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Review:

Bacterial reactive arthritis

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Abstract:

Reactive arthritis (ReA) is a kind of inflammatory that affects the joints which develops as a result of several forms of genitourinary or gastrointestinal infections, illustrating the typica interaction between the host and the environment. Spondyloarthropathies are a kind of arthritis that affects the spine (SpAs). A triad of symptoms involving the synovium, conjunctiva, and urethra characterizes the normal sickness; nevertheless, the majority of people doesn't have this ternary. ReA can be post venereal (Chlamydia trachomatis [Ct]) or post dysentery (*Campylobacter*, *Yersinia*, *Shigella* and *Salmonella*) however various additional bacteria were linked to the disease. For a variety of reasons, conducting epidemiologic and prospective research on ReA has been problematic. Over-reliance on the typical trio of symptoms, as well as the numerous words and eponyms used to define the ailment, has confused the illness description and definition.

Introduction:

Reactive arthritis (ReA) is a kind of rheumatoid disease that occurs after a gastrointestinal or genitourinary infection that lasts several days to weeks. Arthritis, urethritis, and conjunctivitis are frequently referred to as the "classic trinity". It used to termed as "Reiter syndrome," after the first person to describe it, Peter Reiter. The term "Reiter syndrome" was discontinued once it was discovered that Hans Reiter has been the chairman of the Kaiser Wilhelm Institute of Experimental Therapy and a member of the Nazis, where war captives were exposed to several brutal experiments. The root of the illness is thought to be an aberrant immune response to infection of the gastrointestinal tract that caused by *campylobacter, chlamydia, shigella or salmonella* (Arévalo M et al.,2018).

Etiology:

Infections of the genitourinary tract caused by bacteria (Ureaplasma urealyticum, Neisseria gonorrhea, Mycoplasma hominis and Chlamydia trachomatis) or digestive tract have been linked to reactive arthritis (*Clostridium difficile ,Campylobacter jejuni, Shigella flexneri, Yersinia enterocolitica , S. dysenteriae and Salmonella enteritidis).* Following a urogenital infection, most commonly caused by Chlamydia trachomatis, the incidence ranges from 0% to 15%, and after infections of gastrointestinal caused by *Campylobacter, Shigella , Salmonella* or *Yersinia,* the incidence ranges from 0% to 15%.

This might be influenced by epidemiological, environmental, and bacterial pathogenicity, as well as variations in study approaches. Enteric ReA is a frequent complication of enteric diseases. Chlamydia-associated ReA, on the other hand, is widespread, particularly in industrialized nations (Generali E et al.,2018).

Epidemiology

The incidence of reactive arthritis is estimated to be 0.6 to 27 per 100,000 in population-based research. Adult males are more prone to reactive arthritis in their second and third decades of life. (Muilu P et al., 2019).

An episode of arthritis affects around 1-3 percent of people with nonspecific urethritis. In general, poorer socioeconomic people have more disease activity and have less functional capability.

Pathophysiology

Reactive arthritis is a kind of immune-mediated arthritis that is brought on by a recent infection. Bacterial components such as lipopolysaccharide and nucleic acids are hypothesized to activate T lymphocytes whenever invasive germs penetrate the systemic circulation. These cytotoxic T cells had been activated subsequently use molecular mimicry to assault the synovium and other self-antigens. Anti-bacterial cytokine response is thought to be disrupted in reactive arthritis, resulting in bacterial clearance being reduced. However, it is unknown why inflammation is localized in this way.

In individuals with reactive arthritis, the prevalence of HLA-B27 is believed to be between 30% and 50%, while the numbers vary greatly. Frequencies as high as 60% to 80% have been recorded in hospital-based investigations with more seriously afflicted individuals.

Histopathology

At initially, psoriasis and reactive arthritis have similar skin histological features Synovial fluid contains large macrophages, reiter cells conveying

phagocytosed neutrophils, plasma cells and lymphocytes. The occurrence of widespread pannus is exceptional.

Evaluation:

Seronegative spondyloarthropathies impact the axial skeleton, and Reactive Arthritis is one of them. Ankylosing spondylitis and psoriatic arthritis are also part of this category. The involvement of the joints is oligoarticular and asymmetric.

Reactive arthritis diagnostic criteria were issued by the American College of Rheumatology in 1999. Two categories of criteria were created:

Essential:

- Lower extremity asymmetric oligo-arthritis or mono-arthritis
- Symptoms of either enteritis or urethritis that appear 3 to 6 weeks before the start of arthritis

Secondary:

- Culture positive indicates the presence of a triggering infection.
- Involvement of the synovium that persists

With genitourinary symptoms, involvement of the metatarsophalangeal joint, HLA-B27 positivity and increased C reactive protein, the diagnosis of reactive arthritis has a 69 percent sensitivity and 93.5 percent specificity (Selmi C, and Gershwin ME ,2014)

Despite the fact that reactive arthritis is a clinical diagnosis, laboratory testing to identify the causative bacteria and contemporaneous or antecedent infections is frequently utilized to support the diagnosis. Serological screening for Chlamydia trachomatis is restricted due to serological cross-reactivity with Chlamydia pneumonia. Serological testing for Salmonella, Yersinia, and Campylobacter is available; however it is not practical in clinical practice. There are additional infections of gastrointestinal, such as *Shigella*, for which there are no adequate serological tests.. Enteric pathogens can be detected using a stool culture. (Shohat N,et al.,2018).

It's crucial to recognize some problems, such as uveitis. In acute iritis, a slit-lamp examination is useful for identifying cells in the anterior chamber. As a result, if a suspected patient exhibits eye problems, an ophthalmologist should be consulted very away. Acute discomfort, photophobia, visual impairment, scleral injection, and hypopyon are the most common symptoms of uveitis.

HLA B 27 can be assessed since it corresponds with illness seriousness, however it is not a diagnostic test. It is also crucial in the diagnosis of arthritis.

HLA B 27 positive persons are more likely to develop sacroiliitis (Ikeda M,and , Yu DT ,1998).

Treatment / Management

Antimicrobial therapy is strongly suggested if pathogen was already confirmed as a stimulus to reactive arthritis, usually for a period of 3 to 6 months. It has the potential to shorten the duration to remission in half (Bojovi J et al., 2014). If there is an underlying concurrent infection, treatment should be started very away. A patient who doesn't have an active illness are ineffective when given antibiotics. (Carter JD,et a l.,2010). Chlamydia-positive people have been treated with a combination of rifampin and doxycycline or rifampin and azithromycin for a 6-month double-blind prospective triple placebo trial. Despite the fact that the trial's power was insufficient to find the best antibiotic combination, the treatment arm obtained statistically significant symptom remission and PCR negative results.

In reactive arthritis, the objective of treatment is to alleviate symptoms and avoid chronic consequences. Nonsteroidal anti-inflammatory medicines (NSAIDs) will be the first line of protection in the acute period. Orthotics and insoles are mechanical devices that can be beneficial. Glucocorticoids are only used systemically in severe polyarthritis, cardiac, and ocular symptoms. In both acute and chronic ReA, sulphasalazine and other disease-modifying antirheumatic drugs (DMARDs) can help.

Physical activity should be encouraged for all patients. Long-term therapy to prevent muscle loss must include strengthening activities.

Differential Diagnosis:

The doctor should have the ability to exclude any illnesses which have comparable clinical signs and symptoms. Among the most common differential diagnosis to consider are:

- Psoriatic arthritis
- Tubercular arthritis
- Still disease
- Secondary syphilis
- Gouty arthritis
- Rheumatoid arthritis
- Rheumatic fever
- Septic arthritis
- Gonococcal arthritis

- Ankylosing spondylitis

Prognosis:

Reactive arthritis is generally self-limited, with symptoms disappearing in 3 to 5 months. Symptoms that remain longer than six months suggest that the condition is persistent. The most prevalent chronic joint involvement is sacroiliitis. HLA-B27 positive patients have a greater chance of ReA recurrence. ReA can cause long-term arthritis or other joint problems in 15-30% of individuals. Hip involvement, non-responsiveness to NSAIDs, and an ESR greater than 30 all indicate a poor prognosis.

Complications of infection:

ReA has a number of Complications , including:

- Cystoid macular edema
- Chronic arthritis or sacroiliitis
- Recurrent arthritis (15 to 50%)
- Urethral stricture
- Aortic root necrosis
- Ankylosing spondylitis
- Cataracts

Salmonella:

Salmonella is a vast genus with global public health implications, since it is the most common cause of foodborne diseases, resulting in thousands of fatalities globally (Odoch et al., 2017). *Salmonella are rod-shaped bacteria , Gram-negative belonging to family of Enterobacteriaceae who are facultative anaerobes*. *Salmonella* enteric a and *Salmonella Bangor* are the two broad species that make up the genus *Salmonella* So date, over 2600 serovars of S. enterica have been discovered, with Many of them are able to infect animals and humans (Mezal *et al*., 2014).

The genus is mostly found in the digestive systems of humans and animals. Salmonella infection can thus be found in different habitats such as water, food and the environment (Yue and Schifferli, 2013).

Pathogenicity and Virulence Factors

Many techniques, such as invasion or intracellular reproduction inside host cells, have led to the discovery of numerous single genes that contribute to virulence features at the molecular cellular level, such as screening for attenuated mutants, to approach important virulence features and components of S. aureus (Gerlach, and Hensel, 2007). Virulence factors have been demonstrated to play a variety of functions in Salmonella infection

pathogenesis, including capsules, Flagella, adhesion systems, plasmids, and type 3 secretion systems (T3SS), which are encoded on Salmonella pathogenicity islands (SPI)-1 and SPI-2, as well as additional SPIs (Sabbagh et al., 2010). Salmonella colonizes its host by sticking to, invading, surviving, and outsmarting the host's defense mechanisms, which include stomach acidity, defensing and gastrointestinal proteases, as well as intestinal microbiome aggressing. (Yue and Schifferli, 2013).

After Salmonella enterica infection, the clinical presentation of Reactive Arthritis (ReA) shows a mixed relation with HLA-B27 (Ajene et al., 2013). Some studies suggest that those who carry the HLA-B27 gene are more vulnerable to ReA or have a greater risk of Salmonella infection, while others have found no link. (Tuompo et al., 2013) S. enterica grows in a specific membrane-bound compartment known as the Salmonella-containing vacuole prior to cellular escape and dispersion (SCV) (Ramsden et al., 2007). Despite the fact that the mechanism between intracellular bacteria and HLA-B27 is unclear, mammalian cell lines expressing HLA-B27 have been reported to have higher levels of internal Salmonella(Saarinen et al., 2002). The SCT was used to investigate if HLA-B27 misfolding influences endocellular proliferation and S. enterica localization in infected cells. We also looked at how S. enterica affects the activation of the UPR pathways mediated by XBP-1 and ATF6. (Ekman et al., 2002).

Salmonella mostly dwells in an altered peripheral cellular localization in the existence of misfolding HLA-B27. As a result, HLA-B27 may have an impact on SCV biogenesis and intracellular mobility. Salmonella survival and replicative capacity are influenced by SCV maturation and bacterial cellular localization (Holden, 2002).

Symptoms

Reactive arthritis signs and symptoms usually appear 1- 4 weeks following exposure to a triggering illness. They might consist of the following::

- Stiffness and discomfort The most common symptoms of reactive arthritis are joint pain in the knees, ankles, and feet.
- Soft tissue inflammation where it penetrates the bone (enthesitis). Muscles, tendons, and ligaments may all be affected.
- Inflammation of the eyes. Many persons with reactive arthritis develop conjunctivitis (inflammation of the eyes).
- Toes or fingers that are swollen. Your toes or fingers may swell to the point of resembling sausages in rare circumstances.
- Low back discomfort is a common ailment. The discomfort is usually worst at night or first thing in the morning (Vorwerk et al., 2015).

Laboratory testing and reporting *Salmonella* infection

- When Salmonella bacteria are found in feces, bodily tissue, or fluids, an infection is identified. A culture might be used to isolate the

bacterium, or a culture-independent diagnostic test (CIDT) might be used to identify the organism's genetic material.

- The CDC (Centers for Disease Control and Prevention) advises laboratories to cultivate specimens that have received a positive CIDT result. "Reflex culturing" is the name for this method.
- Salmonella isolates are delivered to public health laboratories in each state for serotyping and DNA fingerprinting..
- The National Salmonella Reference Laboratory of the Centers for Disease Control and Prevention (CDC) receives atypical serotypes from public health laboratories for additional characterization or confirmation (Walter et al., 2015).

Chlamydia trachomatis

Chlamydia trachomatis is a gram-negative bacteria that can only multiply within the cells of its host. The bacteria take on two different forms during the C. trachomatis life cycle. Basic bodies range in size from 200 to 400 nanometers in diameter and are encased in a strong cell wall that permits them to survive outside of their host cell. This form can begin a new infection if it comes into contact with a susceptible host cell. Reticulate bodies, which vary in size from 600 to 1500 nanometers in diameter, are found only in host cells (Chaurasia et al., 2016).

Chlamydia causes salpingitis, cervicitis, pelvic inflammatory disease, lymphogranuloma venereum, trachoma, and ongonococcal urethritis. Chlamydia trachomatis is the most common infectious cause of blindness and the most common sexually transmitted bacterium (Butrimiene et al., 2004).

Pathogenesis and virulence factors

According to research, Chlamydia trachomatis (Ct) is a common infection that causes ReA. In fact, Ct has been found in 50% of people who have ReA genitourinary infections. In addition, the CDC estimates that three million new Ct infections develop each year in the United States. According to studies, bacterial components of persistent Ct cause chronic inflammation (Droemann et al., 2007). This is due to the Ct's ability to block the combination of phagosomes and lysosomes that allows Chlamydia to remain in cells. Persistence may indicate the host's attempt to confine Chlamydia, with illness flares linked to chlamydial escape from persistence resulting to acute inflammatory responses, according to Droemann et al., 2007). Another research validated this conclusion, demonstrating that a considerable quantity of IL-10 was released in the synovial fluid of 11 ReA patients, but only a minor quantity of IFN- and TNF- was detected (Yin et al., 1997). In contrast, some investigations have found that TNF- levels are raised in chronic ReA (Butrimiene et al., 2004), indicating that this cytokine has a dual function in disease etiology. IL-17 levels have been identified in the synovial fluid of CiReA patients in studies. Salmonella adventitia proteins might induce synovial immune cells to generate IL-17 or IL-23, according to another

research concentrating on patients with type S. typhoid ReA. (Chaurasia et al., 2016). Another recent research of S. typhimurium-related ReA patients reveals that Salmonella outer membrane protein can increase the production of interleukin (IL)-17/IL-23 in synovial immune cells (Chaurasia et al., 2016).

Clinical signs and symptoms

Chlamydia infections, which can be asymptomatic or mimic gonorrhea infection, is a sign and symptom of C. Infection of the genitalia with T. trachomatis. Urethritis and pelvic inflammatory disease can be caused by either of these factors. C. The most frequent infectious agent associated to blindness (trachoma) also affects the eyes, causing inclusion conjunctivitis, which accounts for around 19 percent of adult conjunctivitis infections (Chaurasia et al., 2016).

Diagnosis of *chlamydia*

Nucleic acid amplification tests (NAATs), cell culture, and other methods can be used to diagnose chlamydia. The most sensitive tests are NAATs, which may be performed on easily available materials such vaginal swabs (either collected by the clinician or the patient) or urine.

Although chlamydial culture is not commonly accessible, it might be used for rectal or pharyngeal specimens. When it comes to recognizing C. trachomatis in non-genital locations, NAATs have been shown to have higher sensitivity and specificity than culture. When compared to culture, NAATS have showed better sensitivity and specificity for the identification of C. trachomatis at rectal locations, and certain laboratories have satisfied regulatory standards and validated NAAT testing on rectal and pharyngeal swab specimens (Droemann et al., 2007).

Yersinia enterocolitica

Yersinia bacteria may cause a variety of illnesses, including enteritis and bubonic plague (Black Death). In Hong Kong in 1894, the first characterization of this genus took place. Shibasaburo Kitasato and Alexandre Emile John Yersin identified Yersinia pestis (previously known as Pasteurella pestis) as the cause of bubonic plague there (Peruzy et al., 2017).

The first recognized description of five human isolates of Yersinia enterocolitica was published in 1939 by Schleifstein and Coleman of the United States. Despite this, in 1934, McIver and Pike isolated one of these clinical strains, but misidentified it as Flavobacterium pseudomallei .Cells with peritrichously flagellated flagella are motile. At temperatures ranging from 0 to 45 degrees Celsius, Yersiniae develops on non-selected and selective media, with an ideal range of 25–28 degrees Celsiu (Kraushaar et al., 2011).

Pathogenesis and virulence factors

Bio/serotypes 2–3/O:9, O:5, and 4/O:3 are frequently seen together. Biotype 1B is likewise thought to be highly pathogenic, despite its rarity in Europe .YE biotype 1A has been assumed to be avirulent since it lacks the recognized Yersinia virulence factor plasmid (pYV). The inv and hreP virulence genes are

present in Yersinia enterocolitica biotype 1A, but not the ystA or virF genes. (Peruzy et al., 2017).

The absence of substantial virulence markers in YE biotype 1A strains, notably ail, has been interpreted as showing that these strains are non-pathogenic to humans. Biotype 1A strains have recently been discovered to contain a lot of genetic variety, with ail positive strains accounting for 2% of YE biotype 1A strains. The bacterium travels throughout the joint, causing it to swell and become inflamed. Yersinia heat shock protein 60 and Yersinia urease 19 kd protein cause T cell responses in infected joints (Thiel et al., 2000).

A cytokine imbalance and a paucity of T-helper cytokines define the patient's response, which may allow the triggering microorganism to remain. While YE biotype 1A is commonly thought to be non-pathogenic, it may cling to epithelial cells and infiltrate them, as well as persist in macrophages. Macrophages can also release proinflammatory cytokines (IL-6, IL-8, and TNF) when exposed to human isolates of YE biotype 1A. (Sieper, 2004). It's also been suggested that Yersinia adhesin (yadA) has a role in ReA development (Gripenberg-Lerche et al.,).

Symptoms:

Diarrhea, abdominal pain, and fever are common symptoms of acute YE infection; mesenteric lymphadenitis and terminal ileitis are sometimes misinterpreted for acute appendicitis. After a YE infection, inflammatory sterile arthritis, reactive arthritis ,and erythema nodosum may ensue (Kraushaar et al., 2011).

Laboratory diagnosis:

The germs might be detected in the patient's excrement, blood, or vomit, among other places. Some countries rely on serology since isolating yersiniae from feces is difficult. Separating the bacterium from the meal is simple. Y. enterocolitica can be presumptively identified in 36-48 hours. (Peruzy et al., 2017).

Shigella:

Gram Negative Enterobacteriaceae family includes Shigella bacteria (rod-shaped, nonsporulating).Shigella flexneri, Shigella sonnei, Shigella boydii and Shigella dysenteriae are the four types of Shigella. Shigella bacteria are diffuse through the feces, and their prevalence is linked to inadequate water sanitation. Shigella bacteria penetrate colonic epithelial cells indirectly through microfold cells (Mcells), where they first come into contact with macrophages, after infection. The cause of apoptosis in macrophages prevents breakdown. The bacteria then grow and move laterally, infecting neighboring epithelial cells. This mechanism triggers proinflammatory signaling, which leads to the activation of NK cells and polymorphonuclear mononuclear cells (PMNs), which kill the bacteria but induce ulceration, inflammation, and bleeding in the mucosa. Shigellosis causes diarrhea (mucoid bloody), stomach cramps, and tenesmus (McNally et al., 2006). Our patient's colonoscopy revealed

symptoms of atypical colitis with aphthoid ulcerations, and a stool culture revealed Shigella flexneri infection..

Pathogenesis and virulence factors:

There are likely to be various factors: some are random, such as the infectious dosage, and others, such as comorbidities like subclinically inflamed joints (for example, weight bearing joints), where organisms may be more easily transported inside macrophages or neutrophils (Cook et al., 2004). Genes will play a role as well—more ReA is found in groups with a high incidence of HLA-B27—but other genes, such as the extracellular and intracellular sensors of bacterial infection, are also likely to play a role. Toll-like receptors16 17 and CARD molecules are the two molecules in question. Crohn's disease is linked to mutations in CARD15, but not ankylosing spondylitis. (Ogura et al., 2001). There have been no investigations on ReA-related connections yet. The alterations affect CARD15's capacity to modulate macrophage responses to bacterial cell walls detected by Toll-like receptor 2. Intracellular organisms, particularly CD8+ T cells, must take precautions to avoid being detected by the adaptive immune system.

Such peptides have previously been linked to HLA-B27 variants that lack the b2-microglobulin (Ferreiros-Vidal et al., 2003). These variants can bind traditional peptides eluted from intact B27 trimolecular complexes, as well (Watanabe et al., 2004). The question of whether atypical types of B27, maybe produced by intracellular infection, have a role in the immunological responses that promote ReA is now being debated.

In any event, these theories would link ReA to Shigella's intracellular niche and its impact on intracellular antigen processing, and this would hold true for both S sonnei and S flexneri. Whether or when more research into ReA cases caused by Shigella infection will provide insight on the arthritis's pathophysiology, the practical point made by Hannu et al is clear: Suspect Shigella as the causative organism in patients with inflammatory arthritis who have recently returned from sunny climes, and keep an eye out for it. (van der Paardt et al., 2003).

Symptoms of shigellosis

Diarrhea (sometimes bloody) and Fever are two examples. If you have any of the following symptoms, you should contact your healthcare provider:

- Dehydrated.
- Bloody diarrhea.
- Fever
- Feel very sick
- Cramping or soreness in the stomach. (van der Paardt et al., 2003).

Diagnosis:

Microscopic examination Stool smears with a larger number of PMN cells show up under the microscope. They are Gram-negative, non-motile, and non-capsulated tiny rods. (Ferreiros-Vidal et al., 2003).

Biochemical analysis and Culture

- To distinguish pale non-lactose-fermenting colonies from other enterobacteria, conventional biochemical and sugar consumption assays are performed after an overnight incubation period.
- Convex colonies are seen on Hektoen agar blue green.
- Nonmotile organisms that do not create H2S, create acid but not gas in the butt and have an alkaline slant in TSI agar media should be exposed to *Shigella* slide agglutination.
- The majority of S. *dysenteriae s*trains are negative for mannitol fermentation and catalase production, however they are occasionally positive for o-nitrophenyl-b-D-galactopyranoside (ONPG) (Van der Paardt et al., 2003).

Serology:

- Vero and HeLa cell tests, as well as immunoassays for the Verocytotoxin generated by specific E. coli strains, can identify *Shiga* toxin expression.
- Patients infected with S. dysenteriae 1 develop antibodies to the lipopolysaccharide antigens in their blood and saliva, but these antibodies are not frequently tested (Ferreiros-Vidal et al., 2003).

Molecular methods:

- (PCR) assays targeting the genes that encode the invasion plasmid antigen H can identify Shigella strains (ipaH).
- The ShET-2 PCR may be used to detect the genes encoding an aerobactin-mediated iron uptake system.
- There are a number of commercial NAATs that can detect shigellae and other important enteric pathogens directly in feces (Ogura et al., 2001).

Campylobacter jejuni:

In humans, *Campylobacter jejuni* seems to be the most common bacterial infection enteritis, responsible for 5–14% of all diarrheal infections worldwide. (Rautelin and Hanninen, 2000). The majority of infections are sporadic, although outbreaks occasionally occur. Campylobacter, for example, is responsible for 59 percent of water or food-borne diarrhea episodes in Canada, and its prevalence is rising (Hannu et al., 2002). Human campylobacteriosis is expected to affect 2.1–2.4 million people in the United States each year. C. jejuni is the most prevalent Campylobacter serotype, accounting for 90–95 percent of positive stools. Only 5–10% of C. coli infections are caused by the second most prevalent serotype. (Friedman et al., 2004).

Symptoms:

Joint and musculoskeletal (MSK) involvement is the most prevalent symptomatology, although mucous membranes , gastrointestinal, skin, cardiac symptoms and ocular have also been recorded and should be investigated independently. (Hannu et al.,2005).

The symptoms of joint pain range from moderate mono- or oligoarthralgia to severe polyarthritis. The arthritis prefers joints in the lower extremities, notably the knees and ankles, although it is not always axially involved. Anyone with a mono- or oligoarthritis of uncertain aetiology should consider ReA in their differential diagnosis (Hannu et al., 2004).

Pathogenesis and virulence factors

The chance of developing post-enteric ReA appears to be slightly higher for Salmonella and Yersinia infection than for Campylobacter infection, although further research is needed to confirm this (Hill Gaston and Lillicrap, 2003). The pathogenesis is unclear, however it is thought that an interaction between the host HLA-B27 and particular bacteria is important in the development of ReA.

There was no connection between HLA-B27 and Campylobacter-associated ReA in a population-based study. Patients with more severe or chronic illness (HLA-B27+ as high as 70% in hospital-based research) may face a referral bias to tertiary care institutions. (Calin and Taurog ,1998). This would prefer increased HLA-B27 prevalence, showing that HLA-B27 isn't essential for ReA development, but it might aggravate disease severity and chronicity. ReA arises after a urogenital or intestinal infection, albeit the organism is rarely detected (Butrimiene et al., 2004).

ReA synovitis is hypothesized to be caused by molecular mimicry. Self-antigens are confused with viral antigens in a process known as molecular mimicry. There are a lot of interesting review papers concerning self/molecular mimicry tolerance (Braun et al., 2000).

Diagnosis:

A synovial fluid culture and microscopy should be undertaken to rule out septic arthritis and crystal-induced arthritis. Salmonella, Yersinia, and Campylobacter can remain for a long period after an initial infection, thus stool should be cultured as well (Butrimiene et al., 2004). Serological methods can also be used to detect Campylobacter infection, albeit their sensitivity and specificity appear to be lower than those for *Salmonella* and *Yersinia* pestis (Braun et al., 2000). High IgG titres to Campylobacter aren't always indicative of a recent infection, as the bug can be found in foods like chicken and eggs. As a result, rising IgG and/or chronically elevated IgA are diagnostically preferred (Fendler et al., 2001). There are no standardized criteria for ReA, which is a key flaw in the diagnosis process.

Consultations:

The patient should see his primary care physician and an orthopedic physician on a frequent basis to examine the extent of the infection's damage.

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