TREATMENT

* CALCULATED FROM PUBLISHED DATA. (KEAN & ANASTASSIADES – 1979)
PUBLICATIONS

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