dentalcetoday.com
Powered by Dentistry Today

Continuing Education

Course Number: 179

TMD Rediscovered: A New Paradigm, Part One

Authored by
Lawrence Gottesman, DDS

Upon successful completion of this CE activity 2 CE credit hours may be awarded

A Peer-Reviewed CE Activity by

DENTISTRY TODAY
is an ADA CERP Recognized Provider

ADA C·E·R·P®
Continuing Education Recognition Program

Dentistry Today, Inc, is an ADA CERP Recognized Provider. ADA CERP is a service of the American Dental Association to assist dental professionals in indentifying quality providers of continuing dental education. ADA CERP does not approve or endorse individual courses or instructors, nor does it imply acceptance of credit hours by boards of dentistry. Concerns or complaints about a CE provider may be directed to the provider or to ADA CERP at ada.org/goto/cerp.

Academy of General Dentistry
PACE
Program Approval for Continuing Education

Approved PACE Program Provider
FAGD/MAGD Credit Approval does not imply acceptance by a state or provincial board of dentistry or AGD endorsement. June 1, 2012 to May 31, 2015 AGD PACE approval number: 309062

TMD Rediscovered: A New Paradigm, Part One

Effective Date: 11/1/2014 Expiration Date: 11/1/2017

LEARNING OBJECTIVES

After participating in this CE activity, the individual will learn:

- Evidence-based support for arthritis of the temporomandibular joint (TMJ) as an infectious disease.
- Elements of inflammation as a vascular event that damages blood vessels supporting the TMJ.

ABOUT THE AUTHOR

Dr. Gottesman received his dental education at New York University College of Dentistry, graduating in 1977, and currently maintains a private practice in Rockville Centre, NY. He has served on the teaching faculty of the Lenox Hill Hospital Dental Service and has also been on the faculty of the New York University College of Dentistry TMD/orofacial pain program, where he served as director of neuropathic pain in the advanced orofacial pain/TMD graduate teaching program. Together with Dr. G. William Arnett and Dr. Stephen B. Milam, Dr. Gottesman has co-authored the acclaimed 2-part article, "Progressive Mandibular Retrusion—Idiopathic Condylar Resorption" which was published in the *American Journal of Orthodontics* in July and August of 1996. For comments, questions, or lecture information, he can be reached at lgotteswim@aol.com.

Disclosure: *Dr. Gottesman reports no disclosures.*

INTRODUCTION

The human temporomandibular joint (TMJ) has been most eloquently described by Benjamin Moffett:[1] *It reigns as the paladin of joints, for, having served as the evolutionary deliverer of the middle ear, it gallantly became the enduring hinge on which woman's emancipation continually swings. Its versatility fills us with respect for a structure so magnificent in function that at one moment it is the sliding pivot of trituration and mastication, at the next, the gnashing safety valve of rage and fury, and, in moments of sublime creativity, the proprioceptive junction for poetry and song.*

The TMJ is a structurally unique joint positioned at the intersection of many vital cross-system interactions. Moffett's article[1] underscores the sophisticated and intricate physiologic role the TMJ plays in simultaneously coordinating multiple functions under the influence of varying functional demands.[2]

Much has been said about temporomandibular joint disorders (TMDs) in the dental literature. The large album of symptoms and associated diseases which seem to defy assignment to a common root cause is problematic, controversial, and confusing. The historical discourse written by Nelson and Landau[3] chronicles the diverse causal heritage of TMD from 1887 forward, and features the contributions made by many professional icons of their time. No doubt, many of our esteemed colleagues have had a strong hand in shaping our professional outlook regarding TMD as a complicated, multifaceted abnormality. However, despite the many hypotheses associated with loss of normal function and degenerative joint changes, the etiopathogenesis of TMD remains unclear.

As a female gender-biased disorder, the list of symptoms and causative factors are strikingly varied, ranging from occlusal discrepancies and prematurities; occlusal pattern abnormalities; malocclusions; variations from centric relation; bruxism; jaw pain; joint pain; clicking; popping; masticatory muscle discomfort; limited range of motion; ear pain; headache; tinnitus; sore throat; neck pain; stress; anxiety; tension; psychosocial issues; tooth loss; accompaniment by back pain, autoimmune syndromes, hormonal and reproductive disorders, sleep disturbances, and gastroesophageal reflux disease, to mention a few.[4-15]

With such a broad band of wide-ranging associations, co-mingling, and co-morbid factors, where can practitioners look to find the foot that will fit the glass slipper?

The mystery may be solved by close examination of the key factors associated with disorders of the TMJ: cytokine profiles, inflammation, and coagulation.

Part one of this article is devoted to a supportive literary review presenting arthritis of the TMJ and other joints as an infectious disease. This portion highlights important

elements of inflammation as a vascular event which involves activation of the coagulation system and causes damage to blood vessels supporting the joint structure and failure of hard tissues.

Part 2 will channel the academic findings discussed in the first part into the clinical setting. The second article will help prepare the clinician to identify TMD and orofacial pain patients with a comprehensive questionnaire targeting disease forms and symptoms from the position of infectious diseases and thrombophilia (pro-clotting disorders) as a mixed entity. Case studies or portions of case reports will be used to demonstrate blood abnormalities and potential blood studies which can be authorized to validate or dismiss coagulopathies and the evidentiary trail of infection. An MRI sequence prescription and clinical examination companioned with this concept will be forwarded. Part 2 will also briefly address 2 imperative questions. First, why does the gender bias exist on this platform, and second, if TMD had its origin as an occlusomuscular disorder, why would a splint work if an infection was at the core foundation?

DECODING THE MYSTERY

Cytokines

Cytokines are proteins that serve as signaling molecules, some of which have pro-inflammatory properties, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), IL-6, interferon gamma, granulocyte-macrophage colony-stimulating factor (GM-CSF), and IL-8, to name the most commonly cited. Pro-inflammatory cytokines have been implicated in joint pain, TMJ closed lock, inflammation, internal disc derangements,[16-22] and joint effusions.[23-27] Other cytokines are anti-inflammatory, including IL-1 receptor antagonist, IL-4, IL-6, IL-10, IL-11, and IL-13,[28] and may reflect an immunomodulatory dampening counterbalance to the cytotoxic response precipitated by the pro-inflammatory group.[29]

Cytokine profiles in asymptomatic controls differ from abnormal TMJ patients.[30] Both pro- and anti-inflammatory cytokines are frequently found together in symptomatic patients.[22,31,32] Additionally, several members of this signaling family have dual roles in modulating the inflammatory immune response and other regulatory processes as demonstrated by IL-6.[32,33-37]

Cytokines maintain a fundamental role as part of the innate immune system, serving as acute phase reactants in the initial nonspecific response to infection. The innate immune cells comprise a population of predominantly white blood cells (WBCs) forming the frontline of defense when our barrier system(s) have been breached. Cytokines are released by resident members of this WBC lineage, including neutrophils, natural killer cells, dendritic cells, monocytes, basophils, eosinophils, and local tissue mast cells and macrophages.[38-44] As part of a complicated and orchestrated system, the cytokines are responsible for immune cell recruitment and other cell-mediated trafficking functions.[45-47]

Pro-inflammatory cytokines, free radicals, and oxidized low-density lipoprotein are among the molecules that can activate nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kβ). The receptor activator of NF-kβ, called RANK, is active in bone regulation, and upon exposure to cell-mediated pro-inflammatory cytokines can initiate osteoclastogenesis.[48]

The key element, however, in understanding the character of cytokines is that *they are most commonly activated in response to microbial pathogens*.[49] Therefore, part of the differential diagnosis in the pathophysiology of TMD must include infection, a lexicon missing from our current common wisdom.

Central to the theme of inflammation is activation of the coagulation system. Triggered by the cytokine release in response to bacterial, viral, fungal, and parasitic organisms, activation of the clotting cascade ensues with the production of tissue factor (thrombin formation) and induces a local or more global systemic vascular response, resulting in a hypercoagulable state,[49] whereby the blood becomes thickened (more viscous). In 1856 the German physician, Rudolf Virchow, described the trio of damage to the blood vessels and changes in blood viscosity leading to this hemostatic abnormality called Virchow's Triad: vascular endothelial injury, blood stasis, and hypercoagulability of the blood. This phenomenon contributes to the domino effect of disturbed flood flow, impaired oxygen delivery to tissues, and hypoxia, and raises the risk for venous thromboembolism or deep vein thrombosis.[50,51] At the tissue level, larger vessels that become obstructed by

thrombus formation may give rise to emboli, which can have catastrophic consequences such as a pulmonary embolism, myocardial infarction, or stroke. However, medium and small portions of the vascular system can also be adversely affected, leading to local ischemic changes and peripheral nerve involvement as the blood-nerve barrier is breached, compromising the blood supply to sensory and motor nerves with resultant motor and painful sensory neuropathies.[52,53]

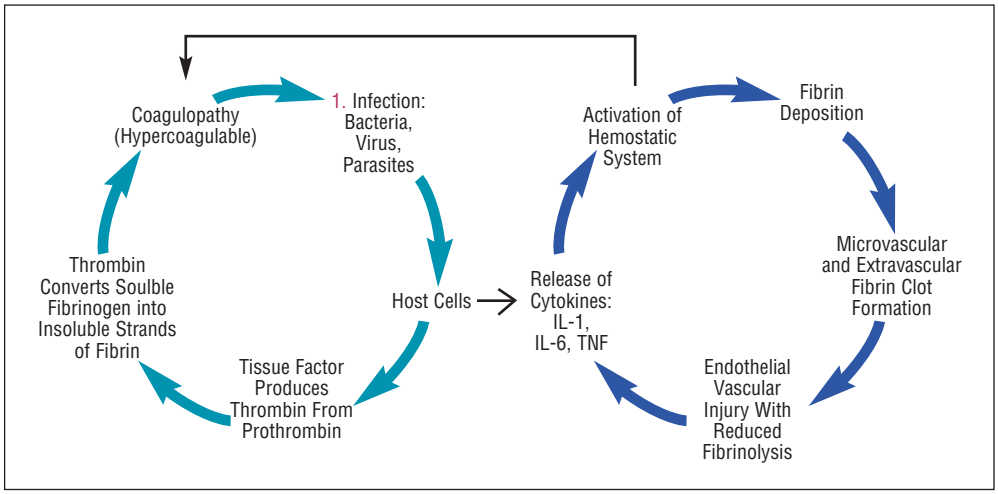

Figure 1. The relationship among microbial pathogens, cytokines, inflammation, and coagulation.

Further, the activation of the hemostatic system concomitant with inflammatory changes leads to fibrin generation with the formation of fibrous tissue in both intravascular and extravascular fluid spaces.[54] Patients with synovitis,[55-57] rheumatoid arthritis,[58,59] adhesions,[60] and the consequential development of free radicals[61] demonstrate fibrin production in association with joint abnormalities and other inflammatory diseases. As the endothelium of the blood vessel, particularly the venous component, becomes paved and thickened with fibrin, its lumen caliper narrows, partially or fully obstructing the venous outflow. Changes in the integrity of the vascular wall lead to arteriosclerosis (stiffening of the blood vessel wall) and decreased compliance.[62] These sequelae set the stage, creating the potential for a static backflow system with an increase in venous pressure and reduced arteriole blood flow influx. With changes in blood flow rate, vascular endothelial wall shear stresses are altered. Adverse modifications in hemodynamics escort and enhance fibrin generation on the venous end, while the arteriolar transformation favors a platelet-rich environment which will ultimately be enriched by the incorporation of fibrin strands into the platelet aggregate.[54,62]

Such abnormalities in blood flow can have profound and dramatic consequences for a joint that is literally being suffocated to death; the accompanying disturbances are implicated in the development of bone marrow lesions[63] and osteonecrosis.[64]

In 2011, Jennewein et al[65] stated that: "Coagulation is fundamental for the confinement of infection and/or the inflammatory response to a limited area. Under pathological inflammatory conditions such as arthritis, multiple sclerosis, or sepsis, an uncontrolled activation of the coagulation system contributes to inflammation, microvascular failure, and organ dysfunction."

The purpose of coagulation is to limit infection and enhance the inflammatory response with the hope of immune functions isolating and quelling an infectious or injurious event.[66,67] The intimacy of cross-talk between systems is essential in trying to strike a balance that addresses the diseased state. The relationship between the severity of the inflammatory reaction and the rigor of the hemostatic response may be beneficial, but not without consequence.[68] Despite what we might insinuate is nature's purpose, the cytokines and other acute phase reactants which are first responders in an attempt to kill microbial trespassers[44] have a highly cytotoxic effect on both the micro-organisms and resident tissues. Ultimately, human body parts caught in the crossfire summarily fall victim to "friendly" fire (Figure 1).

While much attention has been devoted to the biomechanical aspects of joint loads and the influence forces have on the local structures as a rationale for TMD,[69-71] the cytokine profiles in joint studies which have explored the potential for pro-inflammatory cytokine production during cyclic compressive forces are disparate

as demonstrated by Muroi et al in 2007,[72] whereby TMJ synovial tissue surgical explants exposed to mechanical compressive forces produced mostly matrix metalloproteinases along with the chemokine IL-8, without the expression of TNF-α, IL-1ß, IL-6 in their recordable assays. At this juncture, the lack of TNF-α, IL-1ß, and IL-6 cytokine expression during mechanical compressive loading becomes a very important issue. If these cytokines have a primary allegiance to the innate immune system, but are not produced during load testing studies, then it raises the likelihood that part of the root cause for TMD arises from infections. The failure of the joint as an organ could occur at multiple tissue levels[73] without the introduction of mechanical overload and could be potentiated by persistent clotting abnormalities introduced by temporary or persistent microbial invaders.[49]

Orhan et al[74] have demonstrated, via MRI, TMJ bone marrow shifts in patients with anemia without the requirement for disc displacement or internal derangement. The prospect that inherited intrinsic genetic risk factors such as thrombophilia (pro-clotting disorders) may precipitously amplify the clotting cascade during infection must also be considered.[64]

Is TMD an Infectious Disease?

The literature supporting TMD as an infectious disease is largely succedaneous and reactive to the greater number of articles written by researchers within the medical profession. However, the lesser body of evidence in the dental space demonstrating the presence of pathogenic organisms either in the peripheral venous blood, or TMJ tissues or fluid, warrant merit and lend credence to the concept that infection is involved with TMJ disturbances, and may be the leading cause. Although many of the dental articles are highly conserved in the pursuit and identification of only singular microbial species, there are a few studies which utilize a more broadband analysis in parallel with the medical writings to demonstrate co-infection or polymicrobial diversity related to TMJ disease.

Chlamydia trachomatis, one of the organisms responsible for sexually transmitted diseases, occupies a very large presence in both the medical and dental literature and is classified symptomatically under the umbrella of reactive arthritis. Henry et al[75,76] have demonstrated the presence of *C trachomatis* in internal derangement surgical studies where the peripheral blood analysis was positive for immunoglobulin antibodies demonstrating cases of both past and active infections. In a more comprehensive search, Henry et al[75,76] expanded their investigation beyond *C trachomatis*, and included *Mycoplasma fermentans* and *orale*, *Mycoplasma genitalium*, and the organisms associated with food poisoning, *Campylobacter jejuni* spp., *Yersinia enterocolitica* spp., *Salmonella* spp., and *Shigella* spp.[77] The latter group has also been included under the auspices of reactive arthritis. Surgical tissue samples were harvested from the bilaminar zone of 26 surgical patients. Of the 26 patients (24 female and 2 male), 42% had *C trachomatis*, 35% *M genitalium*, and 23% *M fermentans/orale*. The food poisoning group was negative in this study. Eight percent of the group tested positive for 2 organisms (*M fermentans/orale* and *M genitalium*), while 4% were positive for a combined cluster of 3 organisms (*C trachomatis, M fermentans/orale*, and *M genitalium*).[78] In 1999 and 2007, Henry et al[76,79] conducted more constrained studies, looking only for *C trachomatis* and *serovars* from the bilaminar zone of surgical specimens. Of 70 patients in the 2007 study, 46% were positive for *C trachomatis*.[76] Further, in the same investigation, Henry et al[76] found differences in the cytokine profiles between symptomatic *Chlamydia* positive patients and the control group, showing elevated levels of TNF-α and IL-6 in the symptomatic population tested for these cytokines.

Kim et al[77] in 2003 performed a relatively expanded synovial fluid study and found the presence of *M genitalium* in 86% of the 43 patient samples with a 1:1.69 male to female ratio. Of this group, 33 symptomatic participants had a displaced disc, and 10 participants were asymptomatic non-disc displacement recruits. The other organisms investigated were *Staphylococcus Aureus*, present in 52% of the population tested; *M fermentans/orale* 37.2%; *Actinobacillus actinomycetemcomitans* (a highly pathogenic periodontal disease-related species) 25.6%; and *Streptococcus mitis* 7.0%. The conclusions drawn predicated on the higher levels of *S Aureus* present in the symptomatic displaced disc group versus the non-displaced disc asymptomatic volunteers was

that *S Aureus* was implicated as causal to TMD.[77]

Adachi[80] shows the involvement of *Mycobacterium* in the TMJ. Sun et al[81] provide a broadband peak cell rate (PCR), 16s ribosomal RNA analysis of synovial fluid confirming the presence of 11 species and substantiating that a wide variety of bacteria can be associated with TMD. Other authors have made significant contributions to this area as well.[82-84] Jeon et al[85] have identified that the source of infection can be hematogenous with respect to the TMJ, and corroborates a statistical correlation among TMJ disease, sinusitis, rhinitis, pharyngitis, and tonsillitis.[86]

In order to help consolidate and provide a clinical perspective, the addition of some of the comparable medical literature may prove helpful. In recapitulating what has been stated thus far, some salient points which need to be placed into context will be reviewed.

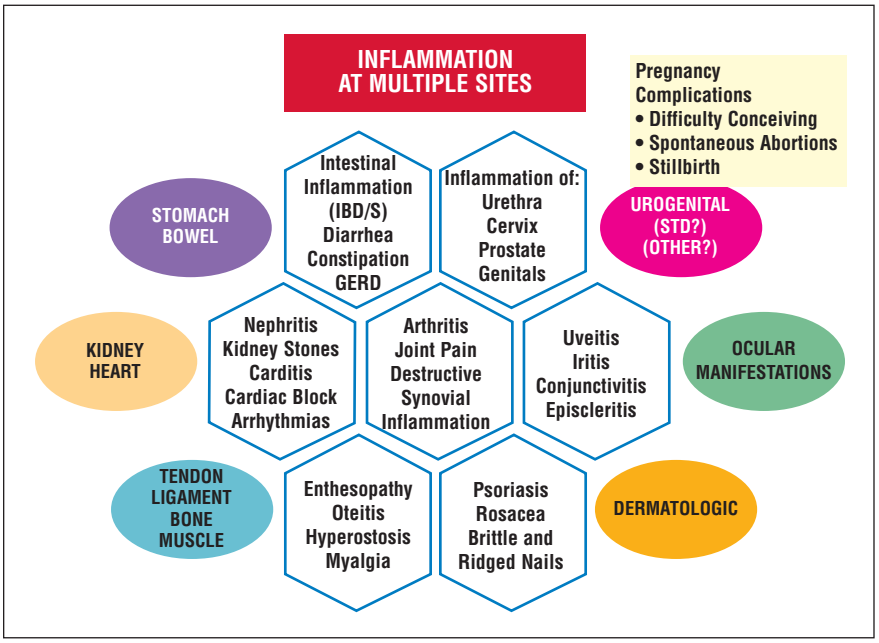

Figure 2. Symptoms of reactive arthritis.

First, there is a regional flavor for the path of origination and dissemination to the TMJ from neighboring structures. Sinuses, nasal passages, pharynx, upper respiratory, and tonsils are all in close proximity to the TMJ. Infections in these nearby areas are potential origination sites for resident organisms to gain migratory access through the vascular or lymphatic systems in order to reach and occupy a niche environment.[85,86]

Secondly, the oral cavity is a substantial reservoir for micro-organisms. The study by Kim et al[77] demonstrates involvement of the periodontal pathogenic organism *A actinomycetemcomitans*. However, to strengthen the case for the involvement and presence of oral pathogens in joint diseases, the work of Moen et al[87,88] validates the oral-systemic link in identifying the DNA from oral bacteria in the synovial fluid and serum from patients with rheumatoid, psoriatic, and osteoarthritis. Moen et al[87,88] found greater diversity and concentrations of DNA from oral micro-organisms in the synovial fluid than the serum. Both rheumatoid and psoriatic arthritis had greater bacterial variety and content when compared to osteoarthritis. There was some disease-related specificity with respect to the organisms present and associated arthritic form. Moen et al[87,88] suggest that the synovial tissues are a preferred niche environment for many organisms; perhaps due to their rich vascularity, presence of a basement membrane, and anatomical form, joints are an attractive sink-hole for colonization.[89]

Blood serum has reduced diversity and numbers of bacteria compared to synovial tissues and fluid. This can be problematic from an investigative standpoint when performing blood studies because the immune response mounted in the peripheral blood often becomes pale in comparison to inflammatory changes in the joint. The patient may not manifest with blood draw biomarker abnormalities due to this phenomenon. The confirmation of this difficulty is established by Lyme polymerase chain reaction studies with analysis from different sites. Comparing blood, cerebrospinal fluid, synovial fluid, and skin tissue, positive markers were significantly higher in synovial fluid and tissue.[90] Also, it is important to mention that most micro-organisms have evolved evasive strategies to avoid immune detection, making positive identification difficult.[91-93]

Further, organisms can migrate from sites distant from the initiating source of the infection, to joints and other sites.

This is particularly true of the organisms associated with sexually transmitted diseases[89] and the *Mycoplasma* group.[94] Organisms included in the reactive arthritis group may originate from the urogenital tract, or gut, as in the food poisoning group, associated with *Campylobacter jejuni* spp., *Yersinia enterocolitica* spp., *Salmonella* spp., and *Shigella* spp.[95]

Microbial pathogens may also entertain occupancy in tissues other than joints, finding their way to mucosa-associated lymphoid tissue as is the case with *Helicobacter pylori* in oral glandular tissue and its contribution to Sjögren's disease symptoms.[96] Most importantly, while on their pilgrimage, organisms may affect many tissues, causing considerable and sometimes serious disturbances. What we may have considered as referred pain patterns and loosely associated disorders more accurately reflects the effect of pathogenic tenancy with genetic and metabolic alterations at multiple locations. The expressions of seemingly unrelated symptoms often seen in association with TMD are more likely to have a common denominator, under the wings of this platform, than previously thought.

This concept is manifest in the reactive arthritis symptom profiles (Figure 2 [symptoms of reactive arthritis]; Table [organisms associated with "infectious" reactive arthritis]).

Cox et al[97] and Kempsell et al[98] provide valuable information in investigating the viability of bacterial organisms in synovial tissue samples from arthritic patients. Using a reverse transcriptase-PCR analysis of bacterial ribosomal RNA, they were able to detect and characterize the bacterial diversity and existence of live organisms associated with the arthritides.[97,98] They make a significant contribution to our understanding of joint diseases. In the Kempsell et al study,[98] 23 participants were evaluated. A comparative bacterial analysis was performed between rheumatoid arthritis (RA) and non-RA patients. Nine patients were classified as having RA. In the non-RA group, the breakdown was as follows: 7 patients had osteoarthritis (OA), 4 patients had undifferentiated arthritis (UA), and 3 patients were normal (no arthritis). Collectively, synovial tissue samples from the RA group showed the presence of 92 living individual species

Table. Organisms Commonly Cited as Associated With Infectious or Reactive Arthritis

GENITOURINARY	GI TRACT	RESPIRATORY TRACT	VECTOR-BORNE	ORAL/MIXED
STD	SHIGELLA *Flexneri*	MYCOPLASMA	LYME DISEASE	MYCOPLASMA
CHLAMYDIA *Trachomatis*	YERSINIA *Enterocolitica*, *Pseudotuberculosis*, *Sonnei*	*Pneumoniae*	RICKETTSIA	• Fermentans • Salivarium
NEISSERIA *Gonorrhoeae*	SALMONELLA *Entiritidis*, *Typhimurim*	CHLAMYDIA *Pneumoniae*, *Psittaci*	ANAPLASMA	*P gingivalis* Treponema *Denticola* *A actinomy-cetemcomitans* *PREVOTELLA* (*Nigrescens*, *Intermedia*) *B forsynthia*
TREPONEMA *Pallidum*	CAMPYLOBACTER *Jejuni* *Shigella*, *Yersinia*, *Salmonella*, and *Campylobacter* = food poisoning group.	STAPH, *Aureus*	BABESIA	
				BIOFILM
RHEUMATOID ARTHRITIS (RA) REACTIVE ARTHRITIS	H PYLORI	PSEUDOMONAS *Aeurginosa*	BARTONELLA	**FUNGI**
MYCOPLASMA	E COLI	STREP, *Pyogenes*, *B-hemolytic*	EHRLICHIA	**PROTOZOA**
• *Fermentans*	C DIFFICILE		COLORADO TICK FEVER	**UNKNOWN ORGANISMS**
• *Genitalium*	TOXOPLASMA GONDII	**SKIN**	Q FEVER	
• *Homonis*	ENTAMOEBA HISTOLYTICA	STAPH, *Epidermis* *P* Acnes MRSA	ROCKY MOUNTAIN SPOTTED FEVER	
	GIARDIA LAMBLIA			
UREAPLASMA	BRUCELLA ABORTUS	**VIRAL**		
• *Urealyticum*	*T Whipplei*	HIV		
		MEASLES		
		HHV		
		EBV		
		CYTOMEGALOVIRUS		
		B19		

Note: The term *infectious arthritis* within the context of this article is used to describe the association of microbial pathogens with autoimmune disorders like RA, as an infectious process affecting joints and other tissue structures.
Combined adaptation from references 1 to 3.

1. Martinez-Martinez RE, Abud-Mendoza C, Patiño-Marin N, Rizo-Rodríguez JC, Little JW, Loyola-Rodríguez JP. Detection of periodontal bacterial DNA in serum and synovial fluid in refractory rheumatoid arthritis patients. *Journal of Clinical Periodontology*. 2009;36(12):1004-1010.
2. Ogrendik M. Rheumatoid arthritis is linked to oral bacteria: etiological association. *Mod Rheumatol*. 2009;19(5):453-456.
3. Sibilia J, Limbach FX. Reactive arthritis or chronic infectious arthritis? *Ann Rheum Dis*. Jul 2002;61(7):580-587.

compared to 50 species in the non-RA control group. Overall, the 2 groups shared 21 species. The normal group had no organisms (Figure 3)!

The following is a synopsis of the article outcome:

- The RA group had a greater number of species and bacterial load than the non-RA group.
- There were many species unique to the individual groups and many organisms.
- There were many unidentified novel organisms which did not conform to any data sets of known organisms.
- Previously thought to be sterile, the joints in diseased patients contain multiple bacterial species.
- These organisms are difficult to cultivate or are culture-resistant, owing to the requirement of unknown fastidious culture mediums or sensitivity to osmotic gradients consistent with cell-wall deficient (CWD) bacteria.
- The colonization suggested these organisms could live in a biofilm.
- There was no uniformity with respect to synovial tissue colonization.
- Not all parts of the same tissue carry the same bacterial load or organisms.
- Microcolonization of different tissue areas is likely.
- Organisms could occupy both intracellular and extracellular locations.
- Commensals from the gut and skin were frequently found in joints and suggested trafficking from these sights.
- The presence of biofilm may confer antibiotic resistance and therapeutic challenges.
- These infections are often slow growing and can take many years to mature.

The findings by these 2 authors and others confirm the realities confronting our profession in the diagnosis and etiology of TMD. Cox et al[97] and Kempsell et al[98] have authenticated that even in the case of classical osteoarthritis, which was thought to be related to the biomechanical "wear and tear" of a joint, significant amounts of bacterial organisms are present. Olmez et al[99] recapitulates this theme in OA patients with *C trachomatis* and *Chlamydia pneumoniae*.

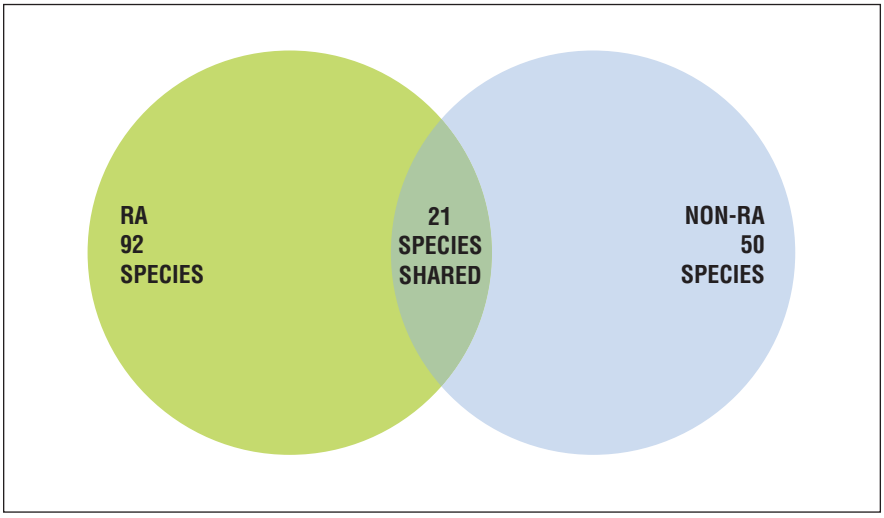

Figure 3. Rheumatoid arthritis (RA) and non-RA subjects shared 21 species of microbial organisms.

CONCLUSION

Pivotal to the supportive arguments presented are the thought processes that should accompany the clinician's diagnostic investigations. Inflammation and coagulation are interdependently linked, especially when infection is the precipitating source. This discourse brings together several elements which have not been brought to the general attention of the dental profession as causal to TMD. Pathogenic microbes that migrate to, and homestead, a particular site will violate the security of our defense systems, activate the release of inflammatory cytokines, and trigger the clotting cascade. These series of events, as part of the inflammatory response, will cause endothelial dysfunction, disturbed blood flow, and oxygen impairment, and lead to the breakdown of the TMJ on multiple levels.

REFERENCES

1. Moffett B. The morphogenesis of the temporomandibular joint. *Am J Orthod*. 1966;52:401-415.
2. Grünheid T, Langenbach GE, Korfage JA, et al. The adaptive response of jaw muscles to varying functional demands. *Eur J Orthod*. 2009;31:596-612.
3. Nelson DA, Landau WM. Jaws: diversities of gnathological history and temporomandibular joint enterprise. *J Neurol Neurosurg Psychiatry*. 1999;67:141-147.
4. Gremillion HA. Multidisciplinary diagnosis and management of

orofacial pain. *Gen Dent*. 2002;50:178-188.
5. Nebbe B, Major PW, Prasad NG. Adolescent female craniofacial morphology associated with advanced bilateral TMJ disc displacement. *Eur J Orthod*. 1998;20:701-712.
6. Okeson JP. Joint intracapsular disorders: diagnostic and nonsurgical management considerations. *Dent Clin North Am*. 2007;51:85-103, vi.
7. Gunson MJ, Arnett GW, Formby B, et al. Oral contraceptive pill use and abnormal menstrual cycles in women with severe condylar resorption: a case for low serum 17-estradiol as a major factor in progressive condylar resorption. *Am J Orthod Dentofacial Orthop*. 2009;136:772-779.
8. Pullinger AG, Seligman DA, Gornbein JA. A multiple logistic regression analysis of the risk and relative odds of temporomandibular disorders as a function of common occlusal features. *J Dent Res*. 1993;72:968-979.
9. Pullinger AG, Seligman DA, Solberg WK. Temporomandibular disorders. Part II: Occlusal factors associated with temporomandibular joint tenderness and dysfunction. *J Prosthet Dent*. 1988;59:363-367.
10. Tallents RH, Macher DJ, Kyrkanides S, et al. Prevalence of missing posterior teeth and intraarticular temporomandibular disorders. *J Prosthet Dent*. 2002;87:45-50.
11. Arnett GW, Milam SB, Gottesman L. Progressive mandibular retrusion—idiopathic condylar resorption. Part I. *Am J Orthod Dentofacial Orthop*. 1996;110:8-15.
12. Arnett GW, Milam SB, Gottesman L. Progressive mandibular retrusion-idiopathic condylar resorption. Part II. *Am J Orthod Dentofacial Orthop*. 1996;110:117-127.
13. Ramirez Aristeguieta LM, Sandoval Ortiz GP, Ballesteros LE. Theories on otic symptoms in temporomandibular disorders: past and present. *Int J Morphol*. 2005;23:141-156.
14. Rouse JS. The bruxism triad: sleep bruxism, sleep disturbance, and sleep-related GERD. *Inside Dentistry*. 2010;6(5):32-44.
15. Lavigne GJ, Khoury S, Abe S, et al. Bruxism physiology and pathology: an overview for clinicians. *J Oral Rehabil*. 2008;35:476-494.
16. Kubota E, Kubota T, Matsumoto J, et al. Synovial fluid cytokines and proteinases as markers of temporomandibular joint disease. *J Oral Maxillofac Surg*. 1998;56:192-198.
17. Matsumoto K, Honda K, Ohshima M, et al. Cytokine profile in synovial fluid from patients with internal derangement of the temporomandibular joint: a preliminary study. *Dentomaxillofac Radiol*. 2006;35:432-441.
18. Nishimura M, Segami N, Kaneyama K, et al. Comparison of cytokine level in synovial fluid between successful and unsuccessful cases in arthrocentesis of the temporomandibular joint. *J Oral Maxillofac Surg*. 2004;62:284-288.
19. Ogura N, Tobe M, Sakamaki H, et al. Tumor necrosis factor-alpha increases chemokine gene expression and production in synovial fibroblasts from human temporomandibular joint. *J Oral Pathol Med*. 2005;34:357-363.
20. Sato J, Segami N, Nishimura M, et al. Expression of interleukin 6 in synovial tissues in patients with internal derangement of the temporomandibular joint. *Br J Oral Maxillofac Surg*. 2003;41:95-101.
21. Sato J, Segami N, Nishimura M, et al. Expression of interleukin 8 in synovial tissues in patients with internal derangement of the temporomandibular joint and its relationship with clinical variables. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103:467-474.
22. Takahashi T, Kondoh T, Fukuda M, et al. Proinflammatory cytokines detectable in synovial fluids from patients with temporomandibular disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998;85:135-141.
23. Emshoff R, Puffer P, Rudisch A, et al. Temporomandibular joint pain: relationship to internal derangement type, osteoarthrosis, and synovial fluid mediator level of tumor necrosis factor-alpha. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2000;90:442-449.
24. Güler N, Uçkan S, Imirzalio lu P, et al. Temporomandibular joint internal derangement: relationship between joint pain and MR grading of effusion and total protein concentration in the joint fluid. *Dentomaxillofac Radiol*. 2005;34:175-181.
25. Kaneyama K, Segami N, Sun W, et al. Levels of soluble cytokine factors in temporomandibular joint effusions seen on magnetic resonance images. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2005;99:411-418.
26. Kaneyama K, Segami N, Yoshimura H, et al. Increased levels of soluble cytokine receptors in the synovial fluid of temporomandibular joint disorders in relation to joint effusion on magnetic resonance images. *J Oral Maxillofac Surg*. 2010;68:1088-1093.
27. Takahashi T, Nagai H, Seki H, et al. Relationship between joint effusion, joint pain, and protein levels in joint lavage fluid of patients with internal derangement and osteoarthritis of the temporomandibular joint. *J Oral Maxillofac Surg*. 1999;57:1187-1193.
28. Opal SM, DePalo VA. Anti-inflammatory cytokines. *Chest*. 2000;117:1162-1172.
29. Zhang R, Liu Y, Yan K, et al. Anti-inflammatory and immunomodulatory mechanisms of mesenchymal stem cell transplantation in experimental traumatic brain injury. *J Neuroinflammation*. 2013;10:106.
30. Kim YK, Kim SG, Kim BS, et al. Analysis of the cytokine profiles of the synovial fluid in a normal temporomandibular joint: preliminary study. *J Craniomaxillofac Surg*. 2012;40:e337-e341.
31. Hamada Y, Kondoh T, Holmlund AB, et al. Cytokine and clinical predictors for treatment outcome of visually guided temporomandibular joint irrigation in patients with chronic closed lock. *J Oral Maxillofac Surg*. 2008;66:29-34.
32. Sultani M, Stringer AM, Bowen JM, et al. Anti-inflammatory cytokines: important immunoregulatory factors contributing to chemotherapy-induced gastrointestinal mucositis. *Chemother Res Pract*. 2012;2012:490804.
33. Elenkov IJ, Iezzoni DG, Daly A, et al. Cytokine dysregulation, inflammation and well-being. *Neuroimmunomodulation*. 2005;12:255-269.

34. Kim EY, Moudgil KD. Regulation of autoimmune inflammation by pro-inflammatory cytokines. *Immunol Lett*. 2008;120(1-2):1-5.
35. Sanjabi S, Zenewicz LA, Kamanaka M, et al. Anti-inflammatory and pro-inflammatory roles of TGF-beta, IL-10, and IL-22 in immunity and autoimmunity. *Curr Opin Pharmacol*. 2009;9:447-453.
36. Shachar I, Karin N. The dual roles of inflammatory cytokines and chemokines in the regulation of autoimmune diseases and their clinical implications. *J Leukoc Biol*. 2013;93:51-61.
37. Erta M, Quintana A, Hidalgo J. Interleukin-6, a major cytokine in the central nervous system. *Int J Biol Sci*. 2012;8:1254-1266.
38. Ait-Oufella H, Taleb S, Mallat Z, et al. Recent advances on the role of cytokines in atherosclerosis. *Arterioscler Thromb Vasc Biol*. 2011;31:969-979.
39. Gruys E, Toussaint MJ, Niewold TA, et al. Acute phase reaction and acute phase proteins. *J Zhejiang Univ Sci B*. 2005;6:1045-1056.
40. Kaneyama K, Segami N, Nishimura M, et al. Importance of proinflammatory cytokines in synovial fluid from 121 joints with temporomandibular disorders. *Br J Oral Maxillofac Surg*. 2002;40:418-423.
41. Scott K, Manunta M, Germain C, et al. Qualitatively distinct patterns of cytokines are released by human dendritic cells in response to different pathogens. *Immunology*. 2005;116:245-254.
42. Bennouna S, Denkers EY. Microbial antigen triggers rapid mobilization of TNF- to the surface of mouse neutrophils transforming them into inducers of high-level dendritic cell TNF- production. *J Immunol*. 2005;174:4845-4851.
43. Lacy P, Stow JL. Cytokine release from innate immune cells: association with diverse membrane trafficking pathways. *Blood*. 2011;118:9-18.
44. Stenger S, Röllinghoff M. Role of cytokines in the innate immune response to intracellular pathogens. *Ann Rheum Dis*. 2001;60(suppl 3):iii43-iii46.
45. Oizumi S, Strbo N, Pahwa S, et al. Molecular and cellular requirements for enhanced antigen cross-presentation to CD8 cytotoxic T lymphocytes. *J Immunol*. 2007;179:2310-2317.
46. Saalmüller A. New understanding of immunological mechanisms. *Vet Microbiol*. 2006;117:32-38.
47. Stäger S, Kaye PM. CD8+ T-cell priming regulated by cytokines of the innate immune system. *Trends Mol Med*. 2004;10:366-371.
48. Zhao B, Ivashkiv LB. Negative regulation of osteoclastogenesis and bone resorption by cytokines and transcriptional repressors. *Arthritis Res Ther*. 2011;13:234.
49. Levi M, Keller TT, van Gorp E, et al. Infection and inflammation and the coagulation system. *Cardiovasc Res*. 2003;60:26-39.
50. Chung I, Lip GY. Virchow's triad revisited: blood constituents. *Pathophysiol Haemost Thromb*. 2003;33(5-6):449-454.
51. Mazza JJ. Hypercoagulability and venous thromboembolism: a review. *WMJ*. 2004;103:41-49.
52. Topp KS, Boyd BS. Structure and biomechanics of peripheral nerves: nerve responses to physical stresses and implications for physical therapist practice. *Phys Ther*. 2006;86:92-109.
53. Finsterer J. Systemic and non-systemic vasculitis affecting the peripheral nerves. *Acta Neurol Belg*. 2009;109:100-113.
54. Neeves KB, Illing DA, Diamond SL. Thrombin flux and wall shear rate regulate fibrin fiber deposition state during polymerization under flow. *Biophys J*. 2010;98:1344-1352.
55. Muto T, Kawakami J, Kanazawa M, et al. Histologic study of synovitis induced by trauma to the rat temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998;86:534-540.
56. Muto T, Shigeo K, Kanazawa M, et al. Ultrastructural study of synovitis induced by trauma to the rat temporomandibular joint (TMJ). *J Oral Pathol Med*. 2003;32:25-33.
57. Zhang S, Liu X, Yang C, et al. Intra-articular adhesions of the temporomandibular joint: Relation between arthroscopic findings and clinical symptoms. *BMC Musculoskelet Disord*. 2009;10:70.
58. Ho PP, Lee LY, Zhao X, et al. Autoimmunity against fibrinogen mediates inflammatory arthritis in mice. *J Immunol*. 2010;184:379-390.
59. Sánchez-Pernaute O, Largo R, Calvo E, et al. A fibrin based model for rheumatoid synovitis. *Ann Rheum Dis*. 2003;62:1135-1138.
60. Hase M. Adhesions in the temporomandibular joint: formation and significance. *Aust Dent J*. 2002;47:163-169.
61. Dijkgraaf LC, Zardeneta G, Cordewener FW, et al. Crosslinking of fibrinogen and fibronectin by free radicals: a possible initial step in adhesion formation in osteoarthritis of the temporomandibular joint. *J Oral Maxillofac Surg*. 2003;61:101-111.
62. Chiu JJ, Chien S. Effects of disturbed flow on vascular endothelium: pathophysiological basis and clinical perspectives. *Physiol Rev*. 2011;91:327-387.
63. Bouquot JE, McMahon RE, Glueck CJ. Bone marrow edema: mild or nascent variant of ischemic bone disease. *J Oral Maxillofac Surg*. 2008;66:205-208.
64. Glueck CJ, Freiberg RA, Wang P. Detecting thrombophilia, hypofibrinolysis and reduced nitric oxide production in osteonecrosis. *Semin Arthroplasty*. 2007;18:184-191.
65. Jennewein C, Tran N, Paulus P, et al. Novel aspects of fibrin(ogen) fragments during inflammation. *Mol Med*. 2011;17(5-6):568-573.
66. Boos CJ, Goon PK, Lip GY. The endothelium, inflammation, and coagulation in sepsis. *Clin Pharmacol Ther*. 2006;79:20-22.
67. Levi M, van der Poll T, Büller HR. Bidirectional relation between inflammation and coagulation. *Circulation*. 2004;109:2698-2704.
68. Iba T, Kidokoro A, Fukunaga M, et al. Association between the severity of sepsis and the changes in hemostatic molecular markers and vascular endothelial damage markers. *Shock*. 2005;23:25-29.
69. Gallo LM, Nickel JC, Iwasaki LR, et al. Stress-field translation in the healthy human temporomandibular joint. *J Dent Res*. 2000;79:1740-1746.
70. Iwasaki LR, Petsche PE, McCall WD Jr, et al. Neuromuscular objectives of the human masticatory apparatus during static biting. *Arch Oral Biol*. 2003;48:767-777.

71. Tanaka E, Rodrigo DP, Miyawaki Y, et al. Stress distribution in the temporomandibular joint affected by anterior disc displacement: a three-dimensional analytic approach with the finite-element method. *J Oral Rehabil*. 2000;27:754-759.
72. Muroi Y, Kakudo K, Nakata K. Effects of compressive loading on human synovium-derived cells. *J Dent Res*. 2007;86:786-791.
73. Brandt KD, Radin EL, Dieppe PA, et al. Yet more evidence that osteoarthritis is not a cartilage disease. *Ann Rheum Dis*. 2006;65:1261-1264.
74. Orhan K, Delilbasi C, Paksoy C. Magnetic resonance imaging evaluation of mandibular condyle bone marrow and temporomandibular joint disc signal intensity in anaemia patients. *Dentomaxillofac Radiol*. 2009;38:247-254.
75. Henry CH, Pitta MC, Wolford LM. Frequency of chlamydial antibodies in patients with internal derangement of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2001;91:287-292.
76. Henry CH, Whittum-Hudson JA, Tull GT, et al. Reactive arthritis and internal derangement of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;104:e22-e26.
77. Kim SJ, Park YH, Hong SP, et al. The presence of bacteria in the synovial fluid of the temporomandibular joint and clinical significance: preliminary study. *J Oral Maxillofac Surg*. 2003;61:1156-1161.
78. Henry CH, Hughes CV, Gérard HC, et al. Reactive arthritis: preliminary microbiologic analysis of the human temporomandibular joint. *J Oral Maxillofac Surg*. 2000;58:1137-1142.
79. Henry CH, Hudson AP, Gérard HC, et al. Identification of Chlamydia trachomatis in the human temporomandibular joint. *J Oral Maxillofac Surg*. 1999;57:683-688.
80. Adachi N, Matsumoto S, Tokuhisa M, et al. Antibodies against mycobacterial antigens in the synovial fluid of patients with temporomandibular disorders. *J Dent Res*. 2000;79:1752-1757.
81. Sun W, Dong L, Kaneyama K, et al. Bacterial diversity in synovial fluids of patients with TMD determined by cloning and sequencing analysis of the 16S ribosomal RNA gene. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;105:566-571.
82. Leighty SM, Spach DH, Myall RW, et al. Septic arthritis of the temporomandibular joint: review of the literature and report of two cases in children. *Int J Oral Maxillofac Surg*. 1993;22:292-297.
83. Paegle DI, Holmlund AB, Östlund MR, et al. The occurrence of antibodies against Chlamydia species in patients with monoarthritis and chronic closed lock of the temporomandibular joint. *J Oral Maxillofac Surg*. 2004;62:435-439.
84. Watanabe T, Shibata K, Yoshikawa T, et al. Detection of Mycoplasma salivarium and Mycoplasma fermentans in synovial fluids of temporomandibular joints of patients with disorders in the joints. *FEMS Immunol Med Microbiol*. 1998;22:241-246.
85. Jeon HS, Hong SP, Cho BO, et al. Hematogenous infection of the human temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2005;99:E11-E17.
86. Jeon YD, Lee JI, Cho BO, et al. Statistical correlation between pharyngitis and temporomandibular joint disease. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2005;99:677-681.
87. Moen K, Brun JG, Madland TM, et al. Immunoglobulin G and A antibody responses to Bacteroides forsythus and Prevotella intermedia in sera and synovial fluids of arthritis patients. *Clin Diagn Lab Immunol*. 2003;10:1043-1050.
88. Moen K, Brun JG, Valen M, et al. Synovial inflammation in active rheumatoid arthritis and psoriatic arthritis facilitates trapping of a variety of oral bacterial DNAs. *Clin Exp Rheumatol*. 2006;24:656-663.
89. Espinoza LR, García-Valladares I. Of bugs and joints: the relationship between infection and joints. *Reumatol Clin*. 2013;9:229-238.
90. Babady NE, Sloan LM, Vetter EA, et al. Percent positive rate of Lyme real-time polymerase chain reaction in blood, cerebrospinal fluid, synovial fluid, and tissue. *Diagn Microbiol Infect Dis*. 2008;62:464-466.
91. Alcami A. Viral mimicry of cytokines, chemokines and their receptors. *Nat Rev Immunol*. 2003;3:36-50.
92. Finlay BB, McFadden G. Anti-immunology: evasion of the host immune system by bacterial and viral pathogens. *Cell*. 2006;124:767-782.
93. Rooijakkers SH, van Strijp JA. Bacterial complement evasion. *Mol Immunol*. 2007;44(1-3):23-32.
94. Rivera A, Yáñez A, León-Tello G, et al. Experimental arthritis induced by a clinical Mycoplasma fermentans isolate. *BMC Musculoskelet Disord*. 2002;3:15.
95. Meyer-Bahlburg A, Brinkhoff J, Krenn V, et al. Infection of synovial fibroblasts in culture by Yersinia enterocolitica and Salmonella enterica serovar Enteritidis: ultrastructural investigation with respect to the pathogenesis of reactive arthritis. *Infect Immun*. 2001;69:7915-7921.
96. El Miedany YM, Baddour M, Ahmed I, et al. Sjogren's syndrome: concomitant H. pylori infection and possible correlation with clinical parameters. *Joint Bone Spine*. 2005;72:135-141.
97. Cox CJ, Kempsell KE, Gaston JS. Investigation of infectious agents associated with arthritis by reverse transcription PCR of bacterial rRNA. *Arthritis Res Ther*. 2003;5:R1-R8.
98. Kempsell KE, Cox CJ, Hurle M, et al. Reverse transcriptase-PCR analysis of bacterial rRNA for detection and characterization of bacterial species in arthritis synovial tissue. *Infect Immun*. 2000;68:6012-6026.
99. Olmez N, Wang GF, Li Y, et al. Chlamydial nucleic acids in synovium in osteoarthritis: what are the implications? *J Rheumatol*. 2001;28:1874-1880.

POST EXAMINATION INFORMATION

To receive continuing education credit for participation in this educational activity you must complete the program post examination and receive a score of 70% or better.

Traditional Completion Option:

You may fax or mail your answers with payment to *Dentistry Today* (see Traditional Completion Information on following page). All information requested must be provided in order to process the program for credit. Be sure to complete your "Payment," "Personal Certification Information," "Answers," and "Evaluation" forms. Your exam will be graded within 72 hours of receipt. Upon successful completion of the post-exam (70% or higher), a letter of completion will be mailed to the address provided.

Online Completion Option:

Use this page to review the questions and mark your answers. Return to ***dentalcetoday.com*** and sign in. If you have not previously purchased the program, select it from the "Online Courses" listing and complete the online purchase process. Once purchased the program will be added to your ***User History*** page where a ***Take Exam*** link will be provided directly across from the program title. Select the ***Take Exam*** link, complete all the program questions and ***Submit*** your answers. An immediate grade report will be provided. Upon receiving a passing grade, complete the online evaluation form. Upon submitting the form, your ***Letter of Completion*** will be provided immediately for printing.

General Program Information:

Online users may log in to ***dentalcetoday.com*** any time in the future to access previously purchased programs and view or print letters of completion and results.

POST EXAMINATION QUESTIONS

1. **Cytokines that have pro-inflammatory properties include:**
   a. Tumor necrosis factor-alpha (TNF-α).
   b. Interleukin-1 beta (IL-1β).
   c. IL-4.
   d. Both a and b.

2. **Cytokines are proteins that serve as signaling molecules. Both pro- and anti-inflammatory cytokines are frequently found together in symptomatic TMJ patients.**
   a. The first statement is true, the second is false.
   b. The first statement is false, the second is true.
   c. Both statements are true.
   d. Both statements are false.

3. **Cytokines are most commonly activated in response to microbial pathogens.**
   a. True.
   b. False.

4. **Cytokines maintain a fundamental role as part of the innate immune system. Cytokines serve as acute phase reactants in the initial nonspecific response to infection.**
   a. The first statement is true, the second is false.
   b. The first statement is false, the second is true.
   c. Both statements are true.
   d. Both statements are false.

5. **Under pathological inflammatory conditions such as arthritis, multiple sclerosis, or sepsis, an uncontrolled activation of _____ contributes to inflammation, microvascular failure, and organ dysfunction.**
   a. IL-4.
   b. The coagulation system.
   c. IL-6.
   d. All of the above.

6. **Research by Muroi found that mechanical compressive loading of the TMJ produced mostly:**
   a. IL-1β cytokine.
   b. IL-6 cytokine.
   c. Matrix metalloproteinases and IL-8 cytokine.
   d. TNF-α cytokine.

7. **Research has found a statistical correlation between TMJ disease and:**
   a. Sinusitis.
   b. Rhinitis.
   c. Pharyngitis and tonsillitis.
   d. All of the above.

8. **Blood serum has reduced diversity and numbers of bacteria compared to synovial fluid.**
   a. True.
   b. False.

9. **Microbial organisms can migrate from sites distant from the initiating source of infection, to joints and other sites. This is particularly true of organisms associated with sexually transmitted diseases.**
   a. The first statement is true, the second is false.
   b. The first statement is false, the second is true.
   c. Both statements are true.
   d. Both statements are false.

10. **Kempsell et al's study of patients with rheumatoid arthritis (RA) found that:**
    a. The RA group had fewer number of microbial species than the non-RA group.
    b. There was uniformity with respect to synovial tissue colonization by microbial species.
    c. Previously thought to be sterile, joints in diseased patients contain multiple bacterial species.
    d. None of the above.

PROGRAM COMPLETION INFORMATION

If you wish to purchase and complete this activity traditionally (mail or fax) rather than online, you must provide the information requested below. Please be sure to select your answers carefully and complete the evaluation information. To receive credit you must answer at least 7 of the 10 questions correctly.

***Complete online at:* dentalcetoday.com**

TRADITIONAL COMPLETION INFORMATION:

Mail or fax this completed form with payment to:

Dentistry Today
Department of Continuing Education
100 Passaic Avenue
Fairfield, NJ 07004
Fax: 973-882-3622

PAYMENT & CREDIT INFORMATION:

Examination Fee: $40.00 **Credit Hours:** 2.0

Note: There is a $10 surcharge to process a check drawn on any bank other than a US bank. Should you have additional questions, please contact us at (973) 882-4700.

❑ I have enclosed a check or money order.

❑ I am using a credit card.

My Credit Card information is provided below.

❑ American Express ❑ Visa ❑ MC ❑ Discover

Please provide the following (please print clearly):

Exact Name on Credit Card

Credit Card # Expiration Date /

Signature

Academy of General Dentistry PACE Program Approval for Continuing Education

Approved PACE Program Provider FAGD/MAGD Credit Approval does not imply acceptance by a state or provincial board of dentistry or AGD endorsement. June 1, 2012 to May 31, 2015 AGD PACE approval number: 309062

ADA C·E·R·P® Continuing Education Recognition Program

Dentistry Today, Inc, is an ADA CERP Recognized Provider. ADA CERP is a service of the American Dental Association to assist dental professionals in indentifying quality providers of continuing dental education. ADA CERP does not approve or endorse individual courses or instructors, nor does it imply acceptance of credit hours by boards of dentistry. Concerns or complaints about a CE provider may be directed to the provider or to ADA CERP at ada.org/goto/cerp.

PERSONAL CERTIFICATION INFORMATION:

Last Name (PLEASE PRINT CLEARLY OR TYPE)

First Name

Profession / Credentials License Number

Street Address

Suite or Apartment Number

City State Zip Code

Daytime Telephone Number With Area Code

Fax Number With Area Code

E-mail Address

ANSWER FORM: COURSE #: 179

Please check the correct box for each question below.

1.	❑ a	❑ b	❑ c	❑ d	6.	❑ a	❑ b	❑ c	❑ d
2.	❑ a	❑ b	❑ c	❑ d	7.	❑ a	❑ b	❑ c	❑ d
3.	❑ a	❑ b			8.	❑ a	❑ b		
4.	❑ a	❑ b	❑ c	❑ d	9.	❑ a	❑ b	❑ c	❑ d
5.	❑ a	❑ b	❑ c	❑ d	10.	❑ a	❑ b	❑ c	❑ d

PROGRAM EVAUATION FORM

Please complete the following activity evaluation questions.

Rating Scale: Excellent = 5 and Poor = 0

Course objectives were achieved. _____

Content was useful and benefited your clinical practice. _____

Review questions were clear and relevant to the editorial. _____

Illustrations and photographs were clear and relevant. _____

Written presentation was informative and concise. _____

How much time did you spend reading the activity and completing the test? _____

What aspect of this course was most helpful and why?

What topics interest you for future *Dentistry Today* CE courses?