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Abstract

Periodontal diseases can affect people throughout their life, from puberty to well into the geriatric years. However, differences between the sexes play a large role into how the diseases progress over time. Women have a monthly cycle of hormones that effects how the disease and the symptoms present themselves in the patients. This review will discuss the history, definition, treatments, and the effects periodontal diseases have on women. Specifically, this review will discuss how the different life stages of women interact with treatments and symptoms.

The Adverse Effects Periodontal Diseases Has on Women

This review extensively covers the history, definition, and the treatments of periodontal diseases. More specifically, topics covered include: the historical roots of periodontal disease, the difficulties in defining periodontal diseases, and various treatments for periodontal disease. Furthermore, how periodontal diseases affect women throughout their life span will be examined in depth. Given that background, the review seeks to answer the research question: How does periodontal disease affect women through the different life stages?

History

Periodontal diseases have been documented since the earliest record of humans was discovered. Paleopathological records show that damaging periodontal disease was present in ancient Egyptian civilizations as well as pre-Columbian Americans (Newman, Takie, Klokkevold & Carranza, 2006). In the earliest medical records, periodontal problems as well as considerations as to how different systemic diseases may be involved in the manifestation of the oral diseases was written about extensively (Newman, Takie, Klokkevold & Carranza). In spite of the initial ideas behind what causes periodontal disease, modern treatment of periodontal diseases was not developed until the 18th century (Newman, Takie, Klokkevold & Carranza).

During ancient Egyptian times, there was evidence found that good oral health and care were an extremely important part of their lives (Newman, Takie, Klokkevold & Carranza, 2006). In many excavation sites, elaborately decorated golden toothpicks were found buried with many people (Newman, Takie, Klokkevold & Carranza). Along with toothpicks, tablets outlining treatments like herbal medications and gingival massage were found in Babylonian and Assyrian tombs (Newman, Takie, Klokkevold & Carranza). Interestingly, one of the most common

diseases that plagued the Egyptian people was periodontal disease. Embalmed bodies from that time show extreme recession of the gum lines (Newman, Takie, Klokkevold & Carranza). The Ebers papyrus from this time contains many references and suggested prescriptions to strengthen the teeth and gums (Newman, Takie, Klokkevold & Carranza). Many of the suggested prescriptions include the use of plant products as well as different minerals, honey pastes, and beer residues, which were to be applied to the gums (Newman, Takie, Klokkevold & Carranza).

The advent of early science emerged out of Greek culture and an early contributor to our understanding of health was the Greek physician, Hippocrates. Hippocrates is known as the father of modern medicine. He was the first to perform the systematic examinations of patients in regards to their pulse, sputum, temperature, excreta, and respiration (Newman, Takie, Klokkevold & Carranza). He was also the first person to write and discuss the eruption of the teeth out of the gums and the etiology of periodontal disease (Newman, Takie, Klokkevold & Carranza).

After Hippocrates emerged more Greek scientists were making discoveries into what was happening in the mouth. Celsus was a second century Greek scientist who lived from 25 BCE-50 CE (Newman, Takie, Klokkevold & Carranza, 2006). In his writings, Celsus spoke about the diseases that affect the soft parts of the mouth (Newman, Takie, Klokkevold & Carranza, 2006). He was the first to describe how the looseness of teeth was caused by the weakness of the gums (Newman, Takie, Klokkevold & Carranza). In his writings, Celsus also describes the use of a toothbrush like tool and using it for gingival massage as an important part of having good oral hygiene (Newman, Takie, Klokkevold & Carranza).

The fall of the Roman Empire was followed by the Middle Ages and eventually the Renaissance period. During these periods of time, advances in the area of human anatomy and physiology were uncovered, specifically during the Renaissance period. At this time, Girolamo Cardano, an Italian scientist and physiologist, became the first person to differentiate and describe all of the different types of periodontal diseases that were present during this time period (Newman, Takie, Klokkevold & Carranza, 2006). One of the biggest advances during this time was the invention of the microscope by Anton van Leeuwenhoek (Newman, Takie, Klokkevold & Carranza). Leeuwenhoek was the first to look at blood cells, sperm, and bacteria under at the microscopic level (Newman, Takie, Klokkevold & Carranza). In many of his texts, he identifies and describes the bacteria that inhabited his mouth and others, which made him the first person to document the bacteria found in normal human flora of the mouth (Newman, Takie, Klokkevold & Carranza). Furthermore, different periodontal tools, including scalers and files were invented (Newman, Takie, Klokkevold & Carranza). In the writings from this time period, the procedure of scaling was described in detail as well as a thorough description of diseases and treatments of the mouth and throat (Newman, Takie, Klokkevold & Carranza).

The 18th century is considered the time when modern dentistry was developed mainly in England and France (Newman, Takie, Klokkevold & Carranza, 2006). Pierre Fauchard, a French physician, is regarded as the father of modern dentistry as we know it today (Newman, Takie, Klokkevold & Carranza). He was self-taught and created a systematic approach to doing dental work and made significant advances in the instruments used for proper dental work (Newman, Takie, Klokkevold & Carranza). Fauchard wrote a book called the *The Surgeon Dentist*, which served as the primary text for many dentists who immigrated to America in the early times of the country (Newman, Takie, Klokkevold & Carranza).

The early American dentists advanced the field of dentistry in astonishing ways through the application of scientific discoveries. For example, Horace Wells and William Morton discovered anesthesia (Newman, Takie, Klokkevold & Carranza, 2006). In their work, Wells and Morton discovered the analgesic effect that nitrous oxide and ethers had on dental patients (Newman, Takie, Klokkevold & Carranza). These discoveries made the practice of dentistry easier on both the patient receiving treatment and the dentist practicing the medicine. Keeping the patients sedated prevented them from moving around which in turn made performing the procedure by the dentist easier.

Further discoveries during this period aided in the understanding of oral health and disease. Louis Pasteur disproved the theory of spontaneous generation of organisms and the germ theory of disease was adopted (Newman, Takie, Klokkevold & Carranza, 2006). German physicist Wilhelm Röntgen developed the radiograph, which has been crucial in the field of dentistry specifically in the field of periodontics (Newman, Takie, Klokkevold & Carranza). Other scientists were beginning to understand the pathogenesis of periodontal disease and how interactions of local and systemic factors cause disease within the mouth (Newman, Takie, Klokkevold & Carranza).

The first oral microbiologist was Willoughby D. Miller. Miller studied basic sciences at the University of Michigan and received dental training from the Pennsylvania Dental College (Newman, Takie, Klokkevold & Carranza, 2006). When he was in Germany, he worked in microbiologist Robert Koch's lab, which started his microbiology research vocation (Newman, Takie, Klokkevold & Carranza). Miller made discoveries into which bacteria led to dental caries as well as identifying bacteria found in normal oral flora (Newman, Takie, Klokkevold &

Carranza). Knowledge of which bacteria are found in the mouth at any given time allowed for the identification of specific bacteria that cause periodontal diseases.

From the discoveries the Egyptians made to the research still being conducted, the field of periodontal disease is continuing grow. The bacteria involved in the manifestation of periodontal diseases and how they destroy the tissues are two factors that make these diseases so complex. Furthermore, the different systemic risk factors, such as added risk of coronary heart disease and stroke, and how the disease affects every patient differently also adds to the complexity of understanding and treating periodontal diseases (Beck, Garcia, Vokonas & et al, 1996).

Defining Periodontal Disease

Defining periodontal disease is challenging given the variety and complexity of the diseases that fall under the umbrella of "periodontal disease". Unlike other diseases, such as cancer, periodontal disease encompasses many different infections, active and inactive, where the gums (gingiva), teeth, alveolar ligament, the maxillary bone, and the mandible are involved (Newman, Takie, Klokkevold & Carranza, 2006). Periodontal diseases include both periodontitis and gingivitis. Explained further, gingivitis refers to the breakdown and destruction of the gums where as periodontitis refers to the destruction of the gums plus the connective tissue and the bone (Wrenn, 2011). For the purposes of this paper, periodontal disease will refer to the destruction of both the gum tissue or the gum tissue as well as the connective tissue and bone that support the teeth.

Until recently, periodontal disease was thought to be a disease where the infection acted at a constant rate, continuously causing destruction of the gums, teeth, and alveolar ligament

(Newman, Takie, Klokkevold & Carranza, 2006). It is now known that periodontitis exists in three forms: chronic, aggressive, and a manifestation of systemic diseases (Newman, Takie, Klokkevold & Carranza). The most common of the three forms is chronic periodontitis, which advances slowly with most cases seen in adult patients (Newman, Takie, Klokkevold & Carranza). However, this disease has been seen in children and young adults as well (Furuta, Ekuni, Irie, Azuma, Tomofuji, Ogura & Morita, 2011).

There are many types of bacteria associated with periodontal disease. Most commonly, the two strains of bacteria found in an active infection in a patient with a periodontal disease are *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* **(**Newman, Takie, Klokkevold & Carranza, 2006). These two bacteria are most common in active adult periodontitis where the host tissue cells have been invaded, a common symptom of the active periodontal infection (Newman, Takie, Klokkevold & Carranza). Although these two strains are very different, the basic components of the bacteria are the same.

Both *A. actinomyetemcomitans* and *P. gingivalis* fall under the category of gram-negative anaerobic bacteria (Sutton, 2006). In general, gram-negative bacteria are classified based on the differential stain, the Gram stain. In this differential test, the bacterial cell wall, made up of peptidoglycan, will adhere to the stain based on the amount of peptidoglycan present (Sutton). Peptidoglycan is a rigid layer made up of *N-acetylglucosamine* and *N-acetylmuramic acid* and the amino acids including L-alanine, D-alanine, D-glutamic acid, and lysine or diaminopimelic acid, also known as DAP (Madigan, Martinko, Stahl & Clark, 2012). In gram-negative bacteria, there is very little peptidoglycan present. Because of this, the cells will appear pink in color instead of the purple color that gram-positive bacteria stain (Sutton). Being an anaerobic bacteria means that the optimal condition for the bacteria to grow contains little to no oxygen in

the area (Madigan, Martinko, Stahl & Clark). These requirements for growth make the mouth and the gum pockets around the teeth the most advantageous area for these strains of bacteria to grow.

Beyond these two common types of bacteria, another 500 pathogens have been associated with periodontal diseases (Kim & Amar, 2006). These species have been further classified by their interaction in the disease and the dental tissue. For example, if a specific bacterium plays a role in the early infection of a periodontal disease, it will be classified differently than a bacterium that is strictly seen in a later stage of the disease that solely aids in the destruction of the gum tissue.

The classifications of the aforementioned species of bacteria are the green, yellow, and purple complexes (Gurenlian, 2007). These three complexes have many associated bacteria that are found in the normal human flora within the mouth. These bacteria are the ones that colonize in the subgingival area to begin the periodontal infections (Gurenlian). Past the normal bacteria, the pathogens are then divided into two larger groups based on their common characteristic and the symptoms they cause. The two largest classifications are the orange complex and the red complex (Kim & Amar, 2006).

The first classification of bacteria to arise in a typical patient with active periodontal disease is the orange complex. This complex consists of *Fusobacterium nucleatum/periodonticum* subspecies, *Prevotella intermedia, Prevotella nigrescens, Peptostreptococcus micros, Campylobacter rectus, Campylobacter gracilis, Campylobacter showae, Eubacterium nodatum,* and *Streptococcus constellatus* (Kim & Amar, 2006). These species are linked to the periodontal disease gingivitis and gingival bleeding (Gurenlian, 2007).

The red complex consists of three bacteria: *Tannerella forsythensis, Porphyromonas*

gingivalis and *Treponema denticola* (Kim & Amar, 2006). These three species are what cause the abnormal pocket depth and the bleeding that happens when probing the infected gums (Kim & Amar). It is known that red complex organisms are found in the most advanced stages of periodontal diseases (Gurenlian, 2007).

It has been discovered that some viruses may also be involved in the development of periodontal diseases. In recent research, it was found that some herpes viruses, including human cytomegalovirus (HCMV) and the Epstien-Barr virus (EBV-1) (Slots, Kamma, & Sugar, 2003), also in the destruction of the gums, which is a major symptom of periodontal diseases (Kim &Amar, 2007). The implications of these recent findings will aid in the understanding and treatment of periodontal diseases in patients with these preexisting conditions.

Knowing how the disease works is imperative to treating its effects in a patient's mouth. While it is challenging to define periodontal disease, there are two primary complexes that are involved in the creation of these diseases: the orange and red complexes. The treatments of periodontal disease are chosen based on the progression of the disease and the needs of the patient. Some treatments can be combined to more effectively treat the patient and, depending on the severity, some surgical treatments may be implemented.

Treatments

Once a patient has been diagnosed with a periodontal disease, the key to disease maintenance is treatment. From medication to surgery to simple preventative care, good oral hygiene is important to slow the progression of the infection and keep a patient's gums and teeth in the best condition possible once periodontal disease is contracted.

Preventative care is the key to preventing the contraction periodontal diseases. Preventative care and good hygiene habits begin early in life. Around the age of six months is

when a child's first tooth arrives ("Babies and Kids", 2012). However, before that time it is important to take care of the child's gums to keep them healthy and developing properly. Before any teeth arrive, it is recommended that you wipe down the infants gums with clean wet gauze or washcloth ("Babies and Kids"). This practice helps to ensure that when teeth do start to arrive that no bacteria or infection around the gums can lead to the decay of the new teeth.

When the teeth finally arrive around six months is when brushing of the teeth with a toothbrush and water can begin ("Babies and Kids", 2012). Until the age of two, no toothpaste should be used due to the harm that ingesting too much fluoride can cause in the developing body ("Babies and Kids"). Past the age of two however, a pea-sized amount of fluoride toothpaste can be used on a child-sized toothbrush ("Babies and Kids"). Until children learn the proper technique and can thoroughly and effectively brush their teeth on their own, assistance from a parent is imperative to avoiding early tooth decay and problems such as " baby bottle tooth decay", also known as early childhood caries ("Babies and Kids").

Baby bottle tooth decay is caused by extended exposure to sugary liquids such as formulas or fruit juices (Academy of General Dentistry, 2012). Cases of baby bottle tooth decay are seen more commonly in children who are put to bed with formula or juice in a bottle (Academy of General Dentistry). In extreme cases, oral surgery must be performed in a hospital setting to treat the caries that form (Academy of General Dentistry). Although these caries occur on non-permanent teeth, the effects may be detrimental to the child as they develop. For example, the child may develop speech problems or the adult teeth may become damaged as well (Academy of General Dentistry).

Another fast and easy way to keep a child's oral health in good condition is sealants ("Babies and Kids", 2012). Sealants are made of an acrylic substance that is laid onto the tooth

surface to cover deep pits and grooves (“Babies and Kids”). By sealing the teeth, decay cannot penetrate the tooth surface, which prevents dental caries from developing (“Babies and Kids”).

Regular six-month cleanings is a primary and important way to prevent periodontal disease. During this appointment, the hygienist will do a thorough examination of the mouth (“Oral Care for Adolescence Fact Sheet”, 2012). Many times this appointment will include x-rays of the entire mouth, the removal of plaque and calculus above and below the gum line, polishing the teeth, an application of fluoride, as well as making up a treatment plan and counseling on how to keep the patients mouth healthy (“Oral Care for Adolescence Fact Sheet”).

Once periodontal disease has been diagnosed, care beyond the biannual hygiene appointments is needed. Depending on the stage of the disease determines the amount of care that is needed to keep the disease under control and the patient out of pain (National Institute of Health, 2012). For example, patients may need to come in every three months versus every six months to maintain the health of the mouth. Routine periodontal appointments include the non-surgical treatment of scaling and root planing (National Institute of Health). Scaling refers to the scraping off of the tartar from the teeth above and below the gingiva (National Institute of Health). Root planing is the treatment that is used to eliminate rough spots that have accumulated on the tooth root where the gums come together (National Institute of Health). It is also used to remove the bacteria that cause periodontal disease (National Institute of Health). This method is preferred among patients and dentists alike because it is less invasive than the surgical treatments for periodontal disease and results in less bleeding, discomfort, and swelling (National Institute of Health).

Depending on the severity of the disease, different medications may be added to supplement the preventative care treatment plan to help with disease control outside of the dental

visits. Some of the medications include prescription antimicrobial mouthwash, an antiseptic chip, antimicrobial gel, antimicrobial microspheres, enzyme suppressants, and oral antibiotics (National Institute of Health, 2012).

The prescription antimicrobial mouthwash is used like regular mouthwash but contains chlorohexidine, an antimicrobial reagent (National Institute of Health, 2012). The mouthwash helps to kill and control bacteria growth after gum surgery or outside of the dental hygiene appointments (National Institute of Health). The antimicrobial chip is a small piece of gelatin that contains chlorohexidine (National Institute of Health). This chip is placed in the pockets of the gums after a root planing procedure where the medication is slowly released over time (National Institute of Health). Again, like the antimicrobial mouthwash, the antimicrobial chip controls the growth of bacteria while at the same time reduces the size of the gum pocket (National Institute of Health). Antibiotic microspheres are much like antimicrobial discs in they control the growth of the periodontal disease causing bacteria while working to reduce gum pocket size, except they differ in that they contain the antibiotic minocyclin and will be placed in the gum pocket by a dentist specializing in the care and prevention of periodontal diseases, a periodontist (National Institute of Health).

An enzyme suppressant, like doxycycline, is present in both gel and tablet form (National Institute of Health, 2012). Both forms of enzyme suppressant are used to keep the bodies destructive enzymes from breaking down gum tissue in the presence of the disease. The enzyme suppressants are also used to control the growth of the bacteria and reduce gum pocket depth (National Institute of Health). Again, the enzyme suppressant is used in conjunction with scaling and root planing (National Institute of Health).

Finally, an oral antibiotic may be prescribed for a patient in conjunction with the treatment plan in place for the specific patient's needs (National Institute of Health, 2012). Oral antibiotics are usually prescribed to patients who have acute periodontal infection or locally lasting infection of the gums versus a patient with periodontal infection in their entire mouth (National Institute of Health). The antibiotic is also used in conjunction with other treatments discussed above.

In severe cases of periodontal disease, surgical treatments are necessary (National Institute of Health, 2012). The two types of surgery commonly used are flap surgery and bone and tissue grafts (National Institute of Health). These two procedures are used when antibiotics along with scaling and root planing are not working to control periodontitis (National Institute of Health). If a patient is not responding to the other treatment methods, the treating dentist may decide that surgery is the only way to treat the patient's periodontal disease (National Institute of Health).

In preparation for flap surgery, a dental hygienist will first remove all of the plaque and calculus built up around the teeth (Columbia University of Dental Medicine, 2010). A review of the medications and life practices of the patient is completed to make sure that the patient is healthy enough to undergo the procedure and to make sure the procedure is safe for the patient (Columbia University of Dental Medicine). Because the procedure requires some general anesthesia, it is important to know the health history of the patient in order to keep them as safe as possible.

The surgery begins with the numbing of the area in which the surgery will take place (Columbia University of Dental Medicine, 2010). The periodontist will then separate the teeth from the gums with a scalpel, and the gums are folded and lifted back to form a flap (Columbia

University of Dental Medicine). By doing this, the periodontist can reach the bone and the roots of the teeth with ease and proceed with the surgery (Columbia University of Dental Medicine). During the surgery, swollen tissues will be removed, as well as any defects in the bone will be fixed with a procedure called osseous recontouring (Columbia University of Dental Medicine, 2010). While the gums are pulled back, the periodontist will do scaling and root planing on the exposed portion of the teeth (Columbia University of Dental Medicine). Once the recontouring, scaling and root planing have been completed, the gums are put back in place and stitched in with stitches that dissolve over time (Columbia University of Dental Medicine).

After care is extremely important following surgery. Maintaining a clean mouth is the key to the surgery's success (Columbia University of Dental Medicine, 2010). Normal brushing and flossing in the spots of the mouth not affected by the surgery can take place (Columbia University of Dental Medicine). At the site of the surgery, gentle brushing with a toothbrush is allowed as well as using antimicrobial mouthwash that is prescribed by the periodontist (Columbia University of Dental Medicine). Swelling and pain may occur, and the periodontist often prescribes a pain medication as well as recommending ice on the outside of the face where the surgery occurred (Columbia University of Dental Medicine).

The other surgery option is the bone and tissue graft surgery. This surgery is used to replace old bone and gum tissue to encourage new growth in the area where the damage of periodontal disease has occurred (Columbia University of Dental Medicine, 2010). Guided tissue regeneration is the procedure where a piece of mesh is placed between the bone and the gum so that the gum tissue will not penetrate into where the bone is supposed to grow and allow the bone and connective tissue to regrow normally (Columbia University of Dental Medicine). Results of

this procedure vary between patients because it is hard to say which grafts will take and grow and which ones will not (Columbia University of Dental Medicine).

Treatments for periodontal disease range from routine scaling, root planing, and antibiotics to surgery. The method of treatment appropriate for the patient is decided by the acting dentist or periodontologist and is dependant upon the progression of their disease. Early stages of the disease may require minimum care, like scaling and root planing, where as more advanced stages may require surgery. One step beyond making decisions on treatments based on the stage of the disease is to look at the gender differences between men and women and how that affects the disease.

Women and Periodontal Disease

Although epidemiological surveys show that men present with periodontal diseases more than women, the impact the disease has on women presents a unique challenge on how to design their individual and personalized treatment plan (Furuta, Ekuni, Irie, Azuma, Tomofuji, Ogura & Morita, 2011). The affects that these diseases have on women are different than men. Women react differently to these diseases because of reproductive hormones and cycling.

Throughout the human female life, there are different periods in which the levels of hormones change. These changes are present in the female system due to the reproductive tract having two separate functions; it transports the gametes to the site where they will be fertilized and it also provides a site for where the conceptus will implant and develop (Johnson & Everitt, 2000). Starting around age 11 to 14, most girls experience puberty (Newman, Takie, & Klokkevold, 2006). Puberty occurs when the female experiences an increased cycling in reproductive hormones, specifically estrogen and progesterone (Newman, Takie, & Klkkevold). Because of this, the female body often has an amplified response to food particles in the gums,

plaque, and calculus on the teeth (Newman, Takie, & Klkkevold). If not treated correctly, the tissue has the possibility of becoming “erythematous, lobulated, and retractable” (Newman, Takie, & Klkkevold, p.514). This can lead to inflammation of the gingiva as well as bleeding and the possibility of developing an infection (Newman, Takie, & Klkkevold). To prevent infection from forming and progressing to a periodontal disease, preventative care is essential.

The next phase in the reproductive years of the female is menses. This is when the female reproductive hormones begin cycling monthly. These hormones play a role in the development and severity of periodontal diseases. Once a women beings her menstrual cycle, the hormones begin a cycle that occurs over a period of 28 days and then repeats. The cycling of the hormones of the female reproductive system starts with the hypothalamus (Sherwood, 2008). The hypothalamus, located in the brain, produces a hormone called gonadotropin-releasing hormone (GnRH) (Sherwood). This stimulates the anterior pituitary to release two hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH) (Newman, Takie, Klkkevold, 2006). FSH and LH have influences on the reproductive system of the female and directly and indirectly play an important role in estrogen and progesterone secretions from the ovaries that act on the uterus, which ultimately causes the menstrual cycle (Sherwood).

The monthly menstrual cycle of the hormones can be broken down into two phases. The first phase is called the ovarian cycle, which can be broken down into the follicular phase and the luteal phase (Johnson & Everitt, 2000). FSH is released from the pituitary gland and binds to FSH receptors that become present in late pre-antral amd early antral follicles (Johnson & Everitt, 2000). The binding of FSH to its receptor on the follicle stimulates it to secrete estradiol during its development (Newman, Takie, Klkkevold, 2006). The binding of FSH also stimulates the synthesis of follicular fluid, which causes the swelling of the follicle and the development of

the follicular antrum (Johnson & Everitt). The follicles not only secrete estradiol, they are also found to be responsible for 30-70% of the circulating androgens found in women (Johnson & Everitt).

It is found that there are two cell types that secrete hormones within the follicle (Johnson & Everitt). The cells of the theca interna are found to synthesize androgens, like testosterone and androstenedione, from the conversion of cholesterol and acetate (Johnson & Everitt). The granulosa cells of the follicles secrete estrogens, like estradiol (Johnson & Everitt). Granulosa cells are unable to form androgens (Johnson & Everitt). In fact, when exogenous androgens are present, the granulosa cells of the ovary have the ability to aromatize the androgens to estrogens (Johnson & Everitt).

Two days before ovulation, estradiol peaks and the oocyte of the dominant follicle is released from the ovary into the uterine tube (Newman, Takie, Klkkevold). The release of the follicle happens due to proteases that act on the ovary (Johnson & Everitt, 2000). This ends the follicular phase of the menstrual cycle.

Estradiol works at the cellular level within the gingival tissues through two different receptors, estrogen receptor alpha (ERα) and estrogen receptor beta (ERβ) (Nebel, Bratthall, Ekblad, Norderyd & Nilsson, 2011). When estradiol is present in system, it binds to these two receptors and this causes DNA synthesis to occur in the gingival tissue where the receptors are present (Nebel, Bratthall, Ekblad, Norderyd & Nilsson). In the study done by Nebel, Bratthall, Ekblad, Norderyd and Nilsson, it was determined that the ERβ receptor, not the ERα receptor, was found in all layers of the gingival epithelium as well as in the cells of the lamina propria (Nebel, Bratthall, Ekblad, Norderyd & Nilsson). The same was found in the healthy and diseased

tissue biopsies in regards to the receptors present (Nebel, Bratthall, Ekblad, Norderyd & Nilsson).

During this study, it was also found that high concentrations of estradiol reduced DNA synthesis 60-70% in the gingival tissue sites where the receptors are present (Nebel, Bratthall, Ekblad, Norderyd & Nilsson). Therefore, it was concluded that DNA synthesis occurs at low concentration of estradiol but not high concentrations of estradiol (Nebel, Bratthall, Ekblad, Norderyd & Nilsson). Two days before ovulation is when estradiol peaks during the follicular phase of the menstrual cycle (Newman, Takie, Klkkevold). According to the research study, it is during this time is when DNA synthesis is occurring in the gingival cells. However, when concentrations of estradiol are low, like during pregnancy when progesterone is high, that is when DNA synthesis is not occurring. During times when DNA synthesis is occurring, the rate of cellular turnover of the gingival epithelium is high. A high rate of turnover of any epithelium in the body means that the health of the tissue is maintained and bacterial invasion is low. Therefore, during the time when DNA synthesis is low, like during pregnancy, the rate that the tissue is turning over is lowered and the tissue becomes more susceptible to bacterial invasion.

The second phase of the menstrual cycle is called the luteal phase (Newman, Takie, Klkkevold, 2006). During this phase, the corpus luteum, which is the structure that forms after the dominant follicle ruptures from the ovary (Sherwood, 2008), begins secreting both progesterone and estradiol (Newman, Takie, Klkkevold). If fertilization occurs, the embryo will implant into the endometrium of the uterus, which has been developing for implantation through both the follicular phase and the luteal phase (Newman, Takie, Klkkevold). If implantation does not occur because the egg was not fertilized, the ovum will dissolve, the corpus luteum will

decrease in size, the hormone levels will drop, and the sloughing off of the endometrial tissue will ensue (Newman, Takie, Klkkevold).

During the menstrual cycle is when the differences between males and females are present in regards to periodontal health. The heightened hormones that women experience at the time of the cycle factor into how the tissues of the mouth react as well as how the bacteria found in periodontal diseases develop and mature (Newman, Takie, Klkkevold, 2006). During the time of menstrual bleeding, there is increased gingival bleeding and tenderness (Newman, Takie, Klkkevold). This increased activity of the bacteria and the bleeding there is a need for closer monitoring and maintenance (Newman, Takie, Klkkevold). During this time, it is sometimes suggested that women who have often experienced excessive postoperative hemorrhages or menstrual flow visit their primary care physician to get regular check ups since a risk of anemia is present (Newman, Takie, Klkkevold).

If implantation of a fertilized embryo does occur, the women will not experience the sloughing off of the endometrial lining, but will instead enter the 40 week gestation period that is termed pregnancy. The changes in hormones during pregnancy affects the ways in which periodontal diseases progress (Newman, Takie, Klkkevold, 2006). Pregnancy brings about changes in hormones and other normal body functions such as temperature and how the body facilitates nutrient intake. Because of these changes, there are risks are associated with having periodontal disease and being pregnant (Newman, Takie, Klkkevold).

In a study by Lopez, Smith, and Gutierrez (2002) done on pregnant women, periodontal infection was found to have a detrimental effect on the gestation period of the baby. It was correlated before the study began that preterm low birth weight might be caused by periodontal infection (Offenbacher, Katz, Fertik, Collins, Boyd, Maynor, et al, 1998). Researchers recruited

pregnant women who were then separated into two groups based on the level of their disease. One group of the women had gingivitis or mild periodontitis and had received the appropriate treatment before reaching 28 weeks of gestation (López, Smith & Gutierrez). The second group had gingivitis or mild periodontitis but did not receive any treatment during their pregnancy (López, Smith & Gutierrez).

The participant group contained a total of 881 women (López, Smith & Gutierrez, 2002). All of the women studied were between the ages of 18 and 35, were pregnant for the first time, and were pregnant 21 weeks or less (López, Smith & Gutierrez). Women with the following criteria were excluded from the study: diabetes, fewer than 18 teeth, or an indication of antibiotics because of some sort of invasive procedure (López, Smith & Gutierrez). The women that were excluded did not meet the minimum requirements in order to successfully participate in the study.

During the preliminaries, the examiners did initial measurements in the areas of oral hygiene status, probing depth, clinical attachment level measurements, and gingival inflammation (López, Smith & Gutierrez, 2002). The treatment of periodontal disease and gingivitis included sub-gingival scaling, which was performed by the clinician, and .12% chlorhexidine solution, an antiseptic mouthwash, was prescribed to the women to use once a day (López, Smith & Gutierrez). Per the parameters of the study, all treatment was completed for the women before they reached 28 weeks of gestation. In addition, required maintenance treatment was performed every 2-3 weeks until their babies were delivered (López, Smith & Gutierrez).

Four hundred and fifty-nine women actually received treatment during the study, while two hundred and sixty-three women did not (López, Smith & Gutierrez, 2002). The women who were not treated during the study either did not show up for the first appointment or did not meet

the minimum health requirements for the study (López, Smith & Gutierrez). All of the women were monitored every 4-6 weeks during their gestation to watch for any worsening or changes in the status of their disease (López, Smith & Gutierrez). Upon delivery, all of the women underwent treatment for their periodontal diseases (López, Smith & Gutierrez).

The results in this study showed correlations between periodontal disease and preterm birth. For this study, the definition of preterm birth used was the spontaneous labor or rupture of membranes before 40 weeks gestation (López, Smith & Gutierrez, 2002). Upon delivery, the women who had preterm low birth weight babies were found to have poor periodontal disease status. In addition this group of women had extended and more severe inflammation than women who went full term with their pregnancies (López, Smith & Gutierrez). Along with the correlation found between women with periodontal disease and preterm low birth weight births, it was also found that these women often had fewer than six pre natal visits, low maternal weight gain, and a previous abortion (López, Smith & Gutierrez). Another interesting finding was that the women who were considered overweight had a negative connection with preterm low birth weight babies, meaning that the women who were overweight had a lower risk of having a preterm birth (López, Smith & Gutierrez).

This study shows that periodontal disease is a risk factor for having a preterm low birth weight baby and may increase the chances of having either a low birth weight or preterm birth almost three fold (López, Smith & Gutierrez, 2002). However, the mechanism as to how periodontal disease causes preterm birth in the women with the disease is still under investigation. Another study suggested that the stimulation of the fetal membranes by the synthesis of prostaglandins may be induced by the infected gingival tissues, which may lead to preterm low birth weight (López, Smith & Gutierrez). Another hypothesis that has been studied

in relation to preterm low birth weight is that the endotoxins that are produced by the bacteria associated with periodontal disease may cause decrease fetal growth (López, Smith & Gutierrez).

After pregnancy, the menstrual cycle of the female resumes and its associated problems connected to periodontal disease with it. Around the age of 51, many women enter menopause (National Institute of Aging, 2008). This occurs because the amount of oocytes that the woman is born with is diminished and therefore the normal monthly cycling stops (Newman, Takie, Klkkevold, 2006). When this occurs, estrogen levels steadily drop and LH and FSH rise and the sex hormones fluctuate sporadically. This causes the irregular ovulation that occurs during the time called peri-menopause, which is also linked to unresponsiveness of the ovaries (Newman, Takie, Klkkevold).

Many oral changes occur during menopause. These changes include thinning of the mucosa, "burning mouth" syndrome, recession of the gingiva, changes in how food tastes, xerostomia, bone loss, and alveolar ridge resorption (Newman, Takie, Klkkevold, 2006). Another change that happens to some women during menopause is the development of a condition called menopausal gingivostomatitis (Steinberg, 2000). Like the other life stages of women, menopausal gingivostomatitis occurs due to a change in hormones and how the body reacts to the bacteria involved. This condition is associated with gums that are shiny and dry, bleed easily (Steinberg). The gingiva may range in color from pale pink to extremely red (Steinberg). Menopausal gingivostomatits is a treatable condition and with regular oral hygiene check ups, gingivostomatits can be cured (Steinberg).

Regular maintenance of periodontal disease and regular check ups are important throughout a women's lifetime and is critical during menopause and the time proceeding. Due to the many changes that occur during this time with hormones and the conclusion of the cycling

pattern, many other changes can occur in the body and having regular check ups is important for staying healthy post menopause.

A study conducted with postmenopausal women looked at the use of hormone replacement therapy (HRT) and how it affected the gingival tissues and the possible effects it may have on periodontal disease (Pizzo, Guiglia, Licata, Pizzo, Davis & Glullana, 2011). In this study, the clinical attachment level (CAL), the amount of supragingival plaque, probing pocket depth (PD), and the amount of bleeding on probing (BOP) was measured in both women on HRT and women not on HRT (Pizzo, Guiglia, Licata, Pizzo, Davis & Glullana).

In the areas of CAL and PD, it was found that there was no significant different between the HRT+ and HRT- women, however HRT+ women showed a significantly lower amount of BOP than women that were HRT- (Pizzo, Guiglia, Licata, Pizzo, Davis & Glullana). The researchers looked further into the cause of the differences in the amount of BOP between the two groups (Pizzo, Guiglia, Licata, Pizzo, Davis & Glullana).

One possible cause for the differences between the two groups in the area of BOP was the amount of plaque accumulation (Pizzo, Guiglia, Licata, Pizzo, Davis & Glullana). The amount of plaque accumulation again showed to have no significant difference between the HRT+ women and the HRT- women (Pizzo, Guiglia, Licata, Pizzo, Davis & Glullana).

The researchers in this study concluded that long-term HRT did not affect the periodontal disease status of postmenopausal women (Pizzo, Guiglia, Licata, Pizzo, Davis & Glullana). This study goes on to suggest that HRT does not prevent protection against a woman acquiring peridontal disease post menopause.

Unlike women, men do not have monthly cycling hormones. Due to this fact, periodontal diseases present differently in women than in men. Pre-menses is the first big change in

hormones and it is during this time is when the first signs of periodontal diseases show up like inflammation and infection in the gum tissues. During the regular cycling of hormones during the menstrual cycle, women will experience varying levels of symptoms from their periodontal disease, therefore requiring regular check up and maintenance for the disease by a dentist or periodontist. When women become pregnant, it is extremely important for women with the disease to seek regular periodontal maintenance to keep the risk of preterm low birth weight children low, as well as keep themselves healthy. The last big life stage that is reached by females is menopause. During this time, some women experience menopausal gingivostomatits, a periodontal disease that only affects the menopausal population of women, may develop. Like some of the other periodontal diseases, regular check ups and maintenance of the disease helps to keep the mouth healthy during these changes. Because women are so much different from men in the sense of their hormones and how their bodies react to the changes, special consideration for treating women with periodontal disease is needed.

Conclusion

Periodontal diseases are challenging to define given the number and variety of different oral diseases. This review sought to answer the question: How does a periodontal disease impact a woman throughout the life span? Specifically, this document discussed how, because of the cycling hormones and the effects those hormones have on the different bacteria, women's periodontal diseases differ from men's. Diseases of the mouth were first discovered during the Egyptian period and the information and knowledge about the different diseases advanced as time progressed. From here, non-surgical and surgical treatments were discussed and how each one is used to treat patients and their differing levels of disease. The main focus of this document went into the effects of periodontal disease on women through their life stages such as pre-

pubery, puberty, pregnancy, and menopause. The research into the differences between men and women pertaining to periodontal disease implicates that it is imperative for dentists and periodontist alike to take into consideration the sex of the patient when the treatments and care for the patient are being determined. An area that should be further researched is how menopause affects periodontal diseases, specifically how the bacteria involved play a part in the destruction of the tissue and the accelerated regression of the gum tissue in older patients.

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