5-2019

A Review of Osteoarthritis

Madelin Brooke Session
Utah State University

A REVIEW OF OSTEOARTHRITIS

by

Madelin Brooke Session

**Capstone submitted in partial fulfillment of
the requirements for graduation with**

UNIVERSITY HONORS

with a major in

**Animal, Dairy and Veterinary Sciences
in the Department of Agriculture**

Approved:

Capstone Mentor Dr. Jeffrey Mason	**Departmental Honors Advisor** Dr. Lee Rickords

University Honors Program Director
Dr. Kristine Miller

**UTAH STATE UNIVERSITY
Logan, UT**

Spring 2019

Abstract

Osteoarthritis is a degenerative joint disease which plagues many older animals and humans. It is a disease that is characterized by the degeneration of joint cartilage, inflammation, as well as chronic pain and stiffness that results from this disorder. Unfortunately, most of the treatments for this painful and chronic disease mostly involve pain management and temporary relief strategies. These strategies usually include pain medication, non-steroidal anti-inflammatory drugs, injectable lubricants, as well as surgical techniques. However, because these treatments are just temporary fixes meant for pain management and to improve quality of life they must continue throughout the remainder of the animal's life. The ultimate goal of this review is to compile knowledge about osteoarthritis. This will include everything from the clinical features and prevalence of the disease, as well as some of the possible causes of this disorder. Some of the most common treatments out there to treat pain and relieve inflammation, as well as some of the more experimental treatments that might not be approved for use yet, however they do still show some promise.

Acknowledgments

I would like to thank Dr. Jeffrey Mason and his team for their help with this project. Everything from proofreading to helping me with resources that he thought that I might find helpful. He and his team were always more than willing to offer me any help that I needed. I would also like to thank that college of Agriculture and Applied Sciences for the education that they have provided me with that has provided me with the knowledge needed to complete this project. I would like to also thank my family for always being supportive and sometimes giving me the push that I needed.

Introduction

Osteoarthritis is a disease that plagues many people and animals throughout the world. This is a disease with a very specific set of clinical signs which consist of inflammation and cartilage degeneration mainly in the synovial joints such as the knee and hips. However, when it comes to the cause of this disease there are many possible answers, mostly due to the fact that it is a multifactorial disease which can be caused by both genetic and environmental factors. One such possible cause for OA is genetics. There are many arguments for a large cause of OA being a single-nucleotide polymorphism in several candidate genes that at the very least make the formation of OA more likely. Another possible cause of OA is hormones. Or more specifically the loss of female hormones, which the lack of has been known to be associated with other bone disorders such as osteoporosis. The two that most everybody are familiar with, but in a way go along with some of the others, is the causative factors of age and obesity.

Of course, the causes of OA are only the beginning. Once somebody, human or animal, is diagnosed with OA, then what? Then, as with any disease, you receive treatment from your doctor. Unfortunately, when it comes to many chronic diseases, like OA, there are not many good treatments available to people who are suffering. The most common ones include taking anti-inflammatory medications as well as pain medications. However, in the long term, this can cause many problems, which is why there are many people out there who are working on experimental treatments to provide people who are suffering with a greater measure of comfort at the very least if not halting the progression of the disease entirely.

Clinical Signs

Osteoarthritis is a disease that affects many people and animals throughout the world. In humans it affects roughly 10% of people over the age of sixty (Mei, et al., 2017) and in other

animals, such as cat's osteoarthritis, it was shown to affect the appendicular joints of about 61% of cats above six years of age (Slingerland et al., 2011). OA is a disease that is characterized the cartilage degeneration in the appendicular skeleton which goes hand in hand with inflammation in the joins as well as alterations in the subchondral bone, the bone directly below the surface of the cartilage (Mei, et al., 2017). There are four factors that are believed to produce OA: mechanical overload, inflammatory disease, good bone response, and poor bone response. It is the combination of all of these factors that cause joint destruction and also joint repair that we see evidence of during visual imaging (Flemming & Gustas-French, 2017).

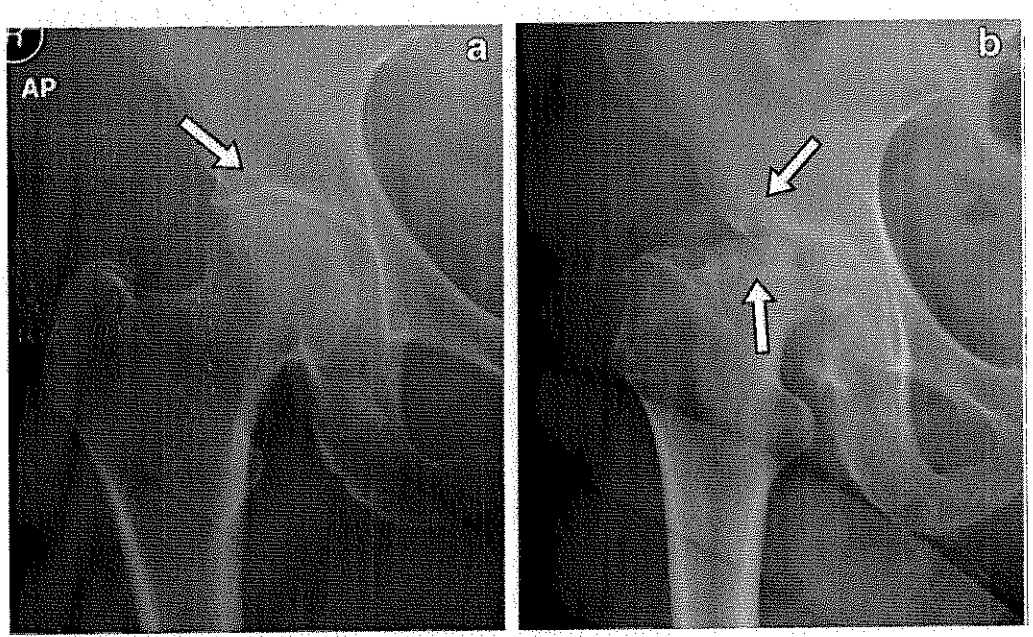

Fig 1: 68 year old woman with RPOA. a Minimal subchondral cyst formation (arrow), medial femoral calcar osteophyte and preserved joint space on seen on initial radiograph. b AP radiograph of the hip obtained 11 months later shows typical flattening of the femoral head which is migrated superior and laterally. Subchondral lucencies are appreciated in the acetabulum and femoral head (arrows). Source: Flemming, D. J., & Gustas-French, C. N. (2017). Rapidly Progressive Osteoarthritis: A Review of the Clinical and Radiologic Presentation. Current Rheumatology Reports, 19(7). doi:10.1007/s11926-017-0665-5

OA is a disease that in most animals, such as cats and dogs, it has a main symptom of lameness. In many animals, such as cats, this can be difficult to diagnose due to them instinctively trying to hide their symptoms from their owners (Slingerland, Hazewinkel, Meij,

Picavet, & Voorhout, 2011). However, once there is a suspicion of OA in an animal then the first course of action towards a diagnosis of OA is to take either radiographs or MRI scans. This is due to the fact that it is non-invasive and provides a measurable form of the progression of the disease, which many other forms of diagnosis do not (Fig 1). In the early stages of OA in the hip, MRI imaging will show a few key things. The first of which is a noticeable loss of articular cartilage along with effusion and synovitis (Flemming & Gustas-French, 2017). However, what is most noticeable on MRI scans is what happens within the bone marrow. In the femoral head, there is a noticeable edema present along with being present in the acetabulum most of the time (Flemming & Gustas-French, 2017).

Causes

Genetics:

OA is a disease which has many possible causes, one of which is genetics. There are several genes which have been pinpointed as being associated with the gene CALM-1 and GDF-5 (Srivastava, et al., 2017). The human skeleton is on average replaced entirely every seven years, which means that bone and cartilage development is under constant genetic control. One of the main genes that control bone and cartilage formation in the body when triggered is known as BMP5, or bone morphologic protein. When this protein is acting the way it's supposed to, it is a big reason behind the normal growth and development of joints, especially synovial joints (Srivastava, et al., 2017).

Due to the proven effects of this gene, it is hypothesized that it plays a very important role in the homeostasis of the skeletal system. After doing a research study in the UK, Sharma, et al. discussed that there was found that five polymorphisms of the BMP5 gene were associated in particular with hip OA in women. It's not just the gene itself that when altered can increase

susceptibility to OA. This gene is also regulated by a promoter, and the promoter itself is regulated by a microsatellite. The microsatellite for the BMP5 promotor has been shown to have allelic variants which alter the transcription of the promotor (Srivastava, et al., 2017). This altering of the transcription of the promotor will, in turn, alter the expression of the BMP5 gene. However, since these microsatellites are just nucleotide tandem repeats, it is very easy to get mutations in their coding especially in genes that have long strings of guanine as those contain prime targets for creating DNA adducts.

Hormones:

OA has been shown over and over again to have a much higher prevalence in women, over the age of fifty, than in men. Past the age of fifty in women is also the approximate age of the onset of menopause. This has been shown to be due to the fact that estrogens have a protective effect for many diseases, including those for bone disorders like osteoarthritis. This is mainly due to the fact that before menopause, mineral storage is very important. This is mainly due to the fact that women before menopause need the minerals a lot more than men or women after menopause. Women before menopause require these minerals for various things, however the main reason that women before menopause require an increased amount of minerals stored in their bones than others is mainly due to the formation of the fetal skeleton during pregnancy as well as breastfeeding a child after pregnancy (Mason, Terry, Merchant, Mason, & Nazokkarmaher, 2015). Once women become older than fifty, most of them have run out of eggs and go through menopause, because of this they no longer need all that mineral storage and therefore their estrogen levels drop which in turn leads to a drop in their bone density.

Based on all of this most people would think that once a woman stops cycling that she could undergo hormone replacement therapy or a similar therapy, and it would greatly reduce the

risk of bone-related disorders like OA. However, this is not always the case. According to several studies, such as "Manipulation of Ovarian Function Significantly Influenced Trabecular and

Cortical Bone Volume, Architecture and Density in Mice at Death" written by Mason, et al., it actually matters when a hormone treatment is administered. In a study with old mice, they transplanted young cycling ovaries into old mice at various points. In this study, they implanted the ovaries into old mice either before they stopped cycling or after they stopped cycling. It turns out that the time where the old mice stopped cycling and lacked those essential reproductive hormones that are so beneficial to bone growth and development made a very big difference in the results. It was shown that when the old mice were implanted with the young ovaries while the old mice were still cycling it appeared to delay the degeneration of bone that is associated with age (Mason et al., 2015). On the other hand, it was shown that when the old mice were implanted with the young ovaries after the old mice had stopped cycling the treatment did not have the intended effects. In these recipients that had already stopped cycling the implantation treatment was shown to actually exacerbate the degeneration of bone that is related to age. These old mice that had stopped cycling before receiving the transplant actually ended up having bone in the worst condition of all the mice in the study, which shows that apparently when there is a gap before a woman receives hormone replacement therapy and when they go through menopause and stop cycling the hormone, replacement therapy can actually do more harm than good (Mason et al., 2015).

While estrogen has been shown to be a strong influencing factor in regard to protection against OA and other bone-related diseases, it doesn't appear to affect all joints equally. OA can affect just about every joint in the body, however, it seems to especially affect the synovial joints

such as the knee, hand, and hip joints. While all these joints can be affected, they appear to have differing and conflicting causes and reactions to estrogen. For all of these joints, some studies reported a change in bone density and volume while some reported no change. A few even reported an adverse change. For example, when it comes to OA in the knee, estrogen replacement therapy appeared to not influence the length of the tibial cartilage volume, but it is associated with tibial cartilage volume (Hussain et al., 2018). However, this is only in some of the studies. In other studies, there was no evidence of postmenopausal estrogen affecting knee OA at all (Hussain et al., 2018). The same is true for both hip and hand OA as well as for knee OA. In hip OA it was shown that there was either no change or there was an even larger risk of requiring hip replacement when estrogen replacement therapy was administered (Hussain et al., 2018). When it comes to hand OA, it was shown that it is the same as in the case as with hip OA, where some studies showed no change when it came to estrogen, some studies showed an increase in OA when the therapy was administered, however unlike with hip OA some studies also showed that not having the estrogen replacement therapy was an increased risk factor for hand OA. So, while OA in all joints shows some kind of response, in most studies they don't all respond the same way as some of the other joints.

Obesity:

Yet another large causative factor for OA is obesity. Obesity is a very large problem facing the world today and it is predicted to only grow larger. Obesity is a condition that is associated with much larger healthcare costs from various conditions and diseases that can come along with it. These are diseases such as hypertension, diabetes, heart disease, and elevated cholesterol. Due to these diseases overweight patients are expected to incur 46% higher costs for inpatients hospital stays and procedures, as well as 27% higher costs for outpatient procedures

and other expenses such as medications. Due to these factors, it is rather unfortunate that obesity has approximately doubled since 1980. Of course, there are many causes for this both biologically as well as socially (Kulkarni, Karssiens, Kumar, & Pandit, 2016). Biologically speaking humans are genetically predisposed to accumulating fat stores for survival, both for heat retention as well as emergency energy stores in case of lack of food. This is mostly due to the fact that it is only recently that we as humans started having reliable sources of food through the domestication of plants and animals making hunting easier as well as giving us a reliable source of food when hunting is scarce through the process of agriculture. Whereas, socially speaking many things have changed since 1980. There has been a great increase in fast food restaurants as well as more greasy fatty food being consumed by people, as well as just more food, in general, being consumed, since after all agricultural practices are improving and therefore there is just more food available to begin with. It was also relatively recently that trans fats were developed, since they don't occur naturally in plants and animals that we consume we don't have enzymes that can break them down, so instead, we just store them in our bodies and they build up. Due to these factors, as well as several others, we as humans and other animals are becoming more and more obese as time goes on, and this, in turn, leads to an increase in OA.

There are many predisposing factors for OA, and OA for each joint has factors which predispose it more than others. For example, it has been proposed that for knee osteoarthritis, obesity is the main risk factor that is associated with it (Kulkarni, Karssiens, Kumar, & Pandit, 2016). The main reasoning for this is that the more obese a person is the greater the weight loading on joints there is. All this additional mass placed on a relatively small surface area puts a great strain on the articular cartilage that is present in that joint. All of this strain eventually causes cartilage degeneration. Like most tissues in the body, cartilage is broken down when it

gets old and then the body produces more to replace it, however, OA is defined as when cartilage is degenerated at a rate faster than the body can produce it (Kulkarni, Karssiens, Kumar, & Pandit, 2016). It's not just that the cartilage gets broken down faster than the body can replace it either, since the body is trying to produce cartilage so quickly to make up for the quick degeneration it often leaves to defects in the cartilage that it generates, which is one of the hallmarks of knee OA, and these defects have been shown to grow with every 1 kg increase of body fat (Kulkarni, Karssiens, Kumar, & Pandit, 2016).

However, there has been much debate on whether weight loss after diagnosis will improve OA in patients. This is mainly due to the fact that there has not been much research done on the subject unfortunately. It has been shown however that a decrease in weight has led to a reduced weight load in the knee joint, with about every 0.5 kg of weight loss results in a two- to four-fold reduction as shown in gait analysis tests (Kulkarni, Karssiens, Kumar, & Pandit, 2016). Unfortunately, OA, especially knee OA, has been shown to increase weight gain in those diagnosed. This is most likely due to the inflammation and pain caused by cartilage degeneration, since the people diagnosed with OA feel so much pain when doing any activity, it severely limits how much they can do, thus greatly reducing their daily caloric expenditure and making losing weight very difficult for people who are afflicted with this disease (Kulkarni, Karssiens, Kumar, & Pandit, 2016). This occurrence of higher BMI's with OA has also been shown to have a very strong association with a patient's need to undergo a total joint arthroplasty surgery, a highly invasive surgery which is considered a treatment of last resort for patients suffering from OA. This trend indicates that the increase in weight of the general population is a good predictor for the increase in the incidences of total joint arthroplasty surgeries that they

require, so much so that requiring a total joint arthroplasty is predicted to increase by 673% in less than thirty years (Kulkarni, Karssiens, Kumar, & Pandit, 2016).

Disease:

While it is not without uncertainty there has been research going on as to whether or not systemic infections could play a role in the causation of joint disease in many animals. In previous studies, they tested synovial samples from a group of dogs with joint damage. It was shown that approximately 37% of these samples contained bacterial DNA when tested (Tomas, Pultorak, Gruen, Breitschwerdt, & Lascelles, 2014). However, it is highly unlikely that infectious bacteria are the sole cause of joint disease and damage. Instead, it is much more likely that they could be a potential trigger for an inflammatory response within the joints which then leads to further damage of the joint (Tomas et al., 2014). While this is likely to be the case, it is also not likely that the bacteria that causes this is the same throughout all species. For example, *Bartonella* is a bacterium that has been implicated in lameness in dogs. However, in cats, it was shown to be the opposite. In cats, studies have shown that cats with higher incidences of joint disease and damage are actually less likely test to positive for *Bartonella* DNA than cats with joint disease and damage (Tomas et al., 2014). It turns out that there is actually a strong association for being negative for *Bartonella* DNA and an increased incidence of joint disease. This could however, have to do with the co-evolution of felines, fleas, and *Bartonella* to the point where there is a benefit to their co-existence, as shown by the association between being positive for *Bartonella* DNA and the decrease of other forms of disease (Tomas et al., 2014). However, this is not to say that another type of bacterium could not perform the same inflammatory trigger function for felines that *Bartonella* does for canines, it simply says that it most likely varies from species to species depending on several factors most likely.

Current Treatments

Pharmacological:

There are many options when it comes to traditional pharmacological treatments for OA. The first of which that is recommended is a topical cream that contains capsaicin. Capsaicin is a chemical that is found in chili peppers. Due to the fact that capsaicin in actuality doesn't cause the effect of spice by activating taste buds, but instead capsaicin causes people to feel spice when the eat it because it actually activates the pain receptors in the mouth instead. However, the reason why it is utilized in a topical cream of OA is that it actually depletes a pain neurotransmitter, substance P, thus desensitizing the pain sensors in the joint that it is applied to (Taruc-Uy & Lynch, 2013). This effect produces a warm numbing sensation on the applied area. However, this treatment is recommended only in accessory to other treatments, this due mostly to the fact that there are concerns that the desensitization of the pain-sensing neurons is not fully reversible (Taruc-Uy & Lynch, 2013).

Another form of pharmaceutical treatment for OA that is commonly recommended to patients is the use of NSAIDs and acetaminophens. These two drugs are two of the main treatment options for OA (Taruc-Uy & Lynch, 2013). Not only do they reduce pain thus improving the quality of life for the patients, but it also has the effect of reducing inflammation as well, thus resulting in less damage to the affected joints in the future. However, these drugs, NSAIDs in particular, carry serious risks. They have a relatively low overdose point of 4 grams per day which for over the counter meds without specific doctor instructions such as acetaminophen like Tylenol and NSAIDs like ibuprofen. As well as the fact that long term usage also carries serious risks of stomach ulcers as well as kidney damage. This is attributed to the

fact that non-steroidal anti-inflammatories work by inhibiting the enzyme cyclooxygenase. There are two forms of this enzyme cyclooxygenase-1 and cyclooxygenase-2. Cyclooxygenase-2 is the enzyme that we want it to target since it is the enzyme that is produced when joints are injured or inflamed (NSAID). However, NSAIDs aren't as discriminatory as we would like them to be. Because of the similarity between cyclooxygenase-1 and cyclooxygenase-2 this class of drugs can target both of them even when we don't want them to. This can be rather unfortunate since cyclooxygenase-1 is the enzyme that is responsible for protecting the stomach lining from the harsh hydrochloric acid that is being produced there as well as maintaining kidney function (NSAID). However, these drugs are not tolerated very well by some people, and in cases like this there are specific cyclooxygenase-2 blockers which can be used in their stead that shouldn't cause the damage that NSAIDs do to the stomach and kidneys since they should not affect cyclooxygenase-1 like NSAIDs do (Taruc-Uy & Lynch, 2013).

A third option for pharmacological treatment of OA is the use of a corticosteroid injection. These injections have been shown to be effective for about 3 weeks but can't be used more than 3 or 4 times per year (Taruc-Uy & Lynch, 2013). The reason for this limit on the number of cortisone injections a patient can receive in a joint is mainly because there is a concern that too many injections could cause cartilage degeneration within a joint (cortisone, 2017). Which, when it comes to OA, would only exacerbate the patient's condition as well as not performing its primary function of relieving inflammation within the joint. Cortisone is one of the most common corticosteroids used for these injections. They belong to a class of chemical which is known to decrease inflammation in the area that they are injected into. When done correctly by a doctor who regularly does these injections there should be minimal discomfort from the injection itself due to the local anesthetic given for the injection. However, there are

still some risks to this procedure just like with any medical procedure no matter how minor. These risks include: joint infection, nerve damage, thinning of skin and soft tissue around the injection site, temporary flare of pain and inflammation in the joint, tendon weakening, thinning of nearby bone, whitening or lightening of the skin, death of nearby bone, as well as a temporary spike in blood sugar (cortisone, 2017). However, as long as these procedures are not performed too often as is recommended, patients follow doctors' instructions post procedure, as well as having an experienced doctor performing the injection, all of these possible risks are greatly reduced.

Surgical:

When it comes to surgical options for the treatment of OA, there are a few options. However, all of these options are to be considered only if non-evasive treatments fail to improve the patient's quality of life enough. The general indicators for this are worsening of disability while on treatment as well as the continuation of pain (Taruc-Uy & Lynch, 2013). The first of these surgical options are fusing the bones in the affected joint. During this procedure, the patient will be under general anesthesia. While under anesthesia the doctor performing the procedure will scrape away all of the cartilage in the affected joint, by doing this it will allow the two bones in the joint to come into direct contact with one another, thus allowing them to fuse. In some cases, the surgeon may also place a piece of bone, harvested from another area of the body near the affected joint, into the joint to promote fusion. The bones will then be brought together through the use of plates, screws, or wires which will most likely be permanent (Fig. 2) (Joint Fusion).

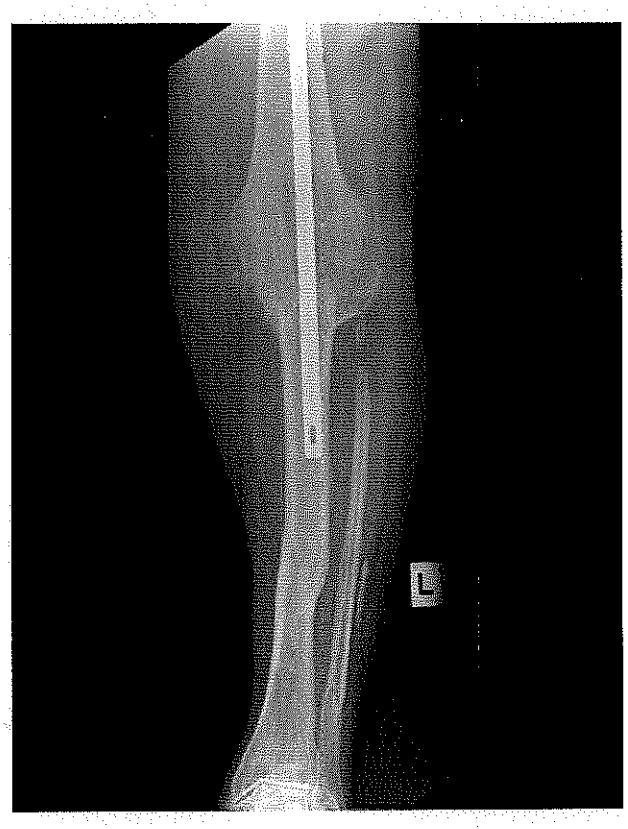

Fig 2. Radiograph of the knee post procedure for joint fusion surgery. Source: https://boneandspine.com/what-is-arthrodesis/

Unfortunately, while this procedure has been deemed safe by doctors, there are still risks to it. One of the biggest risks is from the fact that by performing this procedure, there is increased strain placed on the joints surround the joint that was fused (Taruc-Uy & Lynch, 2013). Due to this increased stress, there is an increase in the likelihood of developing OA in those joints as well in response to the extra strain causing more cartilage degeneration than the body can replace. Of course, since this is an invasive surgical procedure, it comes with all the usual risks of infections, painful scar tissue, bleeding, blood clots, and nerve damage (Joint Fusion). However, due to the fact that not only is this an invasive surgical procedure but since the hardware is left behind after the surgery, there is always a risk of this hardware breaking in the body and causing significant damage to the tissues surrounding the joint. If the hardware left

behind breaks, then the patient will have to undergo another invasive procedure to either get rid of or replace the broken hardware.

A second surgical solution to treating OA is through performing a high tibial osteotomy. Due to the constant wearing down of the articular cartilage, it may develop tears in the cartilage (Knee Surgery). All of these tears coupled with just the constant wear down of the cartilage may not happen symmetrically though. In some cases, it will repetitively wear down on one side more than the other, and as that side wears down more and more it increases the wear that it has on that side in comparison to the other. This is what causes malalignment in the affected joints. A high tibial osteotomy is designed to fix this malalignment. It is designed to fix the malalignment by raising up one side of the joint, this takes the pressure off of the weakened more damaged side and shifts it to the less damaged side (Taruc-Uy & Lynch, 2013). This is an invasive procedure performed by actually cutting into the tibia itself. After the cut in the bone has been made, the two sides are then pulled apart making a wedge-shaped opening. Within the opening created in the tibial bone, the doctor will then insert a bone graft to hold and maintain the tibia in the desired shape, these bone grafts are usually harvested from the patient's pelvis or could be artificial. After the bone grafts are in place, then the doctor will place a metal place on the widest part of the opening and screw it in place to hold the bone grafts in place (Fig 3) (Knee Surgery). Of course, like with any surgical procedure it carries the usual risks of infection, bleeding, as well as many others including hardware breakage damaging surrounding tissue and needing to be removed or replaced. While this procedure is invasive and has a significant recovery time, it is still considered to be a way to avoid having to perform a full knee replacement on a patient (Taruc-Uy & Lynch, 2013). This is why this procedure is generally performed on younger

patients due to the fact that the positive effects from this surgery can last anywhere from 8 to 10 year before a patient ends up having to get a full knee replacement (Knee Surgery).

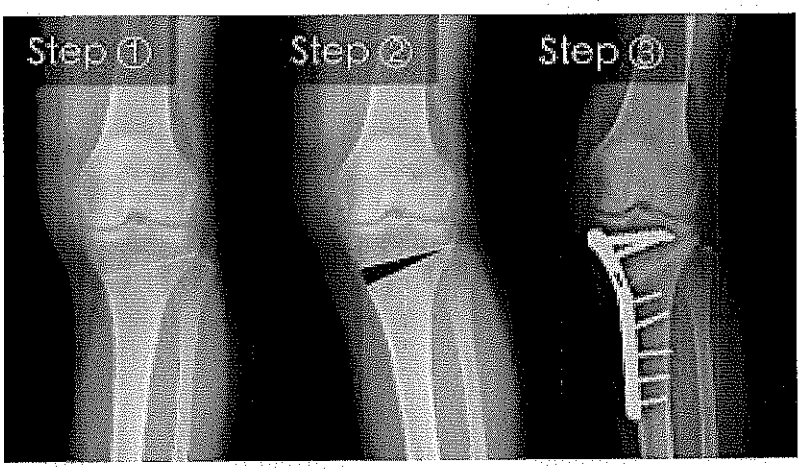

Fig. 3 Radiographs of the knee before during and after performing a High Tibial Osteotomy. Souce: https://imsc.vghtpe.gov.tw/treatment/post/104

Another surgical option for the treatment of OA is through arthroscopy. This procedure is mainly used to remove and debride damaged cartilage tissue (Taruc-Uy & Lynch, 2013). This is a method that is generally greatly preferred over more traditional "open" surgical methods. During surgery using "open" surgical methods it involves making a large incision and essentially peeling back layers of tissue until whatever the doctor intends to operate on is exposed, then after the surgery, everything is closed back up one layer at a time. However, arthroscopy is instead performed by creating a small incision and inserting a scope into the area that is being operated on along with a few other incisions for tools to be inserted into the surgical area as well (Fig.4). Due to its less invasive nature, arthroscopy is preferred in any situation that it can be performed instead of "open" techniques. Since this technique is less invasive than others, it means that patients have a much shorter recovery time, less chance of infections and bleeding, as well as the added benefit of no possible hardware malfunctions. However, like most treatments, it is not perfect. During trials for this technique, results have yet to show an advantage of using

arthroscopy over using different therapeutic together. However, it has been shown to have good results in those that have had it performed, surgery is simply to be avoided when possible due to its possible complications and invasiveness (Taruc-Uy & Lynch, 2013). So even when this technique minimizes many of these complications and invasions, it is still preferred to not use it when other methods that work just as well are available.

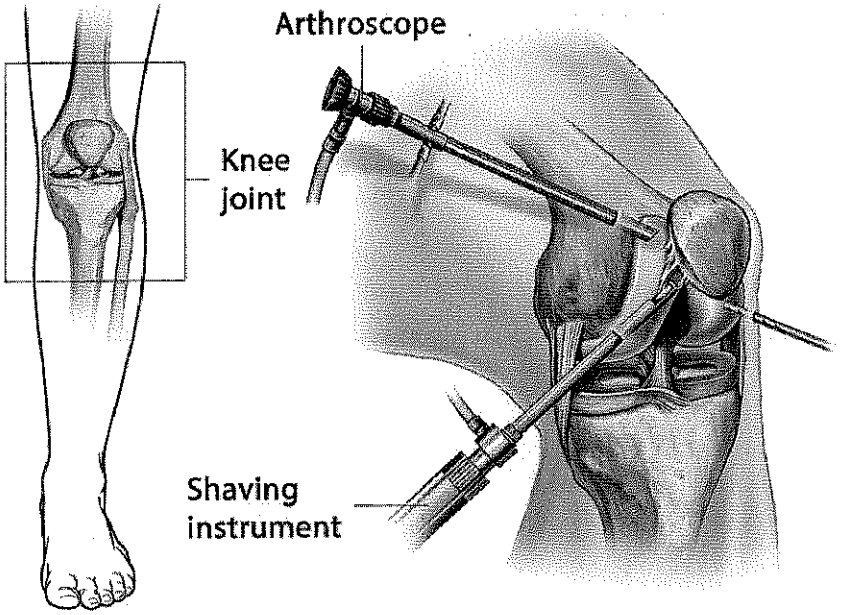

Fig. 4 Procedure for performing a knee arthroscopy. Source: https://www.healthdirect.gov.au/arthroscopy

Then there is the surgery of last resort for damaged joints. Arthroplasty or total joint replacement. This is a procedure that is only performed if all other forms of treatment have been exhausted for the patient (Taruc-Uy & Lynch, 2013). This is a highly invasive procedure that involves fully resurfacing the joint with either metal or plastic (Taruc-Uy & Lynch, 2013). During this procedure, the doctor will remove the damaged surfaces of the knee joint and then replace them with either metal or plastic (Fig. 5). The most common way of securing the prosthesis is through the use of surgical cement, however, it can be attached with a porous surface that the bone can then grow around locking it into place (Knee Replacement). Like with

any other surgical procedure, there is a risk of infection and bleeding. However, arthroplasty also carries with it a high risk of blood clots in the legs and lungs which leads doctors to administer preemptive blood thinners to help prevent this from happening (Knee Replacement). These risks are even higher in patients who are considered to be obese, which is already a risk factor for OA. Operating on obese patients is challenging no matter what operation is being performed, it just so happens that due to their predisposition to OA, a patient with OA is also likely to be obese. Since obese patients are so technically difficult to operate on, the procedure will often result in increased operating time for them, which in turn leads to an increased risk of infection as well as an increased risk of bleeding and other possible complications (Kulkarni, Karssiens, Kumar, & Pandit, 2016). However, despite all of these complications that arise when an obese patient undergoes a total joint arthroplasty, it is simply unrealistic to ask them to lose weight prior to their procedure due to the chronic pain they are in. It is also been shown by a few studies that due to the decrease in pain and stiffness that patients experience post-surgery weight loss. However, these studies are not all converging with their results, some studies have shown that younger patients are actually more likely to gain weight post-surgery, whereas older patients are more likely to lose weight post-surgery. However, what most studies seem to agree on is that all patients show improvement in their mobility as well as in their overall outcomes (Kulkarni, Karssiens, Kumar, & Pandit, 2016).

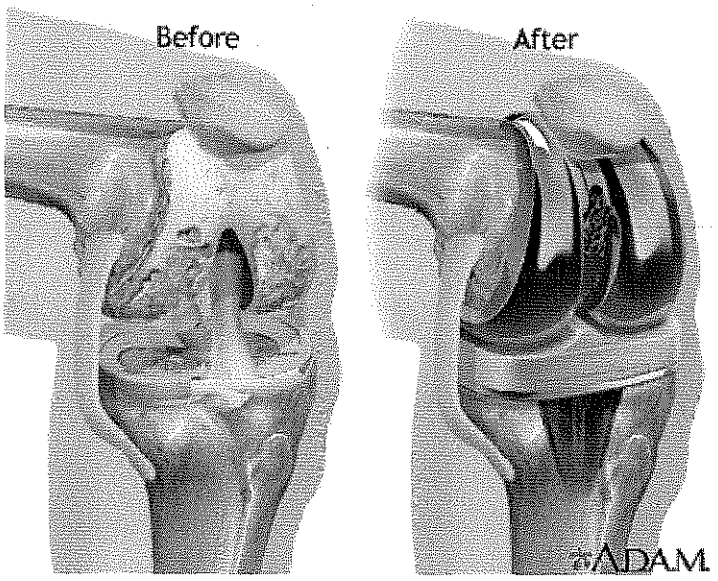

Fig. 5 Before and After of knee arthroplasty surgery. Source: https://medlineplus.gov/ency/article/002974.htm

Non-pharmacological:

When it comes to non-pharmacological and non-surgical treatments for OA, there are a few different options. The first of which is through physical exercise. Physical exercise has been shown to improve pain and improve the function of the affected joints (Taruc-Uy & Lynch, 2013). Unfortunately, due to the inflammation and pain in weight-bearing joints, it makes physical activity very difficult and painful for people with OA (Kulkarni, Karssiens, Kumar, & Pandit, 2016). However, because of people's joint pain levels with OA there needs to be a bit of creativity when it comes to getting people to exercise. The first option is through aquatic exercise. Due to the buoyancy of water, it relieves quite a bit of stress that is normally placed on these joints, thus allowing people to exercise without as much pain. And since swimming requires the use of a lot more muscles than a lot of other forms of exercise, it allows people to perform more caloric expenditure in a shorter amount of time than other forms of exercise can do for them (Kulkarni, Karssiens, Kumar, & Pandit, 2016). There are a few options for exercise methods, especially since in the beginning the people with affected joints probably won't be used to exercise due to the pain they are usually in, therefore it is probably better that they don't start

swimming laps at the very beginning. So, it is probably better for people to start out with performing exercises like scissor kicks, abduction-adduction kicks, and water running (Franco, Morelhão, de Carvalho, & Pinto, 2017). By performing a few cycles of these exercises, it will allow patients ease into physical activity while also lessening pain associated with physical activity. It has been shown that through methods such as these, that individuals pain scores can improve significantly by about five points on a twenty-point scale (Franco, Morelhão, de Carvalho, & Pinto, 2017). As well as a significant improvement on quality of life scale by around ten points on a hundred-point scale (Franco, Morelhão, de Carvalho, & Pinto, 2017).

Of course, aquatic exercise isn't the only form of physical exercise that people with joints affected by OA can perform. People can also exercise on dry land with the proper equipment. While using things like walking canes, braces, and appropriate footwear people can significantly decrease the stress that joints affected with OA experience. Through the use of these types of equipment, people can perform exercises that are more in-line with their regular day to day activities such as going for long walks and other activities that were previously too difficult for them to accomplish (Taruc-Uy & Lynch, 2013).

Another form of physical exercise that is easier for people with joints affected by OA to perform is Tai Chi. Tai Chi is a traditional form of Chinese martial arts that involves slow calculated movements accompanied by deep breathing (Taruc-Uy & Lynch, 2013). In this form of martial arts, your body is in constant motion changing from position to position without pause (Tai Chi, 2018). This is a form of martial arts that many people practice for self-defense purposes as well as the general health benefits that come from practicing most forms of martial arts. However, this form of exercise is particularly appealing to those who are suffering from joints afflicted with OA because it is a form of exercise that is very low-impact and puts minimal stress

on joints and muscles, making it easier for people with joint afflictions such as OA to participate in it (Tai Chi, 2018).

There are also medicinal approaches to treating people with joints affected by OA that are not surgical or pharmacological. The first of which is Pulsed Electromagnetic Field Stimulation. This is a device that creates an electromagnetic field that can penetrate deep through muscles and joints within two to twenty minutes (PEMF, 2017). It has been shown that when you send an electromagnetic field through cells it causes expansion and contraction which can cause many beneficial side effects. The first of which is that it causes an increase of the circulation of nutrients throughout the cells, and in the process of circulating nutrients more efficiently throughout the cell it also causes more efficient movement of oxygen throughout the cells (PEMF, 2017). Since there is an increase of circulation of oxygen and nutrients throughout the cell without actually increasing blood pressure or heart rate, it also causes a decrease in swelling throughout the area this therapy is applied to (PEMF, 2017). There is also an increase in the regeneration of damaged and diseased tissues because of the increase in nutrients circulating through the area now (PEMF, 2017). Due to all of these effects of reducing swelling and increasing the regeneration of damaged tissues, there is a great pain-relieving advantage to this therapy that benefits can last long term (PEMF, 2017).

There is another piece of therapeutic technology that can be used in a similar fashion to pulsed electromagnetic field stimulation. It is known as transcutaneous electrical nerve stimulation. This form of therapy involves the use of low-voltage electrical currents. These electrical currents will travel through the nerve fibers from electrodes that are placed on the active site of pain. As the electrical currents travel through the nerve fibers, they block the pain signals from being sent to the brain, thus decreasing the amount of pain a person feels (TENS).

There are many advantages to using this therapeutic machine over using pulsed electromagnetic field stimulation. One of which is that transcutaneous electrical nerve stimulation does not have to be performed at a doctor's office by a professional. Instead, this therapy can be performed at home by the patient with a portable battery-operated machine, after receiving a small amount of training from their doctor or physical therapist (TENS). However, in many ways, pulsed electromagnetic field stimulation would be preferable to transcutaneous electrical nerve stimulation. The main reason why electromagnetism is preferable in many ways is that it does not just manipulate the nerves in the body. Instead, pulsed electromagnetic field stimulation affects blood and nutrient flow throughout the cells that it penetrates, and through these mechanisms which cause a decrease in swelling and increase in cellular repair mechanisms, decreases pain. So instead of just giving the patient a sense of increased comfort from the decrease in pain that transcutaneous electrical nerve stimulation provides, it actually improves that patients' conditions which in turn causes a decrease in pain.

Experimental Treatments

Of course, scientists are always coming up with new treatments for all types of diseases and disorders. These new treatments can sometimes be controversial due to them not having much research behind them. One of these newer treatments is the administration of Glucosamine Sulfate and Chondroitin Sulfate. Both glucosamine sulfate and chondroitin are substrates of the chemical hyaluronic acid, which is a major component of joint fluid (Taruc-Uy & Lynch, 2013). Glucosamine sulfate and Chondroitin are usually administered together. When they are administered, it is usually orally or sometimes in a topical cream, and even rarer as an intramuscular injection. While glucosamine by itself has not been shown to prevent the onset of OA in patients it has been shown to relieve pain (glucosamine). It is believed that taking

glucosamine supplements will increase the development of either a patient's articular cartilage or the fluid that surrounds their joints (glucosamine). It is also believed that taking these supplements could help to prevent the degeneration of articular cartilage or synovial fluid, or it is entirely possible that taking glucosamine sulfide supplements could even do both, promote the development of these tissues and prevent the degeneration of these tissues (glucosamine). There are a few reasons as to why glucosamine sulfate could promote the development of synovial fluid or articular cartilage. One of these reasons is that glucosamine sulfate is a natural substrate of hyaluronic acid, a key component of synovial fluid. However, it could also help promote the development of articular cartilage because of the sulfate group that it contains, since sulfate groups have been known to be important in the body's ability to produce cartilage. This could be one of the reasons why glucosamine sulfate has been shown to be more effective than some of the other forms of glucosamine such as glucosamine hydrochloride or N-acetyl glucosamine (glucosamine). However, while glucosamine can relieve pain, it does not work quickly, it can take up to four to eight weeks for glucosamine to kick in whereas pain relievers such as ibuprofen and acetaminophen work in less than an hour (glucosamine). Due to this reasoning, glucosamine is often taken in conjunction with other medications, since patients could still have flare-ups of pain despite being on the medication. Administration of this medication orally has been shown to be likely safe, however, when administered through topical creams or by intramuscular injections has been deemed possibly safe. Glucosamine sulfate has some fairly mild side effects such as nausea, constipation, heartburn, and diarrhea, as well as some rarer side effects such as skin reactions and headaches (glucosamine).

Another form of treatment that is still considered to be controversial is the use of anti-nerve growth factor antibodies. These antibodies are designed to attack only nerve growth factors

and are considered being used as an alternative to NSAIDs. However, these compounds are currently still in the testing phase and are not yet approved for use as a treatment for humans (Gruen, et al., 2016). Although, as these drugs are currently undergoing animal trials, there is informative research about their use. One thing that has become apparent is that since this class of drugs is an antibody, and antibodies are extremely specific targeting molecules, they need to be species specific in order to function properly. This is due mostly to the fact that all species, ranging from cats and dogs to humans with many in between, have species-specific nerve growth factors. Nerve growth factors are a protein that is found throughout the body and is believed to have a wide variety of functions. These functions range from immune function, stress response, nerve maintenance, and are also implicated in neurodegenerative diseases. It is known as nerve growth factor due to the role that it plays during embryonic development and how it is responsible for a large part of the growth and organization of the nervous system (Navis, 2007). After much study and research, it was determined that nerve growth factor is actually a signaling protein that is produced by various tissues throughout the body. Research has shown that nerve growth factor is produced by nerves in target tissues, these target tissues are tissues such as skin, muscle, and vascular tissue. After nerve growth factor has been produced it binds to a receptor on the cell surface causing a cascade of reactions which end up leading to the stimulation of growth and guiding of nerve fibers towards the target tissues (Navis, 2007). Admittedly this growth factor is most active during development and its expression tapers off as the animals reach adulthood. The main exception to this is when a traumatic injury occurs which results in the need for nerve growth in order to properly heal (Navis, 2007). Of course, this is not the only time when nerve growth factor is produced in the body, since this growth factor is also related to the function of the immune system, it has also been shown to be produced from bone marrow

leukocytes during a period of stress. These leukocytes also contain a receptor for nerve growth factor. However, another situation that is more relevant to OA is that nerve growth factor is also produced to help protect nerve fibers from the repair processes of nearby tissues ((Navis, 2007). Due to the fact that OA consists of a chronic injury, and the cells within the joint are almost constantly trying to repair the damage to the existing cartilage and trying to keep up with the damage being done to the articular cartilage it stands to reason that nerve growth factor would be produced quite a bit in patients with OA. It is due to this hypothesis that the production of anti-nerve growth factors was created. It is thought that if patients were to have an antibody given to them that attacks and prevents the use of nerve growth factor, then doctors could stop not only the spread of nerves, but they could in theory also take away some of the natural protections that the nerves in the affected joints area have against the effects of tissues repair, thus leaving them open to damage and possibly future deadening of the nerves themselves. Since animals like cats tend to try and hide pain as much as they can as a defense mechanism, veterinarians and researches have to try to look for signs of pain and pain relief in other ways, ways like looking at activity level. After all, when any animal, including humans, are suffering from joint pain they will do their best to try and limit that pain, which in most cases ends up just looking like a decrease in activity level. During the animal studies for the anti-nerve growth antibodies, it was shown that the animals, specifically cats, in this case, had significant improvement of their activity levels after the fourth week (Gruen, et al., 2016). This rise in the activity level was shown to be very favorable when compared to a study that looked at the effects of meloxicam, a common NSAID used to treat OA. In this particular study the duration of one injectable dose of the anti-nerve growth factor antibody was enough to last from around four to six weeks (Fig. 6) (Gruen, et al., 2016).

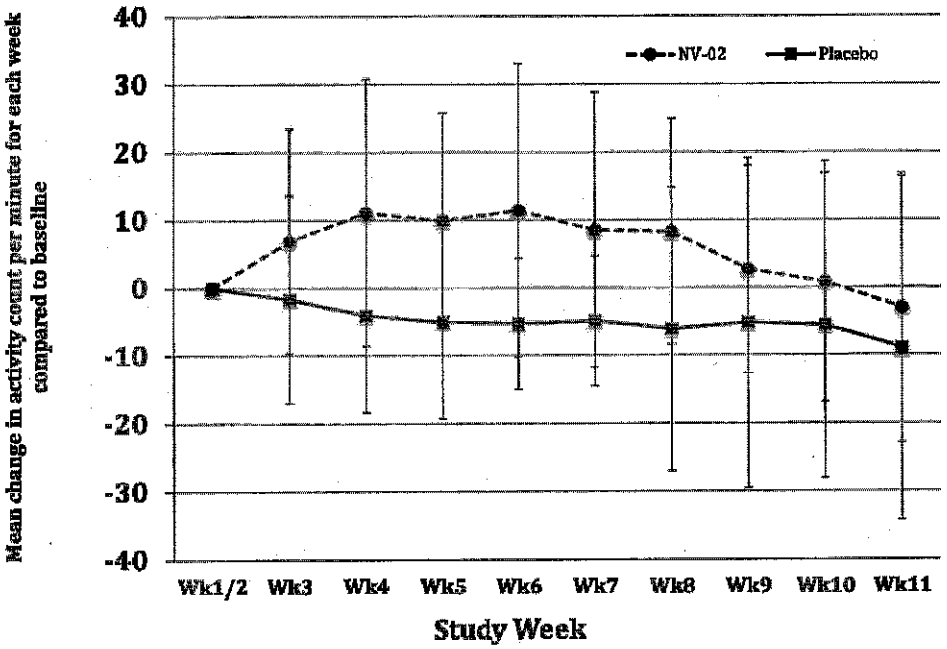

Fig. 6 Plot of percentage change from baseline (average of weeks 1 and 2 activity, before the antibody or placebo being administered) in mean weekly activity counts (originally expressed as average activity count per minute over the week) by group (treatment/placebo), for each week of study. Source: Gruen, M., Thomson, A., Griffith, E., Paradise, H., Gearing, D., & Lascelles, B. (2016). A Feline-Specific Anti-Nerve Growth Factor Antibody Improves Mobility in Cats with Degenerative Joint Disease-Associated Pain: A Pilot Proof of Concept Study. Journal of Veterinary Internal Medicine, 30(4), 1138-1148. doi:10.1111/jvim.13972

Of course, not all experimental forms of treatment for OA are brand new. Most of the time treatments are considered experimental because they are so new that they don't have enough research and trials backing them to be available as a common treatment. However, sometimes a treatment is considered experimental because people were too skeptical of it for a long time to really perform solid research on it. A good example of this type of situation is acupuncture. While acupuncture is just recently started to be accepted in western medical culture as a possible promising treatment for OA in many Asian countries like China it is a treatment that has been common practice for joint pain for thousands of years (Guo, et al., 2019). More recent studies have shown that acupuncture is safe and effective for treating pain, stiffness, as well as improving function (Guo, et al., 2019). Some of these studies made use of resting-state

functional magnetic resonance imaging (rs-fMRI). They did this in order to discover exactly why acupuncture is able to work as well as it has been shown to. The results of these rs-fMRI studies have shown that acupuncture improves pain in patients suffering from OA by enhancing the functional connectivity between the right frontoparietal network and the medial prefrontal cortex, thus regulating the descending pain-modulatory system of patients suffering from OA (Guo, et al., 2019). Several studies have shown a connection between the right frontoparietal network and pain signals. Mainly when performing functional MRIs researchers have discovered that increases in this network were a good indicator of the expectancy of pain (Kong, et al., 2013). While the medial prefrontal cortex is largely associated with executive decision making and memory, there is also a pain processing component. It is believed that the medial prefrontal cortex could serve two roles when it comes to pain, the first of which is that it could mediate the blocking of the detection of painful stimuli. On the other hand, the medial prefrontal cortex could also induce pain turning chronic (Ong, Stohler, & Herr, 2018). Therefore, rs-fMRI has given good results as to why acupuncture will actually work through the process of effecting these two regions of the brain and possibly, in essence, train them to not expect pain and to reduce the chronicity of OA joint pain. When it comes to knee OA, there are generally four points on the lower leg which are commonly used for acupuncture points (Fig 7). The first of which is known as SP9 and is on the medial side of the calf and is inferior to the medial condyle of the tibia. There is also the GB34 point which is on the lateral side of the calf and is inferior to the head of the fibula. Thirdly there is the EX-LEO4 point which is in the depression located on the medial side of the patellar ligament, Lastly, there is the EX-LE5 point which is in the depression located on the external side of the external ligament (Guo, et al., 2019). Of course, the benefits that acupuncture has been shown to have for OA is reliant on who is performing the procedure.

While there may not be any special certifications for performing acupuncture, it is always better when anything is being injected into your body to have it done by somebody who has had education and training in doing so, even if there is no formal education available for the subject.

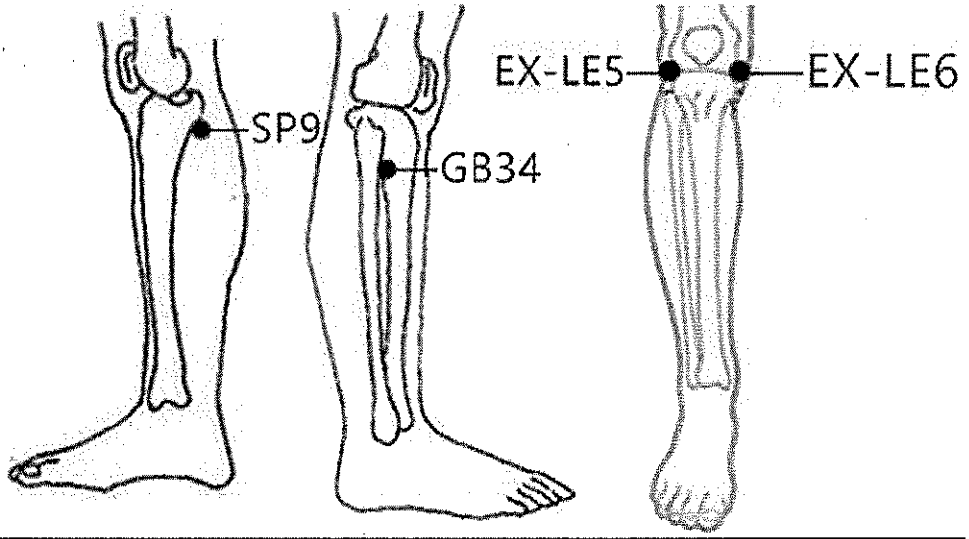

Fig. 7 Locations of acupoints: SP9 (yinlingquan), on the medial side of the shank, at the depression posterior and inferior to the medial condyle of the tibia. GB34 (yanglingquan), on the lateral side of the lower leg, in the depression anterior and inferior to the head of the fibula. EX-LE04 (neixiyan), in the depression located on the medial side of the patellar ligament. EX-LE5 (waixiiyan), in the depression located on the external side of the patellar ligament. Source: Guo, J., Chen, Y., Li, Z., Cheng, S., Tang, C., Dong, X., . . . Liang, F. (2019). The cerebral mechanism of acupuncture for treating knee osteoarthritis: Study protocol for a randomized controlled trial. Trials, 20(1). doi:10.1186/s13063-019-3233-7

Conclusion

In conclusion, osteoarthritis is a multifactorial disease that has a set of symptoms and can have many possible causes. The first of which is genetics, since like all systems in the body, growth, and development of the skeletal system is regulated by various enzymes, protein signals, and other factors that are controlled by genetics. Yet another possible cause for osteoarthritis are hormones, more specifically female associated hormones such as estrogens, as it is known that these hormones are responsible for the regulation of uptake and release of various minerals in the skeletal system which is a component of bone density. Another factor for the cause of osteoarthritis is obesity. This could mostly be attributed to the increased weight putting stress on weight-bearing joints. The last possible cause for osteoarthritis is the previous infection from

bacteria such as *Bartonella*, most likely due to triggering an inflammatory response in the infected joints. Some of the more common treatments such as surgical options, pharmaceutical options, and non-surgical non-pharmacological options that are out there were also discussed as well as the benefits and drawbacks of each. This is in combination with some of the more experimental treatments, that while they might not necessarily be approved for use in humans or have as much research supporting them as they could, they show quite a bit of promise once they have more studies and trials supporting them. All of these things together paint a clearer picture of a disease that plagues many people and animals throughout the world and will hopefully provide a good source of information for those looking for it.

References

1031597873550235. (2017, June 04). Treating Chronic Pain with PEMF Therapy. Retrieved from https://healthcareinamerica.us/treating-chronic-pain-with-pemf-therapy-f4c09dc183d7

Cortisone shots. (2017, December 30). Retrieved from https://www.mayoclinic.org/tests-procedures/cortisone-shots/about/pac-20384794

Flemming, D. J., & Gustas-French, C. N. (2017). Rapidly Progressive Osteoarthritis: A Review of the Clinical and Radiologic Presentation. Current Rheumatology Reports, 19(7). doi:10.1007/s11926-017-0665-5

Franco, M. R., Morelhão, P. K., De Carvalho, A., & Pinto, R. Z. (2017). Aquatic Exercise for the Treatment of Hip and Knee Osteoarthritis. Linking Evidence And Practice, 97(7). doi:10.1093/ptj/pzx043.

Glucosamine Sulfate: Uses, Side Effects, Interactions, Dosage, and Warning. (n.d.). Retrieved from https://www.webmd.com/vitamins/ai/ingredientmono-807/glucosamine-sulfate

Gruen, M., Thomson, A., Griffith, E., Paradise, H., Gearing, D., & Lascelles, B. (2016). A Feline-Specific Anti-Nerve Growth Factor Antibody Improves Mobility in Cats with Degenerative Joint Disease-Associated Pain: A Pilot Proof of Concept Study. Journal of Veterinary Internal Medicine, 30(4), 1138-1148. doi:10.1111/jvim.13972

Guo, J., Chen, Y., Li, Z., Cheng, S., Tang, C., Dong, X., . . . Liang, F. (2019). The cerebral mechanism of acupuncture for treating knee osteoarthritis: Study protocol for a randomized controlled trial. Trials, 20(1). doi:10.1186/s13063-019-3233-7

Hussain, S. M., Cicuttini, F. M., Alyousef, B., & Wang, Y. (2018). Female hormonal factors and osteoarthritis of the knee, hip and hand: A narrative review. Climacteric, 21(2), 132-139. doi:10.1080/13697137.2017.1421926

Joint Fusion Surgery: Purpose, Procedure, Risks, Recovery. (n.d.). Retrieved from https://www.webmd.com/osteoarthritis/guide/joint-fusion-surgery#1

Knee Replacement Surgery Procedure. (n.d.). Retrieved from https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/knee-replacement-surgery-procedure

Knee Surgery: High Tibial Osteotomy. (n.d.). Retrieved from https://www.hss.edu/conditions_knee-surgery-high-tibial-osteotomy.asp

Kong, J., Jensen, K., Loiotile, R., Cheetham, A., Wey, H., Tan, Y., . . . Gollub, R. L. (2013). Functional connectivity of the frontoparietal network predicts cognitive modulation of pain. Pain, 154(3), 459-467. doi:10.1016/j.pain.2012.12.004

Kulkarni, K., Karssiens, T., Kumar, V., & Pandit, H. (2016). Obesity and osteoarthritis. Maturitas, 89, 22-28. doi:10.1016/j.maturitas.2016.04.006

Mason, J. B., Terry, B. C., Merchant, S. S., Mason, H. M., & Nazokkarmaher, M. (2015). Manipulation of Ovarian Function Significantly Influenced Trabecular and Cortical Bone Volume, Architecture and Density in Mice at Death. Plos One, 10(12). doi:10.1371/journal.pone.0145821

Mei, L., Shen, B., Ling, P., Liu, S., Xue, J., Liu, F., . . . Liu, X. (2017). Culture-expanded allogenic adipose tissue-derived stem cells attenuate cartilage degeneration in an experimental rat osteoarthritis model. Plos One, 12(4). doi:10.1371/journal.pone.0176107

Navis, A. R. (2007, October 30). The Embryo Project Encyclopedia. Retrieved from https://embryo.asu.edu/pages/nerve-growth-factor

Ong, W., Stohler, C. S., & Herr, D. R. (2018). Role of the Prefrontal Cortex in Pain Processing. Molecular Neurobiology, 56(2), 1137-1166. doi:10.1007/s12035-018-1130-9

Slingerland, L., Hazewinkel, H., Meij, B., Picavet, P., & Voorhout, G. (2011). Cross-sectional study of the prevalence and clinical features of osteoarthritis in 100 cats. The Veterinary Journal, 187(3), 304-309. doi:10.1016/j.tvjl.2009.12.014

Srivastava, R., Sharma, A., Srivastava, S., Agrahari, A., Singh, A., & Parmar, D. (2017). Evaluation of the association between a single-nucleotide polymorphism of bone morphogenetic proteins 5 gene and risk of knee osteoarthritis. Journal of Postgraduate Medicine, 63(3), 151. doi:10.4103/jpgm.jpgm_450_16

Taruc-Uy, R. L., & Lynch, S. A. (2013). Diagnosis and Treatment of Osteoarthritis. Primary Care, 40(4). doi:10.1016/j.pop.2013.08.003

Tomas, A., Pultorak, E., Gruen, M., Breitschwerdt, E., & Lascelles, B. (2014). Relationship Between Degenerative Joint Disease, Pain, andBartonellaspp. Seroreactivity in Domesticated Cats. Journal of Veterinary Internal Medicine, 29(1), 21-27. doi:10.1111/jvim.12495

Transcutaneous Electrical Nerve Stimulation (TENS). (n.d.). Retrieved from https://my.clevelandclinic.org/health/treatments/15840-transcutaneous-electrical-nerve-stimulation-tens

What Are NSAIDs? - OrthoInfo - AAOS. (n.d.). Retrieved from https://orthoinfo.aaos.org/en/treatment/what-are-nsaids/

Why try tai chi? (2018, September 26). Retrieved from https://www.mayoclinic.org/healthy-lifestyle/stress-management/in-depth/tai-chi/art-20045184

Yang, M., Jiang, L., Wang, Q., Chen, H., & Xu, G. (2017). Traditional Chinese medicine for knee osteoarthritis: An overview of systematic review. Plos One, 12(12). doi:10.1371/journal.pone.0189884

Reflective Writing

The process of creating and completing this capstone project was a lengthy one. As a capstone project, it was designed to accomplish several goals such as: creating a capstone experience for my undergraduate experience, add to my overall education and future goals, deepen my research experience within my major, require critical thinking about topics in my major, and to broaden my experience across disciplines. By accomplishing all of these goals it is in the hope that these capstone projects will make students like myself more rounded and more educated people as well as hopefully becoming more active and engaged within our communities.

When it comes to creating a capstone experience for my undergraduate experience these capstone projects are in a way designed to tie together everything that we as students have learned throughout not just our undergraduate years but before that as well. By creating a large project like this we are forced to draw on our experiences and knowledge that we learned for our different classes as well as past research experiences. Because of this it truly becomes the pinnacle of our undergraduate career as well as a good stepping stone to our future education goals as well as our future lives in our professional careers by giving us a taste of what could be to come for us in our chosen fields.

In regards to adding to my overall education and future goals, my capstone project did this in a few ways. I performed a literary review of a singular disease, in my case osteoarthritis. Due to my future career goals within the profession of veterinary medicine, I will be required to know about many common diseases in depth as they will be dealt with by all veterinarians on a regular basis. Therefore, going through all of this research has given me a taste for what I might be learning in veterinary school as well as the independent research that I will have to perform

once I become a veterinarian. Medicine is always changing, and new research is always coming to light, even when it comes to diseases that have been around for hundreds of years. We are always learning new things and people who are in the field of medicine whether it be human or veterinary need to constantly be able to keep up with it, usually through the use of professional journals in their chosen field. When I was going through all of this research, most of it very recent, it showed to me just how little I knew about a disease that is so commonplace. It really did give me a greater appreciation for what I will be expecting to have to learn both through school and just to keep up with current research.

This capstone project also allowed me to deepen my knowledge in my field. Throughout this project, I learned more about possible treatments, causes, and clinical signs than I have of any one disease than I ever have before. I learned about what would be most commonplace in both human and veterinary medicine when it comes to treatments. I also got to have more experience in reading radiographs while I was going through this research than I have in most other situations. There is also the fact that I go the opportunity to learn more about experimental treatments that are up and coming or have been around for a while and just require more research behind them in order to be approved. Throughout all of my time learning about these new and in some cases improved treatments it was eye-opening as to how even with diseases like osteoarthritis that have been around for hundreds of years we are still trying to develop new treatments and how even those new treatments are still not focused on curing it but instead trying to improve patients' conditions.

Throughout this capstone project, there was also a requirement for more critical thinking than most other things that I have done in my undergraduate career have required. For me, this has mostly involved picking and choosing which research is applicable to what I was trying to

accomplish. I had to learn how to not take everything I see at face value in order to find what I really needed for my capstone project. This will, in turn, be quite helpful with my everyday life outside of school, both in my future professional life as well as my personal life. When it comes to being a Veterinarian you have to be able to take what your clients say about their pets with a grain of salt in order to get the whole truth. Clients will often fudge the truth to make themselves look better or even just outright lie to make others think better of them for the way they treat their pets. All of these critical thinking skills will in the future be very helpful going forward in my life.

This capstone project also allowed me to broaden my experience across disciplines. Throughout the course of this project, I had to perform in-depth research into fields that I wouldn't have expected to have to look into for a skeletal system disease like osteoarthritis such as neurobiology, genetics, as well as even more unexpected topics such as traditional Chinese medicine such as acupuncture. It truly did prove to me that no field of study is truly isolated. All subjects and fields have some sort of tie into others in some way or another. For example, in my research on osteoarthritis when I looked into acupuncture as a possible treatment I ended up having to perform some rather in-depth research into neurobiology as well in order to fully understand just how the researchers were saying that acupuncture affected the body.

In the end, this capstone project helped me improve my knowledge in many fields both academic and otherwise. It showed me beyond a shadow of a doubt that no field is truly isolated from one another, that they all intersect in some way or another. As well as helping me to improve and deepen my knowledge within my own field that I expected to come from this and improve my critical thinking skills from going through so much research to determine what exactly I needed from this project.

Professional Author Bio

Madelin Session is a student at Utah State University and she is currently studying for a major in Animal, Dairy and Veterinary Science with an emphasis in Bioveterinary science along with minors in Chemistry and Biology. She has achieved the dean's list for all the semesters during her undergraduate career. She has participated in undergraduate research with her assistance in Dr. Jeffrey Mason's lab and assisting his graduate students with their projects. As well as performing an internship with Best Friends Animal Society in their kitten nursery as well as working at a 24/7 emergency veterinary hospital. Her future plans are to graduate from veterinary school and go into a residency for specialization.