

IS YOUR ARTHRITIS ACTUALLY CAUSED BY BACTERIA?

If you think so, this study may be for you.

WHAT IS RHEUMATOID ARTHRITIS (RA)?

Rheumatoid arthritis (RA) is an inflammatory form of arthritis that causes joint pain and damage. RA attacks the lining of your joints (synovium), causing swelling that can result in aching and throbbing, and eventually deformity. Sometimes RA symptoms make even the simplest activities — such as opening a jar or taking a walk — difficult to manage.

WHAT ARE THE SIGNS AND SYMPTOMS OF RA?

Signs and symptoms of rheumatoid arthritis may include:

- **Joint pain**
- **Joint swelling**
- **Joints that are tender to the touch**
- **Red and puffy hands**
- **Firm bumps of tissue under the skin on your arms (rheumatoid nodules)**
- **Fatigue**
- **Morning stiffness that lasts at least 30 minutes**
- **Fever**
- **Weight loss**

WHAT IS THE PURPOSE OF THIS STUDY?

Even though there have been many advances in the treatment of RA, psoriatic arthritis (PsA), and other inflammatory arthritis, doctors still do not know what causes the inflammation in your joints. For decades, many theories have been proposed, but none of them have been proven right. Currently, there's no cure for RA. It's likely that RA occurs as a result of a complex combination of factors, including your genes, your lifestyle choices, such as smoking and diet, and things in your environment, such as bacteria or viruses.

We actually think that **bacteria that live in your mouth and intestine are responsible, at least in part, for the development of your Arthritis.** We believe that by killing those bacteria with antibiotics, we might be able to understand how immune system works and maybe what causes arthritis.

WHAT DO WE KNOW ABOUT THE USE OF ANTIBIOTICS TO TREAT RHEUMATIC DISEASE?

Based on scientific studies, clinical trials and patient surveys, we know that certain antibiotics (such as minocycline, doxycycline, hydroxychloroquine and others) slow or stop the progression of rheumatoid arthritis, ease pain, lessen stiffness, diminish swollen joints and enhance the quality of life. Several of them are actually approved by the Food and Drug Administration (FDA) for the treatment of RA.

While conventional therapy uses medications aimed at controlling or suppressing the symptoms — the so-called Disease-Modifying Anti Rheumatic Drugs or DMARDs (including Methotrexate, Leflunomide, Enbrel, Humira, and others) — antibiotics are used with the idea

that perhaps there is an **infectious bacteria (in your mouth or intestine) that actually causes or worsens the inflammation in your joints.**

WHAT DON'T WE KNOW ABOUT THE USE OF ANTIBIOTICS TO TREAT RHEUMATIC DISEASE?

Traditionally when people get an infection, the bacteria that cause it can be identified by performing a “culture” of the affected organ, tissue or body fluid. For instance, when someone gets a urinary tract infection, a doctor orders a urinary culture. After a few days, and if a bacteria “grows” in a special mix of nutrients, a specific antibiotic is prescribed to fight the infection.

However, most of the bacteria that live in our mouths (teeth and gums) and in our intestines cannot be identified by these traditional “cultures.” For that reason, arthritis investigators have been unable to understand which bacteria, if any, are being killed by the antibiotics we use. In fact, some have suggested that these antibiotics have mostly anti-inflammatory properties and that their mode of action is not related to the elimination of bacteria. We would like to investigate this important matter further.

HOW WOULD YOU KNOW WHICH BACTERIA MAY BE ASSOCIATED WITH RA?

New genetic technology can help us identify these bacteria. There are studies in humans and in mice that show a link between the presence of certain bacteria in the gut and the development of arthritis. Using similar techniques, we want to find out if people with RA have different bacteria than people with PsA and healthy people.

Then, we want to test this idea by giving antibiotics to patients with RA (on top of their regular medications) and obtain samples from blood, dental cleanings, urine and stools to look for variations in the expression of genes, immune cells, proteins, enzymes, and oral and intestinal bacteria.

HOW CAN I TAKE PART IN THIS STUDY?

If you agree to participate, we will first ask you several questions regarding the status of your arthritis, the medications you use or have used in the recent past, your social and dietary habits, and your medical and surgical history. If your answers tell us that you are the right patient for our study, we will go over a consent form which describes in more detail how we will study your intestinal and mouth bacteria, the immune cells in your blood and other genes, enzymes and proteins that tell us about your disease status.

SAY I QUALIFY FOR THIS STUDY AND I AGREE TO PARTICIPATE — WHAT ARE THE NEXT STEPS?

VISIT A. First, we will review your history of arthritis in more detail and your personal information will be taken; we will make sure your blood work, X-rays, PPD test (for tuberculosis) and other blood tests related to your health are up-to-date. A thorough physical exam will be performed (including a formal count of your swollen/tender joints) and a questionnaire of your well-being will be filled out. You will then be assigned to one of three treatment groups. You will either receive a type of antibiotics on top of your current RA medications or you will only continue with RA meds (with no antibiotics).

We will then make a follow up appointment within 2 weeks where your first stool and oral samples will be taken and where you will be actually given the antibiotics (***VISIT B***).

VISIT B. This will be what we call the “Baseline Visit.” In this important visit, the most time-consuming one, we will ask you to come to your appointment with your stool sample. A group of 4 people will be guiding you for a few hours of your day. We will meet you at the **NYU College of Dentistry – Bluestone Center for Clinical Research**, at 421 1st Ave. (between 24th and 25th street), 2nd Floor – Clinic 2W, New York. We will receive the questionnaires you have filled out, the stool samples, and will go over a brief physical exam. A dental hygienist will look at your gums and obtain a few samples. You will get a dental cleaning for free if necessary. We will collect blood and urine and give you another stool collection kit for you to bring to your next regular appointment (***VISIT C***). Before you leave, we will assign you to a “treatment group.” You will be given a 2-month supply of either Vancomycin, Doxycycline or placebo (an inactive pill with no medication) for you to take. You will not know what you are taking, so the results of the study are not influenced by what you think.

VISIT C. One month after ***VISIT B***, you will come back to see your regular doctor as usual. You will be asked questions about the study medications you are taking and how you are feeling. If you need a change in pain medication for your arthritis, your doctor can prescribe it for you. We will collect blood and urine and give you another stool collection kit.

VISIT D, E and F. One month after ***VISIT C***, you will be finished with your study medications. You will come back to see your regular doctor as usual (every 6-8 weeks). For these three appointments, we will work together with your doctor so you do not spend too much extra time. The idea is that you get your regular medications for RA and, without your antibiotics, we continue to collect stool samples.

HOW WOULD I KNOW HOW TO COLLECT MY STOOL SAMPLES?

We have prepared an instruction sheet with pictures to explain the process better.

IF I HAVE A QUESTION ABOUT THE STUDY, THE ANTIBIOTICS OR EVEN ABOUT APPOINTMENTS, WHO SHOULD I CONTACT?

You can contact us at any time (24/7) at the following:

- Phone No.: 212-598-6513
- E-mail: MiCRA@nyumc.org

WILL I GET REIMBURSED FOR MY TIME AND TRAVEL EXPENSES?

We will provide lunch for you at ***VISIT B***. At ***VISIT D*** you will receive a reimbursement for your time and travel expenses.

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