Uploaded to VFC Website
October 2012

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

Veterans-For-Change is a 501(c)(3) Non-Profit Corporation
Tax ID #27-3820181

If Veteran's don't help Veteran's, who will?

We appreciate all donations to continue to provide information and services to Veterans and their families.

https://www.paypal.com/cgi-bin/webscr?cmd=_s-xclick&hosted_button_id=WGT2M5UTB9A78

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members.

ANKYLOSING SPONDYLITIS

(REACTIVE ARTHRITIS OF THE SPINE)

Gabe Mirkin, M.D.

If your back is stiff and hurts when you move, if it hurts to touch two points at the side of the top of your pelvis where it joins your spine (the sacroiliac joint), and if your back x ray shows signs of this disease, you probably suffer from ankylosing spondylitis. You may also have pain and swelling in your eyes, lungs, and heart valves. Most doctors think that ankylosing spondylitis is an autoimmune disease in which a person's immunity is so stupid that it attacks and destroys the joints in his back, rather than just doing its job of protecting a person from infection. They treat you with immune suppressants that may make you feel better, but increase your risk for infections and cancers and shorten your life. Nobody really knows why you have this condition, but the overwhelming evidence is that you inherited your susceptibility from your parents and you got this condition from an infection.

When you are infected, your body protects you by making proteins called antibodies and cells called white blood cells that attack and kill the bacteria. Your immunity recognizes each specific germ by the structure of its surface membranes. Ninety percent of people with ankylosing spondylitis have a gene called HLA-B27, which means that their cells have surface membranes that are like the surface membranes on many bacteria, particularly those that grow and live in your intestinal tract. So, if certain bacteria get into your bloodstream, your immunity recognizes these germs by their surface membranes and makes antibodies and cells that attack and kill them. However, if the cells in your body have similar surface membranes, your own immunity can be fooled and think that you are the invading germ and attack and kill your own cells.

There is one more piece to the puzzle. All people with ankylosing spondylitis have changes in their intestines that look like a disease called Crohn's disease in which they develop bloody ulcers in their intestines and sometimes terrible cramping and diarrhea. If intestinal bacteria are to cause ankylosing spondylitis, they have to have a way to get into the bloodstream, and the intestinal ulcers of Crohn's disease could be the portal of entry.

Dr. Joel Taurog and his colleagues at the University of Texas Southwestern Medical Center in Dallas developed laboratory rats that have the same HLA-B27 on their cells as that is found in people who have ankylosing spondylitis. These rats develop the same symptoms that occur in people with ankylosing spondylitis: joint and intestinal swelling and pain, and skin and nail lesions that look like psoriasis.

Hundreds of reports in the literature show that arthritis follows infections with bacteria such as Salmonella that causes typhoid fever , chlamydia that causes burning on urination, and a host of germs that cause diarrhea. Dr. Taurog showed that HLA-B27 rats that are raised in a completely germ-free environment do not develop arthritis or Crohn's disease. This implies that people who have the HLA-B27 surface protein on their cells will not get ankylosing spondylitis or Crohn's disease unless they are infected with certain types of germs.

Reactive arthritis is another type of arthritis that is associated with HLA-B27 genes. It occurs after venereal infections, usually chlamydia. and diarrhea caused by Yersinia or campylobacter. The most promising research going on right now is looking for specific bacteria that have been shown to cause arthritis, and then learn how to protect the body from overreacting to these bacteria, such as Mycobacterium paratuberculosis (that is thought to cause Crohn's disease), paramyxovirus (the measles viruses), Listeria monocytogenes (that causes diarrhea), and abnormal E. Coli that are in your intestines.

Several papers support an infectious cause for ankylosing spondylitis. People with ankylosing spondylitis are more likely to have genital (20) or intestinal symptoms (19) or infections with mycoplasma, chlamydia and ureaplasma (1). Virtually all patients have ulcers or changes in their gut similar to those seen in

Crohn's disease (2,20,21,22). Sufferers often have high blood levels of IGG and IGA antibodies that the body produces to kill Klebsiella bacteria which normally live in the intestines of healthy people (3,4,5,5A,17,24,25). Living with a person with ankylosing spondylitis increases your risk for developing the disease (6).

The surface structure of Klebsiella contains two molecules similar to that of a genetic marker for ankylosing spondylitis called HLA-B27; so does another gut bacteria called bacteroides (6A). When the pain is severe, large amounts of Klebsiella are found in stool samples, and those with ankylosing spondylitis often have intestinal ulcers in the end of the small intestine. A low starch diet that reduces the concentration of klebsiella has been reported to alleviate the back pain (7). Ankylosing spondylitis has been associated with campylobacter, clostridium, salmonella, shigella, yersinia, bacteroides and klebsiella (16).

When patients are in severe pain, many physicians prescribe immune suppressants because they help to control pain, and there is no good evidence that long-term antibiotics help control symptoms. However, I know of no double blinded, extended studies to test the effects of long-term antibiotics on ankylosing spondylitis. I have successfully treated several Crohn's disease patients with a regimen of doxycycline 100 mg twice a day continuously, and metronidazole 250 mg four times a day on alternate weeks, for as long as six months. However, I have not had this success with patients with ankylosing spondylitis. We need research to see if the antibiotic that can kill mycobacterium paratuberculosis that may be the cause of Crohn's disease, will also help control ankylosing spondylitis. In that case, a study should be done to see if clarithromycin, 500 mg twice a day for many months, will help control this condition. The theory that antibiotics may have a role in treatment of Crohn's disease and ankylosing spondylitis is highly controversial and not accepted by most doctors; check with your doctor.

One last point: very often the severe back pain of ankylosing spondylitis can be controlled by taking bisphosphonate drugs that are used to strengthen bones in people who have osteoporosis (18). An exciting study from the University of Alberta in Canada shows that intravenous infusion of pamidronate, a common drug for strengthening bones, helps to control ankylosing spondylitis. Pamidronate is a drug that is used to treat osteoporosis and is safer than most of the drugs used to treat ankylosing spondylitis. The doctor puts around 60 mg of Pamidronate into 500 cc of fluid and runs it into the veins slowly over 4 to 6 hours. When this is done once a week for several weeks, the pains of ankylosing spondylitis often goes away (28)

1) U Lange, M Berliner, W Weidner, HG Schiefer, KL Schmidt, K Federlin. Ankylosing spondylitis and infections of the male urogenital tract: Exploration of urinary tract infection in correlation to rheumatologic parameters. Zeitschrift Fur Rheumatologie 55: 4 (JUL-AUG 1996):249-255.

2) H Mielants, M Devos, C Cuvelier, EM Veys. The role of GUT inflammation in the pathogenesis of spondyloarthropathies. Acta Clinica Belgica 51: 5 (OCT 1996):340-349.

3) O Makiikola, K Lehtinen, K Granfors. Similarly increased serum IgA1 and IgA2 subclass antibody levels against Klebsiella pneumoniae bacteria in ankylosing spondylitis patients with/without extra-articular features. British Journal of Rheumatology 35: 2 (FEB,1996):125-128.

4) O Ardicoglu, MB Atay, H Ataoglu, N Etiz, H Ozenci. Ig A antibodies to Klebsiella in ankylosing spondylitis. Clinical Rheumatology 15: 6 (NOV1996):573-576.

5) Y Tani, H Tiwana, S Hukuda, J Nishioka, M Fielder, C Wilson, S Bansal, A Ebringer. Antibodies to Klebsiella, Proteus, and HLA-B27 peptides in Japanese patients with ankylosing spondylitis and rheumatoid arthritis. Journal of Rheumatology 24: 1 (JAN 1997):109-114. 5A) O Makiikola, R Hallgren, L Kanerud, N Feltelius, L Knutsson, K Granfors. Enhanced jejunal production of antibodies to Klebsiella and other Enterobacteria in patients with ankylosing spondylitis and rheumatoid arthritis. Annals of the Rheumatic Diseases 56: 7 (JUL 1997):421-425.

6) S Weinreich, J Capkova, B Hoebehewryk, C Boog, P Ivanyi. Grouped caging predisposes male mice to ankylosing enthesopathy. Annals of the Rheumatic Diseases 55: 9 (SEP 1996):645-647. 6A) J. Cclin Invest. 1996;98:945-53.

7) A Ebringer, C Wilson. The use of a low-starch diet in the treatment of patients suffering from ankylosing spondylitis. Clinical Rheumatology 15: Suppl. 1 (JAN 1996):62-66.

8) SGM Meuwissen, JBA Crusius, AS Pena, AJ Dekkersaeys, BAC Dijkmans. Spondyloarthropathy and idiopathic inflammatory bowel diseases. Inflammatory Bowel Diseases 3: 1 (SPR 1997):25-37.

9) K Granfors. Host-microbe interaction in HLA-B27-associated diseases. Annals of Medicine 29: 2 (APR 1997):153-157.

10) H Tiwana, C Wilson, RS Walmsley, AJ Wakefield, MSN Smith, NL Cox, MJ Hudson, A Ebringer. Antibody responses to gut bacteria in ankylosing spondylitis, rheumatoid arthritis, Crohn's disease and ulcerative colitis. Rheumatology International 17: 1 (MAY 1997):11-16. Klebsiella in the pathogenesis of AS and Proteus in RA. The role of Klebsiella in inflammatory bowel disease requires further study.

11) W Kuon, R Lauster, U Bottcher, A Koroknay, M Ulbrecht, M Hartmann, M Grolms, S Ugrinovic, J Braun, EH Weiss, J Sieper. Recognition of chlamydial antigen by HLA-B27-restricted cytotoxic T cells in HLA-B*2705 transgenic CBA (H-2(k)) mice. Arthritis and Rheumatism 40: 5 (MAY 1997):945-954.

12) Y Tani, H Sato, N Tanaka, S Hukuda. Antibodies against bacterial lipopolysaccharides in Japanese patients with ankylosing spondylitis. British Journal of Rheumatology 36: 4 (APR 1997):491-493.

13) KC Mounzer, MJ Dinubile. Prophylactic use of antibiotics and vaccines in patients with rheumatologic disorders. Rheumatic Disease Clinics of North America 23: 2(MAY 1997):259.

14) JT Gran, JF Skomsvoll. The outcome of ankylosing spondylitis: A study of 100 patients. British Journal of Rheumatology 36: 7 (JUL 1997):766-771. 15) O Ardicoglu, MB Atay, H Ataoglu, N Etiz, H Ozcenilg. A antibodies to Klebsiella in ankylosing spondylitis. Clinical Rheumatology

15: 6 (NOV 1996):573-576. Ankylosing spondylitis is triggered by Klebsiella.

16) **Lancet** 1998(March 14);351:767-8.

17) SHD Blankenbergsprenkels, M Fielder, TEW Feltkamp, H Tiwana, C Wilson, A Ebringer. Antibodies to Klebsiella pneumoniae in Dutch patients with ankylosing spondylitis and acute anterior uveitis and to Proteus mirabilis in rheumatoid arthritis. Journal of Rheumatology 25: 4 (APR 1998):743-747.

18) WP Maksymowych, GS Jhangri, S Leclercq, K Skeith, A Yan, AS Russell. An open study of pamidronate in the treatment of refractory ankylosing spondylitis. Journal of Rheumatology 25: 4 (APR 1998):714-717. pamidronate may possess antiinflammatory activity in patients with AS.

19)RQ Silva, JB Garcia, JAF Sanchez, FJ Casillas, CO Calvo, RH Mesia, JLS Lombrana, AR Perez. Silent axial arthropathy in inflammatory bowel disease. Clinical, radiological and genetic characteristics. Revista Clinica Espanola 198: 3 (MAR 1998):124-128. high frequency of asymptomatic sacroileitis in patients with IBD. 20) SM Sidelnikova, RM Kutyina, EA Zotikov. HLA-antigens and some pathogenetic aspects of reactive arthritis. Terapevticheskii Arkhiv 70: 5(1998):20-24. infection, ReA with HLA B27.

20) M Leirisalorepo. Therapeutic aspects of spondyloarthropathies - A review. Scandinavian Journal of Rheumatology 27: 5 (1998):323-328. In the pathogenesis of spondyloarthropathies, infection and gut inflammation are the most important external triggering factors. Early antimicrobial therapy to treat urethritis caused by Chlamydia trachomatis is effective in preventing a recurrent reactive arthritis: When the arthritis appear, a short term conventional antimicrobial therapy is unable to modify its course. In acute chlamydia arthritis, patients benefit from a prolonged (3-month) treatment with tetracycline, while such a treatment has not proved to be effective in enteroarthritis or in chronic forms of reactive arthritis.

21) F Dekeyser, D Elewaut, M Devos, K Devlam, C Cuvelier, H Mielants, EM Veys. Bowel inflammation and the spondyloarthropathies. Rheumatic Disease Clinics of North America. 24: 4(NOV 1998):785.

22) E Markerhermann, T Hohler. Pathogenesis of human leukocyte antigen B27-positive arthritis: Information from clinical materials. Rheumatic Disease Clinics of North America 24: 4(NOV 1998):865.

23) SD Khare, HS Luthra, CS David. Animal models of human leukocyte antigen B27-linked arthritides. Rheumatic Disease Clinics of North America 24: 4 (NOV 1998):883.

24) O Makiikola, M Nissila, K Lehtinen, K Granfors. IgA class serum antibodies against three different Klebsiella serotypes in ankylosing spondylitis. British Journal of Rheumatology 37: 12 (DEC 1998):1299-1302.

25) K Ahmadi, C Wilson, H Tiwana, A Binder, A Ebringer. Antibodies to Klebsiella pneumoniae lipopolysaccharide in patients with ankylosing spondylitis. British Journal of Rheumatology 37: 12 (DEC 1998):1330-1333.

26) A Ozgul, K Yazicioglu, S Gunduz, TA Kalyon, O Arpacioglu. Acute brucella sacroiliitis: Clinical features. Clinical Rheumatology 17: 6 (1998):521-523. One of the patients was positive for HLA-B27;

27)JH Ringrose.HLA-B27 associated spondyloarthropathy, an autoimmune disease based on crossreactivity between bacteria and HLA-B27?Annals of the Rheumatic Diseases, 1999, Vol 58, Iss 10, pp 598-610.there is no evident proof that SpA is an autoimmune disease attributable to crossreactivity between bacteria and HLA-B27.

28) A six-month randomized, controlled, double-blind, dose-response comparison of intravenous pamidronate (60 mg versus 10 mg) in the treatment of nonsteroidal antiinflammatory drug-refractory ankylosing spondylitis. Arthritis and Rheumatism, 2002, Vol 46, Iss 3, pp 766-773. WP Maksymowych, GS Jhangri, AA Fitzgerald, S LeClercq, P Chiu, A Yan, KJ Skeith, SL Aaron, J Homik, P Davis, D Sholter, AS Russell. Maksymowych WP, Univ Alberta, 562 Heritage Med Res Bldg, Edmonton, AB T6G 2S2, CANADA

Checked 8/9/05