

My Jaw, My Life



Judy

To write about my TMJ medical history is easy. It's all about dentists, dates, and 5 surgeries. To write about how TMD has forever changed my life is extremely difficult. As you begin to read my story, please be mindful that there is always pain; pain in my mouth, face, neck, shoulders, and upper back—pain that is chronic and debilitating. I haven't driven a car for years because of dizziness.

There is absolutely a ton of guilt when thinking of my children. They have been affected in some ways that I may never discover. Their lives were changed when they had to deal with a mom who ALWAYS seemed to have a headache and a NEW dentist promising relief. My children are now grown and we have close relationships but the guilt remains. People can tell you that you did your best, it is not your fault, but the very bottom line is a sense of sorrow that I feel for not being able to do more for my children. For many reasons, TMD being one of them, my marriage failed. No need to go further.

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We Need Your Support!

When I thanked Judy for sending her thoughts on life with TMJ (see story on this page) she wrote back, “Do you know I’ve known you for 20 years?” Wow! Reading that sentence made me realize that Judy, and many of you, have supported us and cheered us on for many years, even decades. Looking back 26 years, Temporomandibular Disorders (TMD) were advertised as being quickly fixed with a splint or surgery and the science underlying these treatments and conditions was minimal.

Fast forward to today. It is now known that for many patients, TMD is a chronic medical condition accompanied by other pain conditions. It is a complex disorder affected by one’s genes, age, sex, and environmental factors, including dental treatments. This new knowledge represents significant accomplishments in scientific research.

We know so much more now than we did in the '80s, but not nearly enough to understand all the causes, how it progresses and what practices result in treatments that work and don't cause more harm and pain.

We at the TMJA are deeply grateful for your ‘staying the course’ as we advocated for science. It has not been easy and there have been and still are many barriers. It has taken many years to make TMD patients’ needs not just known, but understood.

Back to Judy. As you will read, Judy’s life is affected by TM Disorders every minute of every day. But Judy is just one of 36 million American men and women living life with some degree of TMD pain and/or dysfunction. This means our mission is not accomplished. Our work and cause must go on.

Unfortunately, like many individuals and organizations, TMJA has been adversely affected by the nation’s economic crisis. We have done and continue to do much with little. However, it is getting even more difficult to continue this way. Now, more than ever, we need more than your cheers: We need your financial support. We ask you to please consider a generous donation to support our advocacy and educational efforts. We can assure you that your donation, of any size, will be prudently used to support our continued productive work.

We are really looking forward to hearing from you and appreciate your continued interest and support. ♦

Terrie Cowley, President & Co-Founder

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The TMJ *Communiqué*

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The *TMJ Communiqué* is intended solely as an information guide and source of support for people with Temporomandibular Disorders (TMD). It does not constitute medical or dental advice, nor is it a substitute for medical or dental advice. Always consult your healthcare professional before starting treatment. The TMJ Association, Ltd. does not provide referrals.

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Potent Opiates Without Awful Side Effects?

A generation ago, scientists discovered that the nervous system produces its own morphine-like, pain-relieving substances—the endorphins—which latch onto receptors on the surface of selected nerve cells to initiate their analgesic action. These “opioid” receptors come in several subtypes given Greek letter names (mu, kappa, delta) and respond to a range of opioid drugs such as morphine and codeine. The problem is that cells with opioid receptors are abundant in the nervous system where they serve multiple functions, and prescription opioids are not selective. The result is that most pain patients taking such drugs experience unpleasant side effects, including nausea, constipation, lower respiration rate, and so on, not to mention the potential for addiction. If chemists could refine their drug designs to target selected subtypes of opioid receptors the hope is that these unwanted side effects would be eliminated.

That hope is closer to reality now as a result of the research of two teams of investigators published in the online March 21 edition of *Nature*. A team led by Brian Bobilka and Sébastien Granier at Stanford University School of Medicine has detailed the structure of the mu opioid receptor, which responds to morphine and other analgesics, and a team at the Scripps Research Institute in La Jolla, California headed by Raymond Stevens has done the same for the kappa opioid receptor. The receptor structures are complex molecules that criss-cross the nerve cell membrane and each contains a large pocket that could bind a candidate drug at different spots. The idea would be to design molecules that would bind tightly and selectively to particular subtypes and in such a way as to activate just the right pathways to relieve pain and not produce unwanted side effects. No one is promising that new magic bullet pain drugs will be produced overnight. To complicate matters, researchers are discovering that the receptor structure is not static, but can alter its form, which could in turn alter what compounds could fit into it. At least investigators have a starting point for rational drug design, ushering in what some are already calling a new era in opioid pharmacology. ♦

Joan Wilentz, The TMJ Association

Source: Pain Research Forum, <http://www.painresearchforum.org>

Update: The same teams of investigators have determined the structure of two more opioid receptors. Stanford scientists solved the structure of the delta receptor and the Scripps team the nociceptin/orphan FQ receptor.

More Sophisticated Research

Since early days, TMJA has advocated for research to advance understanding of the TM joint, the most complex joint in the body, urging the National Institutes of Health (NIH) to put more effort into studies of basic anatomy and physiology, and of genetics and risk factors. We are pleased to report that TM joint research is underway and is benefiting from more sophisticated tools and technology. Herewith are some examples of research currently supported by NIH. Note that the grants describe the aims of research rather than new findings.

Alejandro Almarza, Ph.D. at the McGowan Institute of Regenerative Medicine at the University of Pittsburgh, is working to develop a replacement for the TM disc using biologic extracellular matrix material (ECM) tissue. “Extracellular matrix” consists of materials and molecules in the ground substance surrounding various cells and organs in the body. The EMC implant Dr. Almarza is using consists of a powdered form of ECM sandwiched between layers of the same material. The ECM, derived from pig bladders, is shaped to model the TMJ disc and implanted into animal models. Dr. Almarza hopes this research will serve as a template for the formation of new, site-appropriate, functional TMJ disc tissue.

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2013 TMD Report Language

The TMJ Association continues to keep the needs of the TMJ patients on the radar screen of Congress. We want the best science this country has to offer for these devastating conditions and we are fortunate to have the support of members of the Senate Labor, Health and Human Services, Education and Related Services Appropriations Subcommittee, responsible for funding the National Institutes of Health (NIH).

The NIH is the largest funding agency of scientific research for TMD. Our hope for relief lies in the answers only science can provide and that science is largely funded by the NIH. We encourage you to write to the Labor HHS Committee members thanking them for their support. Contact the TMJA for details.

2013 SENATE REPORT LANGUAGE FOR TMJ DISORDERS:

National Institute of Dental and Craniofacial Research [NIDCR]

Temporomandibular Disorders [TMD].—The Committee recognizes the advances that have been made as a result of NIDCR funding toward understanding the pain associated with TMD and encourages the Institute to continue basic and clinical research in this area. The Committee also encourages NIDCR to collaborate with other ICs [Institutes and Centers] regarding the etiology and pathogenesis of TMD as well as the co-morbid chronic pain conditions and disorders that solely or predominately affect women. An under-researched aspect of these disorders is the jaw joint. NIDCR should work with NIAMS [National Institute of Arthritis and Musculoskeletal and Skin Diseases] and NIBIB [National Institute of

Biomedical Imaging and Bioengineering] to develop research opportunities in the area of joint pain and dysfunction. Topics that need further research include: the kinematics and biomechanics of the jaw in normal and disease states; the development of biomarkers in bone, muscle, and cartilage that are predictive of temporomandibular disease progression; the interactions of the temporomandibular joint musculoskeletal system with the nervous system; and the development of non-invasive measures of temporomandibular joint bone, cartilage, and muscle structure, degradation, and repair. The Committee urges NIDCR, NIAMS, NIBIB, and other relevant ICs to organize a workshop to assess the state of the science and identify research gaps and future scientific directions to advance understanding of the temporomandibular joint.

National Institute of Arthritis and Musculoskeletal and Skin Diseases [NIAMS]

Temporomandibular Disorders [TMD].—Many people who have TMD suffer from conditions that routinely affect other joints in the body, such as trauma, arthritis, and fibromyalgia. Therefore, the Committee calls on NIAMS to collaborate with NIDCR and NIBIB to bring the intellectual and scientific resources within these Institutes to the study of the jaw anatomy and physiology and the complex neural, endocrine, and immune system interactions that orchestrate jaw function and trigger jaw joint pathology. NIAMS should integrate findings from studies of the structure, mechanical function, metabolism, and blood flow of bone, joints, and muscles with studies of central and peripheral neural pathways, as well as the endocrine, paracrine, and cytokine factors that impact upon craniofacial structures as a means to understanding the underlying causes of jaw pain and dysfunction. ♦

More on the Role of Estrogens in TMD

That TMD predominantly strikes women in their childbearing years has long intrigued scientists. But studies of the effects of female hormones—exactly how they affect TMD symptoms—remain controversial and inconclusive.

Now scientists in China, in an experiment on female rats with inflamed jaws, suggest that estradiol (the most potent of naturally occurring estrogens in mammals) increases pain sensitivity. It does this by stimulating nerve cells in a part of the brain called the hippocampus to express a specific type of “vanilloid” receptor that responds to pain associated with acid, hot peppers, and heat (including the heat associated with inflammation). This expression of vanilloid receptors amplifies the pain signals coming into the brain from nerves in the inflamed jaws.

The studies involved female rats whose jaws had become painfully inflamed as a result of a chemical injection. The ovaries of the rats had been surgically removed (ovariectomy), but the rats were then given varying doses of replacement estradiol. Compared to a control group of ovariectomized rats without replacement hormones, the estradiol rats proved more sensitive to normally painless pressures applied to the jaw, which they showed by quickly withdrawing their heads to mild pressures. As a further confirmation of their conclusions, the experimenters injected a substance into the hippocampus that blocked the actions of the vanilloid receptors and showed that it significantly reduced the rat’s sensitivity to mild pressures. ♦

Joan Wilentz, The TMJ Association

Source: 17-*B*-Estradiol Enhanced Allodynia of Inflammatory Temporomandibular Joint through Upregulation of Hippocampal TRPV1 in Ovariectomized Rats, <http://www.jneurosci.org/content/30/26/8710.full.pdf>.

Temporomandibular Disorders and Comorbid Pain Conditions

Lim PF, Maixner W, Khan AA. *Temporomandibular disorder and comorbid pain conditions*. JADA 2011; 142(12):1365-67. Copyright ©2011 American Dental Association. All rights reserved. Reprinted by permission.

CLINICAL PROBLEM

A 50-year-old woman who was new to the dental office sought treatment because of a chief complaint of pain in her jaw and teeth “for many years.” During a period of several years, she had seen many dentists who had adjusted her occlusion and restored most of her molars in an attempt to eliminate her pain. However, her facial pain condition did not improve with this treatment approach. Her previous dentist made an oral appliance and told her that there was nothing else he could do for her. She reported that the soreness in her jaw and her headaches had worsened lately. The patient’s medical history included constant headaches, irritable bowel syndrome, vulvar vestibulitis syndrome and fibromyalgia (FM). Is there an association between her chronic facial pain and these other widespread pain conditions?

EXPLANATION

Three distinct patterns of pain distribution—localized, regional and widespread—generally are recognized.^{1,2} Various psychological and general health factors have been identified as risk factors for the development of chronic widespread pain (CWP). These include poor general health, sleep disturbance, fatigue and high levels of psychological distress.^{3,4} In a prospective study, Von Korff and colleagues⁵ found that the presence of one pain condition at baseline was associated with a fourfold increased risk of developing a temporomandibular disorder (TMD). In addition, Aggarwal and colleagues⁶ reported that one of the strongest predictors of chronic TMD pain was a history of having had CWP.

The results of various studies have shown that chronic facial pain often is comorbid with other pain conditions including FM,⁷ headaches,⁸ vulvar vestibulitis syndrome (also known as vulvodynia),⁹ spinal pain¹⁰ and low back pain.¹¹ The results of a prospective longitudinal study showed that participants who developed TMD reported having had a higher experience of joint, back, chest and menstrual pain at baseline.¹² They also were more likely to be experiencing other pains at the time of TMD onset compared with participants who did not develop TMD. **These findings suggest that, for certain patients, regional and widespread chronic pain conditions represent overlapping conditions and should be considered part of a continuum rather than distinct entities with separate etiologies.**

FM represents one end of the CWP continuum.¹³ Study investigators evaluating the overlap between FM and

TMD reported that 35 to 97 percent of patients with FM had signs and symptoms of TMD, while the prevalence of FM in patients with TMD was an estimated 10 to 52 percent.¹⁴⁻¹⁶ These percentages vary widely owing to different inclusion criteria. Similarities reported in the two conditions included typical clinical pain reports, common symptoms such as sleep difficulty and fatigue, and psychopathology such as depression and anxiety disorders; again, this suggests that TMD pain in patients with FM may be an extension of the CWP rather than a separate entity.

Diatchenko and colleagues¹⁷ hypothesized that, irrespective of the peripheral pain location, chronic pain probably is regulated within the body in a similar fashion. These authors proposed that idiopathic pain disorders share common denominators, including exposure to certain environmental events, elevated levels of psychological distress, a tendency toward pain amplification and genetic predisposition.¹⁷ These pathways of vulnerability are interactive, and as a group they influence the patient’s risk of experiencing pain onset and persistence.

Several lines of evidence indicate that alterations in central pain processing play an important role in the onset of CWP, the exacerbation of CWP or both. In an experimental setting, patients with TMD demonstrated abnormal temporal summation (that is, enhanced pain intensity in response to repetitive noxious stimulation), and this enhanced temporal summation usually is not limited to the area of clinical pain.¹⁸ Functional abnormalities of the hypothalamic-pituitary-adrenal axis, which is the major physiological stress response system in the body, are another hallmark of chronic pain conditions. Light and colleagues¹⁹ conducted a double-masked, crossover, placebocontrolled trial and reported that propranolol, a β -adrenergic antagonist, reduced the total number of painful sites and pain ratings in patients with TMD and FM. Taken together, the data from these studies suggest generalized hyperexcitability of the central nociceptive system in patients with chronic pain.

The results of human genetic studies revealed associations between certain genetic polymorphisms and the development of chronic pain syndromes.^{20,21} When coupled with environmental triggers, these genetic factors contribute to enhanced pain perception, psychological dysfunction and an increased risk of onset and persistence of TMD and related idiopathic pain disorders. Diatchenko and colleagues²² identified three genetic variants (haplotypes) of the gene encoding catecholamine-*O*-methyltransferase designated as low-, average- and high-pain sensitivity. The presence of even a single low-pain-sensitivity haplotype reduces by 2.3 times the risk of developing TMD.

CLINICAL IMPLICATIONS

Increased awareness of the overlap between chronic TMD and comorbid pain conditions likely will result in improved diagnoses and more effective pain management.²³ Patients with TMD symptoms often are treated within a narrow dental paradigm while clinicians ignore coexisting pain conditions, resulting in treatment failure and perpetuation of the problem. Raphael and Marbach²⁴ conducted a randomized, controlled clinical trial, the results of which showed that patients with TMD and widespread pain did not experience improvement with oral appliance therapy, whereas those with only local TMD pain did experience improvement. Researchers in future studies need to address the impact of these pathways of vulnerability on the effectiveness of the various treatment modalities for chronic TMD and comorbid pain disorders.

Various simple self-administered questionnaires are available to aid the general dentist in assessing possible comorbid pain conditions. The Fibromyalgia Rapid Screening Tool is a six-item inventory requiring “yes” or “no” responses; it has a sensitivity of 90.5 percent and a specificity of 85.7 percent in the detection of FM.²⁵ The ID Migraine screener is a three-item questionnaire also requiring “yes” or “no” responses; it has a positive predictive value of 93 percent.²⁶ Practitioners also can assess associated symptoms such as depression and anxiety, somatization, insomnia and fatigue by means of various validated short questionnaires, such as the Beck Depression Inventory²⁷ and the State-Trait Anxiety Inventory.²⁸

CONCLUSION

An urgent need exists for a multifaceted approach to the treatment of TMD that is based not only on its etiology but also on the presence or absence of comorbid conditions. According to a recently revised policy statement of the American Association for Dental Research,²⁹ **“unless there are specific and justifiable indications to the contrary, treatment of TMD patients initially should be based on the use of conservative, reversible and evidence-based therapeutic modalities.”** These include patient education and self-management, cognitive behavioral therapy, pharmacotherapy, physical therapy and use of orthopedic appliances. **In patients with comorbid conditions, however, referral to a multidisciplinary pain clinic for assessment and treatment almost always will produce a better outcome for all concerned. ♦**

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Smoking and Allergy Associated with TMD in Females

New research by UNC Chapel Hill investigators shows that young women with Temporomandibular Joint Disorders (TMD) are four times more likely to be current or former smokers than women of any age who have no clinical signs of TMD. Moreover, TMD sufferers of all ages were three times more likely to have a history of skin rashes, allergies or hives or sinus troubles than women without TMD.

The lead investigator, Dr. Anne Sanders, and colleagues in the Center for Neurosensory Disorders at UNC, analyzed data from nearly 300 women aged 18 to 60 enrolled in a case-control study designed to identify factors associated with chronic TMD. TMD cases were identified by clinical examination using the Research Diagnostic Criteria for Temporomandibular Disorders. Perceived stress and inflammatory cytokines were among other variables also considered. “Our findings refute the notion that analgesic properties of nicotine relieve chronic TMD pain,” Sanders said. “In fact, long-term smoking leads to changes in pain perception such that smokers deprived of nicotine are likely to show greater sensitivity to pain triggers.” What these findings indicate is that women, especially young women, should avoid turning to smoking as way to manage their pain and the anxiety it evokes. Although former smokers were more likely than lifetime nonsmokers to have TMD, the association of TMD with smoking was weaker in former smokers than current smokers. While this implies that quitting smoking may help, whether smoking cessation leads to a reduction in TMD pain is not something that could be addressed in this study. The good news is that smoking cessation is likely to have health benefits for inflammation function, psychological health and allergic type conditions such as allergic rhinitis and hives.

The study is the first ever to compare the relationship between smoking and TMD across different age groups. It is also the first study to report evidence that lifetime history of allergy-type conditions are reported more commonly among people with TMD. “While our observation of an association between allergy and TMD is interesting, we have yet to understand the biological processes underlying this association” Sanders noted. The investigators plan to explore these relationships in greater detail in the longitudinal OPPERA study where smoking status and history of allergy are measured in both female and male participants before the first onset of TMD. ♦

We thank Dr. Anne Sanders, Assistant Professor in the Department of Dental Ecology, School of Dentistry at the University of North Carolina at Chapel Hill, for writing this summary article. Support for the study was provided by the National Institutes of Health.

Source: Sanders AE, Maixner W, Nackley AG, Diatchenko L, By K, Miller VE, Slade GD. *Excess risk of temporomandibular disorder associated with cigarette smoking in young adults*. J Pain. 2012 Jan;13(1):21-31.

Support the TMJA in the 2012 Fall Campaigns

September marks the beginning of the **Government’s Combined Federal Campaign (CFC)** appeal. If you are a government employee, please designate The TMJ Association as your CFC charity (**CFC# 12102**). If not, please share this information with your postal carrier, family members or friends serving in the military who may jump at the opportunity to support your charity.



State employees in *Arizona, California, Connecticut, Florida, Maryland, Massachusetts, New Jersey, New York, Ohio, Rhode Island, Washington and Wisconsin* can also contribute through the **State Employee Contribution Campaign** by writing in The TMJ Association.

United Way and other **non-profit corporate donor programs** are a great way to show your support and will soon be underway. Simply write in *The TMJ Association* on your donor form. ♦

The relationship between abnormal dental occlusion, body posture and development of Temporomandibular Disorders (TMD) has been a controversial subject for many years. Based on such concepts, many patients have been subjected to extensive and expensive treatments purported to correct existing occlusal and postural abnormalities. In this article, the authors review the existing literature on this subject, as well as the validity of the various devices and clinical methods that have been used to measure this relationship.

These include surface electromyography (an electrical recording of muscle activity that aids in the diagnosis of neuromuscular disease), kinesiology (the study of the anatomy, physiology, and mechanics of body movement) and postural platforms (devices that measures changes in body position), that have been used to measure this relationship.

Their results show that the literature does not support the idea that occlusal alterations are associated with either the development of temporomandibular joint problems or masticatory muscle disorders, nor is there any relationship to variations in head and body posture. Thus, they conclude that a mechanical approach to treating TMD by means of irreversible methods such as occlusal adjustments, full mouth dental reconstructions or orthodontics is not justified from a scientific viewpoint. ♦

Written by Dr. Daniel Laskin, Clinical Consultant to The TMJ Association and Professor and Chairman Emeritus at the Virginia Commonwealth University, Department of Oral and Maxillofacial Surgery in Richmond, VA.

Source: Manfredini, D., Castroflorio, T., Perinetti, G. and Guarda-Nardini, L. (2012), Dental occlusion, body posture and temporomandibular disorders: where we are now and where we are heading for. *Journal of Oral Rehabilitation*, 39: 463–471. doi: 10.1111/j.1365-2842.2012.02291.x.

My Jaw, My Life

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I most definitely feel that I have missed out on many of life's joys and experiences. I could ramble on about pain but choose not to. To find a surgeon after eighteen years who was able to undo some of the harm to my jaw has been amazing, but I am still finding myself deep in the woods of TMJ. The years of being a guinea pig are both physically and mentally painful and exhausting. As I go from day to day, I deal with the hand I have been dealt quietly and alone. My message to dentists treating TMJ patients: LISTEN and DO NO HARM! To my fellow TMJ patients, I wish you good days and lots of hope for relief, if even in small doses. I wish you a sense of peace as you continue to try to find a way out of the TMD maze. ♦ *Judy*

What You May Want to Know About...

Glucosamine sulfate for the treatment of osteoarthritis in the temporomandibular joint—Although ineffective, glucosamine sulfate has at least been shown to be safe when taken in the recommended dosage. However, when persons do not get any positive effect, they may go beyond the recommended dose and a recent study has shown that this may possibly increase the risk of developing diabetes. This is one more reason to avoid its use. Cahlin BJ, Dahlstrom L, No effect of glucosamine sulfate on osteoarthritis in the temporomandibular joints—a randomized, controlled, short-term study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, <http://www.ncbi.nlm.nih.gov/pubmed/22001199>

Patients with Temporomandibular Disorders have increased fatigability of the cervical extensor Muscles—A recent study showed that the cervical (neck) muscles fatigued more quickly in TMD patients than in control subjects. Armijo-Olivo, S, Silvestre, R, Fuentes, J, da Costa, B, Major, P, Warren, S, Thie, N, Magee, D, Patients With Temporomandibular Disorders Have Increased Fatigability of the Cervical Extensor Muscles, *Clinical Journal of Pain*, http://journals.lww.com/clinicalpain/Abstract/2012/01000/Patients_With_Temporomandibular_Disorders_Have.8.aspx

Effectiveness of education versus an occlusal splint for the treatment of myofascial pain of the jaw muscles—An education program may be more effective than an occlusal splint. Further studies are needed to determine if an education program plus splint therapy would be better than either used alone. Michelotti, A, Iodice G, Vollaro S, Steenks, M, Farella, M, Evaluation of the short-term effectiveness of education versus an occlusal splint for the treatment of myofascial pain of the jaw muscles, *JADA*, <http://jada.ada.org/content/143/1/47>

Acupuncture for Treating Temporomandibular Joint Disorders—Actual acupuncture may be no more effective than sham acupuncture in treating temporomandibular disorders. Jung A, Shin BC, Lee MS, Sim H, Ernst E, Acupuncture for treating temporomandibular joint disorders: a systematic review and meta-analysis of randomized, sham-controlled trials., *J Dent*, <http://www.ncbi.nlm.nih.gov/pubmed/21354460>

Ability to Concentrate & Painful Temporomandibular Disorders—Patients with painful TMD show a significantly higher percentage of an “often” or “very often” impaired ability to concentrate compared to the general population. Schierz, O, Nixdorf D, Singer S, Reissmann D, Self-reported ability to concentrate in patients with painful temporomandibular disorders compared to the general population, *Community Dent Oral Epidemiol*, <http://dx.doi.org/10.1111/j.1600-0528.2012.00692.x>

Lyme Disease—If you think you suffer from TMD, it's very important to see your medical doctor to rule out any other medical conditions such as Lyme disease that could be causing your symptoms. TMJA blog, <http://www.tmj.org/site/blogs/tmj-disorders/2012-05-17-0>

Fentanyl Patch Warning

FDA warns about risks of accidental exposure to fentanyl by children, and don't forget pets. FDA, <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm300803.htm> ♦

Kyriacos Athanasiou, Ph.D., P.E. at the University of California, Davis, and a member of TMJA's Scientific Board, has two grants directed toward developing tissue-engineered replacements for various components of the TM joint. One grant is using co-cultures of fibrocartilage and cartilage cells to mimic the dimensions and make-up of the cartilage surface of the mandible and of the joint disc. By supplying various growth factors in the cell culture medium along with mechanical stimulation, Dr. Athanasiou hopes to enhance the mechanical properties of the constructs enabling them to function as well as healthy native tissue under the various demands of joint function. The constructs will be implanted and tested in an immunodeficient mouse model. A second grant is directed to implanting an anatomically correct and robust TMJ disc, with attachments, to replace a disc with commonly seen disc pathology, including perforations and damage in the lateral regions.

Yiping Chen, Ph.D. at Tulane University School of Medicine in Louisiana, is looking at the underlying genetic, cellular and molecular mechanisms involved in development of the TMJ that could give rise to congenital jaw ankylosis—a condition of limited mouth opening caused by adhesion of the condyle with joint components in the skull. He has identified a major embryonic developmental gene, *Shox2*, which, when conditionally inactivated at a stage in development, causes jaw tissue abnormalities and ankylosis. The aims of his research will be to use a mouse model to determine the genes regulated by *Shox2*, explore how the *Shox2* gene itself can be modulated and compare the mouse gene to its human counterpart.

Sunil Kapila, B.D.S., M.S., Ph.D. at the University of Michigan Dental School, is studying the role of female hormones and their receptors in TMD. Earlier studies indicate that estrogen and/or relaxin contribute to the degeneration of TMJ soft tissues by expression of specific tissue-degrading enzymes called matrix metalloproteinases (MMPs), while progesterone attenuates MMP expression. The new research will explore the dose-response effects of relaxin/progesterone in enhancing/attenuating loss of TMJ disc substance; determine the specific MMPs involved in degradation by using mouse models in which genes coding for specific MMPs are selectively removed (“knocked out”) and, similarly, use mice in which specific estrogen and relaxin receptor genes have been knocked out, to identify which hormone receptors contribute to joint degradation.

Jeffrey Nickel, D.M.D., M.Sc., Ph.D. at the University of Missouri-Kansas City, is studying mechanical fatigue failure of TMJ tissues, which could cause disc dysfunction, inflammation, pain and bony changes. Mechanical fatigue depends on the magnitude of energies exerted on the jaws and the extent of load bearing. His initial findings suggest

that higher energy densities occur in women compared to men, and in individuals with disc displacement compared to a healthy group. His grant will follow up on initial findings and use jaw imaging, and energy and load-bearing measurements, to compare men and women, and subjects with and without disc displacement and/or joint pain. He will factor in genetic analyses to determine if having gene variants that increase sensitivity to pain, along with higher energy density and jaw loading, can predict disc position in subjects with and without joint pain.

Patricia Purcell, Ph.D. at Children's Hospital Boston/Harvard Medical School, is looking at the molecular and cellular mechanisms of TM joint formation. Dr. Purcell believes that using a technique called laser capture microdissection, that isolates different parts of the TM joint in mouse embryonic tissue, will reveal which genes are present in each location, with the final goal of establishing a “blueprint” of the TM joint. She believes this research may provide new “biomarkers” that are increased or decreased in TMJ Disorders, and could be used to predict the risk that an individual will develop TMJ Disorders. Furthermore, the molecular information gained from this research may assist in the devising of alternative therapeutic approaches for TM Joint Disorders, as well as ultimately in bioengineering replacements for defective or damaged TM joint structures.

Gordana Vunjak-Novakovic, Ph.D. at Columbia University, is using stem cells to grow grafts of bone in the shape of the TM joint using a bioreactor and is able to control the factors that enter the bioreactor over time. These factors include essential nutrients, oxygen, and physical factors that keep these large pieces of bone alive and functional. Dr. Vunjak-Novakovic believes this research will someday help patients who have had TMJ implants or may be contemplating implant surgery down the road. The bioengineered bone grafts are currently being tested in an animal model, but the commercial technology is only a few years away.

Hai Yao, Ph.D. at the Medical University of South Carolina, explains that the TMJ disc is a large soft tissue structure without blood vessels and dependent on a nutrient supply for its maintenance and health. Using a pig model, he aims to develop a non-invasive “integrated dynamic measuring system” to establish quantitative relationships between jaw mechanical loading (pattern and magnitude), nutrient concentration profiles (oxygen, glucose, lactate), and metabolic rates in the disc. He believes that nutrient concentration and metabolic rates are sensitive to jaw loading during jaw function and thus could be early bio-indicators for evaluating the effects of mechanical loading on temporomandibular disorders. ♦