The Use of Minocycline in the Treatment of Rheumatoid Arthritis
by Beth A. Malley, RN, CCRC

Introduction
Each year, arthritis results in an estimated 250,000 hospitalizations and nine million out-patient visits (Bruce 2005, Rindfleisch and Muller 2005). According to the Arthritis Foundation, over two million people in the United States are afflicted with Rheumatoid Arthritis (RA). RA is an autoimmune disease that can occur at any age, although it generally occurs between the ages of 40-60 and is two to three times more common in women than men (Centers for Disease Control [CDC] 2008). It is considered a chronic, progressive illness with the potential to cause joint destruction and functional disability (CDC 2008, Shiel 2008). While the cause of RA is unknown, infectious agents such as viruses, bacteria, and fungi have long been suspected as the cause of the disease (Tilley, Graciela, Heyse, Trentham et al. 1995, Eustice 2006).

Because RA is a chronic and progressive disease, lifelong treatment is required. The treatment goal is to reduce inflammation in order to relieve pain and prevent or slow the progression of joint damage caused by the RA. There are several medication options available for the treatment of rheumatoid arthritis. According the CDC, the effectiveness, cost, and management of side effects for the treatment of RA is a true burden for those afflicted (CDC 2008). Historically, treatment of RA with medication has followed a pyramid approach. Corticosteroids and non-steroidal anti-inflammatory drugs (NSAID) were used first, then Disease-Modifying Antirheumatic Drugs (DMARD), and finally biologic response modifiers (BRM) for those who didn’t respond to the previous drugs. Today, a more aggressive treatment approach is being used for people with early RA, for example DMARD are prescribed within three months of diagnosis (CDC 2008).

Over the last 40 years, antibiotics from the tetracycline family, specifically minocycline, have been researched for treatment of RA. The results have led to clinically significant improvements in the treatment of the disease and minimal risk of side effects (Stone 2003; Case 2001; O’Dell 2001, 1997). As mentioned, there are several medications available for the treatment of RA. This article will briefly review current drug options for treating RA and specifically focus on the use of minocycline (CDC 2008).

Diagnosis
The American Rheumatism Association criteria for the classification of rheumatoid arthritis are found in Table 1 (CDC 2008).

When one is diagnosed with RA, the condition can be characterized as a “mild,” “moderate,” or “severe” disease. Severity and number of physical symptoms, along with location and number of specific joints that are affected, blood work results, plus X-ray findings are used to determine how the disease is classified and treated. Treatment for patients with “mild disease” symptoms and normal X-ray findings (no bone erosion) commonly consists of medications such as plaquenil, sulfasalazine, and/or minocycline.
Patients with "moderate" to "severe" disease symptoms and X-ray findings that are positive for bone erosion are usually treated with methotrexate, among other medications. If the symptoms are not controlled, Arava, Imuran, or a combination of drugs may be considered (Rindfleisch and Muller 2005).

**Medication: Effectiveness, Side Effects, and Cost**

There are two classes of drugs for the treatment of RA: fast-acting "first line drugs" and slow-acting "second line drugs," also known as Disease Modifying Antirheumatic Drugs (DMARDs) (Sheil 2008). Two classifications of drug used as fast-acting, "first line" are Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), which include aspirin and naproxen, and corticosteroids, which include drugs such as prednisone among others. In general, the fast-acting medications are used in the first few weeks to months of onset and treat those who suffer with mild, moderate, or severe physical symptoms. These drugs provide rapid improvement and control for symptoms such as pain and inflammation, while a diagnostic work-up is being done and the slow-acting, "second line" medications become effective. Slow-acting medications can take three to four months to become effective. Cost for these "first line" drugs in a generic equivalent is usually <$50.00 for a one month supply (Sheil 2008). Most patients exhibit substantial control of symptoms with the use of these "first line" medications. Corticosteroids (prednisone) can limit bone erosion caused by RA, which make this drug very effective, but short-term use (less than three months) is recommended to avoid the potential of severe side effects (American College of Rheumatology 2008). NSAIDs, on the other hand, show minimal to rare side effects and can be used for a longer periods of time as tolerated (CDC 2008). DMARDs, "second line drugs," promote disease remission and prevent progressive joint destruction. They are increasingly used in the first few months of the RA diagnosis (American College of Rheumatology 2008). The type of DMARD used will dictate the cost and potential side effects associated (Rindfleisch and Muller 2005; Sheil 2008). The cost of first- and second-line drugs used in the treatment of RA varies. Medication cost can range from $63.00 to $1,316.00 per month for the generic form (Table 2). For example, methotrexate has a moderate-to-severe side effects profile and runs about $63 a month. Arava has a more severe side effects profile and costs $374 a month. Imuran’s side effect profile is mild-to-severe, but costs $1,316 a month. Plaquenil ($35) and minocycline ($115) are generally considered low in cost, with few side effects, and well-tolerated. Plaquenil side-effects profile is considered modest, with frequent eye exams required, whereas minocycline side effects are well documented as mild and rare (Rindfleisch and Muller 2005; Sheil 2008).

**Brief History of Minocycline**

Tetracycline is a large family of antibiotics first identified as natural products. In 1990, Nubian mummies from Egypt were found to contain significant levels of tetracycline. Some scientists suggest that the beer brewed at this time was the source of tetracycline (Armelagos 2005). Tetracycline was first discussed by Benjamin Duggar in 1948 and later discovered in the research labs of Pfizer by Lloyd Conover (Klajn, Rafal 2007). The patent of tetracycline sparked the development of many chemically altered antibiotics. Minocycline is one example of a semi-synthetic form of tetracycline. These antibiotics are found to inhibit or stop bacterial growth, decrease inflammation, and act to alter the immune response (Tilley 1995, Suresh 2004). In addition, minocycline is considered a more potent drug and is more rapidly absorbed by the body than other antibiotics in this family (Klajn, Rafal 2007).

Currently, minocycline’s primary use is to treat acne and other skin infections such as certain strains of methicillin-resistant *Staphylococcus*.
Minocycline in RA

> Aureus (MRSA), and Lyme disease. It is also used to treat various other conditions such as anthrax, cholera, gonorrhea, bubonic plague, pneumonia, syphilis, and urinary tract infections (Eustice 2006). There is evidence that it isn’t the antibiotic properties of minocycline that affect the immune system that make minocycline (and other tetracycline drugs) so effective for the treatment of arthritis but the ability to inhibit enzymes that break down cartilage and connective tissue (Miller 2008).

While minocycline is an approved antibiotic, it’s not Food and Drug Administration (FDA)-approved for use with RA. Physicians specializing in Rheumatology are within their scope of practice when prescribing minocycline to treat RA, although it’s not a common practice (Sheil 2008). Minocycline is effective in about 60% of those who use it for RA, although without FDA approval or official guidelines, some physicians remain skeptical, waiting for more evidence related to dosage and long-term use of minocycline (Eustice 2006). As research continues and treatment guidelines change to include the use of minocycline as an acceptable treatment for mild RA, physicians may be more comfortable with prescribing this antibiotic to treat mild rheumatoid arthritis (Eustice 2006).

Brief History of Minocycline in the Use of Rheumatoid Arthritis

The first real evidence that RA could have an infectious cause came in 1939, by Drs. Swift and Brown with the finding of mycoplasmas in the tissue of patients with RA (Road Back Foundation 2008). Mycoplasmas are microorganisms that fall into a category between a virus and the bacteria. They can grow in tissue fluids (blood, joint, heart, chest, and spinal fluids) without killing the cell (Road Back Foundation 2008). In 1950, the National Institutes of Health (NIH) awarded a research grant for studying RA and, the following year, reported mycoplasmas as the suspected organism responsible for the body’s immune system response. In 1985, a retrospective observational study reported the use of minocycline to be valuable in the management and improvement of disease symptoms for those with rheumatoid arthritis (Road Back Foundation 2008). In 1988, Thomas McPherson Brown and his colleague Henry Scammell published The Road Back – Rheumatoid Arthritis, Its Cause and Its Treatment. In this book, they described arthritis as an infectious process. Dr. Brown, through 52 years of medical practice and research experience, maintained the idea that RA was an infectious process and treated his patients with minocycline, even though the antibiotic was not FDA-approved.

Researchers continue to gather evidence, some based on clinical trials, to validate the safe and effective use of minocycline for the treatment of arthritis. In a review and analysis of ten randomized clinical control trials (RCTs), with a total of 535 subjects, between 1966-2002, a group of scientists found tetracycline (mostly minocycline), to be associated with a reduction in disease activity and “no absolute” increased risk of side effects (Stone 2003). In addition, there are several RCTs that have shown that minocycline is an effective DMARD in RA, when compared to placebo (sugar pill) or hydroxychloroquine (Plaquenil) (Tilley 1995; O’Dell 1997, 1999, 2001). Since the generic form of minocycline is available, it may never become FDA-approved for treating RA. This often happens when a medication becomes available in a generic form, because the testing and sale of the drug does not become “commercially viable” for companies to pursue (The Road Back Foundation 2008).

Benefits and Risks

Similar to and consistent with the significant findings that tetracycline, (particularly minocycline) decrease disease activity. Side effects associated with the use of these antibiotics are described as minimal, and the drug is well-tolerated (as shown in Table 1). Most of the literature describes a few potential side effects such as dizziness, nausea, headaches, and, on rare occasion, lupus-like syndrome and reversible grey pigmentation of the skin can occur.

Conclusion

Considering the results of the last 40 years of research, some physicians and researchers think there is sufficient evidence that minocycline is a safe, effective, and low-cost treatment approach for those afflicted with mild RA. Research continues in an effort to find the best treatment approach for those afflicted with RA. On June 15 2008, The College of Rheumatology provided recommendations for the use of nonbiologic and DMARDs in rheumatoid arthritis. These treatment guidelines, in short, included the use of plaquenil or minocycline in the treatment of patients with mild disease symptoms of rheumatoid arthritis (Saag, Teng, Patkar, Anuntiyo, Finney, Curtis et al. 2008).

For a health care consumer diagnosed with rheumatoid arthritis, the role of education in the management of this disease is of utmost importance. The risks and benefits of using minocycline...
as a treatment option need to be explored by both the patient and physician. A proactive approach includes thoroughly educating oneself and finding a physician who is knowledgeable and open to discuss the different medications available for the treatment of rheumatoid arthritis. Since the release of the treatment recommendations (2008) as noted above, physicians may now be more comfortable with the use of minocycline as an option for the treatment of RA. Suggested resources include The Road Back Foundation: www.roadback.org, The Arthritis Foundation: www.arthritis.org, American College of Rheumatology: www.rheumatology.org, The Center for Disease Control and Prevention: www.cdc.gov, and The US Food & Drug Administration: www.FDA.gov.

**References**


**Minocycline in RA**


**Physician Formulated**

**ResveraCaps**

**Resveratrol Extract**

60 Vegetarian Capsules

One Capsule provides:

**Resveratrol**: 500 mg (polygonum cuspidatum) extract (standardized to contain 20% trans resveratrol)

**Other Ingredients**: Silicon dioxide, Kosher rice flour, VegiCap (hypromellose)

**Recommended Usage**: As a dietary supplement, take one capsule per day between meals or as recommended by your health care professional. Consult a physician before using, if pregnant or lactating.

**ResveraCaps features 500 mg of high-quality polygonum cuspidatum standardized to contain 20% (100 mg) total resveratrols. Resveratrol promotes cardiovascular health through its antioxidant action, and ongoing research is revealing that resveratrol may possess benefits that prevent the loss of vital metabolic functions required for long life.**

**Rx Vitamins**

Physician Formulated

Scientifically Advanced Nutritional Supplements

For more information about our full product line or to place an order call: 1-800-Rx2-2222 or 914-592-2323

Fax orders toll free to 1-888-800-8068

visit us at www.rxvitamins.com • email: info@rxvitamins.com

Optimal Nutritional Support