TMJ disorders are a complex set of disorders often involving central or peripheral pain, muscles of mastication and the TMJ. The TMJ may have internal derangement, inflammatory disorders or joint degeneration. Many patients also have psychological disorders stemming from the pain or other sources. About 6% to 12% of the U.S. population have TMD. About 80% of them have TMJ involvement. The cause of this disorder is unknown. Current diagnostic approaches depend on clinical history, clinical exam and imaging. At the present we don’t have an understanding of what initiates the disease process.

Current therapies are all based on alleviating the signs and symptoms:

If there is pain, analgesics are prescribed; if there is bruxism, habit control is undertaken; if there is muscle involvement, muscle relaxants and anti-inflammatories are prescribed as well as a splint for muscle reprogramming. When most of these modalities fail, then surgical approaches including lavages and joint replacements are attempted. Since the etiologies of these disorders are not understood, we are not in a position to use disease-modifying agents. In other words, we are just managing the disorder rather than using rational therapies.

ON THE HORIZON

Biomedicine has become an increasingly important discipline in dentistry. Examples of biomedicine at work in dentistry include tissue regeneration of periodontal tissues with growth factors and biomarkers of periodontal disease. The biomedical part of this process comes into play with genetics and understanding the biological bases for disease mechanisms. Such knowledge can then be used for diagnosis, monitoring disease progression and monitoring response to therapy.

What are disease biomarkers? Examples are RNA, DNA, or proteins. They can be identified in blood, saliva, urine, and synovial fluid. These markers have to be sensitive and specific to be useful for diagnosis.

The introduction of 3D imaging and Cone Beam CT scans is another exciting area in diagnosis of TMJ disorders and orthodontic treatment planning. Its utility is going to increase in the coming years, as more clinicians rely on it, and more research is completed. Dr. Kapila believes that this technology will become important in the early detection of TMJ diseases.

AGE AND GENDER DISTRIBUTION FOR TMD

The incidence of TMJ disorders is very high in women between the second and fifth decade of life (20-45 years), the prime reproductive age. Women in this age group also have a high incidence of TMJ clicking and tenderness. The female to male ratio in the population is between 3:1 to 10:1, again a high predisposition for women of reproductive age.

Such statistics have led many investigators, including Dr. Kapila’s own group, to hypothesize a connection between hormones and TMJ disorders. Several public health studies have shown an association between the use of exogenous hormones such as estrogen replacement therapy and oral contraceptives to TMJ pain. Several other studies have shown the presence of estrogen and progesterone receptors in the TMJ. It has also been shown that Estrogen can effect the collagen content of the joint structures in rats.

There is no conclusive evidence, however, that reproductive hormones play a role in a subset of TMJ disorders. We do not yet understand how hormones contribute to TMJ disease. There are other reproductive hormones, for example, relaxin, that have not been looked at as potential culprits in TMJ disorders.

Relaxin is a hormone found in small amounts in women of reproductive age and in pregnant women. It is not present systemically in men. It has a crucial role in tissue turnover and in childbirth, where it helps relax the pubic symphysis, hence the name relaxin.

The pubic symphysis is a fibrocartilage, also found in the TMJ, where it is the main component in the disc and articular surfaces. The main components of fibrocartilage are collagen and proteoglycans. If either breaks down, the joint won’t function properly.

Do female reproductive hormones contribute to the degradation of the TMJ fibrocartilage? Is there an asso-
Citation between local and systemic hormone levels and TMJ disease in women? Animal studies have shown that relaxin and estrogen induce certain tissue degrading enzymes (MMPs) in the TMJ disc. The induction of these enzymes leads to loss of collagen and proteoglycans in the disc and can lead to joint degeneration. Progesterone has been shown to have a protective effect. These enzymes are capable of degrading everything within the TMJ. They are very highly regulated. The hypothesis is that hormones and other agents turn on these enzymes. Once activated, they degrade the collagen and proteoglycans and cause degeneration of the disc and articular surfaces, which leads to loss of matrix molecules and the inability to sustain function, leading to degenerative joint disease.

Studies have also shown that TMJ cells that have been primed with estrogen can make them more sensitive to relaxin. Relaxin in turn induces the enzyme collagenase, which degrades the matrix. It is important to note that this enzyme is induced at physiologic concentration of relaxin.

The knee meniscus and the knee articular cartilage however do not respond to these hormones. Why don’t they? A close look shows that the expression levels of estrogen receptors ER-α and ER-β in the TMJ disc is very similar to the fibrocartilage in the pubic symphysis. Relaxin receptor LGR7 is highly expressed in the TMJ disc and the pubic symphysis but not in the knee meniscus. The receptors ER-α and LGR7 are thought to be responsible for expression of enzymes such as collagenases.

The expression of these receptors can be helpful as potential biomarkers as well. Enhanced levels of relaxin may indicate an increased risk of degenerative joint disease. Matrix breakdown products can also be used as biomarkers for joint disease.

IMAGING

There are three basic imaging modalities used to diagnose TMJ disorders:

**Tomograms**—Tomograms have traditionally been used for diagnosing TMJ disorders. Tomograms, however, relate very poorly to patient symptoms. What is happening at the radiographic level is not what is going on at the biological level. This means that abnormalities seen on tomograms indicate disease at a relatively late stage.

**CBCT**—Cone Beam CT scans are an increasingly popular way of imaging the TMJ joint. With CBCT we are able to look at the hard tissues and the relationship of these tissues to each other.

**MRI**—These are also 3D images but have the advantage of showing the soft tissue in the joint, namely the disc.

CBCT is the preferable method of viewing the TMJ. It is good for visualization of significant detail, for 3D volumetric reconstruction, for the overlay of tissues, and for looking at sections of interest on demand. They are accurate in diagnosis with or without adjuncts.

TISSUE ENGINEERING

Joint replacement has been done with allografts or costochondral grafts. More recently, however, tissue engineering is being used in this area. Tissue engineering is basically making the same tissue for the patient in culture or in animals.

Some common terms of tissue engineering are:

**Scaffolds**—These are physical constructs, made of various artificial materials.

**Cells**—preferably from the patient who is going to get the tissue and ideally pluripotent mesenchymal stem cells. Stem cells will be more a part of treatment in the future.

**Bioreactor**—where tissues grow in vitro.

**Bioactive agent**—such as bone growth factors

The process is to derive the cell of interest or the stem cell for the patient, culture them in vitro, isolate the stem cells, expand the cell population, then impregnate the scaffold with the cells and bioactive material and grow that tissue either in an animal or in vitro. Once the bone and the cartilaginous structures are developed in vitro, the surgeon can place that tissue in the patient’s joint. This would be most valuable for patients where the disease is not caught early on.

Application of such work would be in the replacement of defects that are site-specific and patient-specific by autologous, in-vitro created condyles. Dr. Kapila believes clinical trials are only a few years away. The ultimate goal would be total joint replacement.

There is a tremendous amount of science and increasing body of knowledge that is being developed and created in the area of TMJ disorders. It is evident that the current method of managing the symptoms rather than the etiology will not be adequate for effective treatment. The future is in biomedicine, diagnostic markers, rational therapies and in improvements in applications of new imaging technologies in diagnosis. The hope is that with these improvements we will be able to treat our patients in a much more sophisticated and specific manner.