Vascularity and the Hormonal Cycle in Female Classical Singers

D.M.A. Document

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Abstract

The female classical singer is a highly functioning vocal athlete who relies on extreme efficiency of her instrument to yield finely nuanced vocalism. Yet many of these singers endure dysphonia during the premenstrual days of the hormonal cycle. This document explores the existence of laryngopathia premenstrualis and its etiologies: not only the hormonal imbalance of high levels of progesterone and mid-level estrogen, but also the possible influence of increased vascularity and vascular congestion of vocal fold tissue. These components may give rise to increased risk of vocal pathologies. Further research into this topic will be proposed and supported.

Dedication

This document is dedicated to my husband, Carlos Monzón,

and in loving memory of my parents, Robert and Virginia Walker.

Acknowledgments

I am profoundly grateful to my advisor and mentor, Dr. Scott McCoy. Your guidance has been invaluable, without which this document would not have been possible. I greatly admire and respect your integrity, your knowledge, and your unfailing commitment to the edification of your students. I consider myself extremely fortunate to be one of them. Eternal esteem and gratitude to Dr. Robin Rice for his cultivation of my voice, for sharing his knowledge of the teaching of singing, and for navigating me through this degree and career path. You are priceless. Thank you to Regan Tackett and Julie Tucker for your editing eyes and brains, and for your unending friendship and support. My appreciation to Michelle Toth and Dr. Laura Matrka at the Ohio State University Voice and Swallowing Disorders Clinic, my professors at OSU, my advising committee, and to the OSU School of Music for an irreplaceable experience and education.

And last but most; undying love and thankfulness to my husband and children. Thank you for believing in me, cheering me on, lifting me up, and loving me always. Eloquence escapes me, there are no words. Thank you.

Vita

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Table of Contents

List of Tables

List of Figures

Chapter 1: Classical Singer as Vocal Athlete

Each year, Sports Illustrated releases a list of the "Fittest 50" athletes in the world, encompassing all areas of sports. Their panel of adjudicators includes sports performance experts, athletic trainers, and strength and conditioning coaches. They level the playing field and chose fifty men and fifty women at the top echelon of athletic ability. Athletes are judged based on their performances in the last year, the demands of their respective sports, their training regimens, and the following physical benchmarks: speed, strength, endurance, agility, flexibility, and power.[1] Could not the world's finest classical singers be adjudicated based on the exact same criteria?

Singers are in fact judged on the same physical benchmarks of the voice: speed of coloratura, power and strength of tone, stamina, agility, and flexibility of the voice. The most elite classical singers have extensive training regimens, vocal coaches and trainers that are experts in the field, and very demanding performance schedules to maintain. The classical singer is a highly functioning vocal athlete, relying on highly nuanced fine muscle coordination at the laryngeal level (in synchronization with the muscles controlling resonance and articulation in the vocal tract) as well as the muscles of respiration throughout the entire torso. Just as sports athletes train intensively to shave a few milliseconds off their fastest time, classical singers prepare rigorously for vocally and physically demanding roles, at times rarely

[1] "Sports Illustrated Fittest 50," Sports Illustrated, accessed May 21, 2019, https://www.si.com/specials/fittest50-2017/index.html.

leaving the stage during a four-hour opera, or perhaps performing a twenty-minute aria filled with vocal gymnastics, stretching the voice to its fullest capacity.

Consider the vocal load of the working classical singer. Between gigs, the professional is preparing for what comes next, perhaps an upcoming concert performance or an operatic role. These preparations could take place within a few weeks or a few months, depending on how engaged the singer is. The vocal load could include: one to two hours of daily practice, a weekly one-hour voice lesson, and anywhere from one to four hours per week with various vocal coaches to prepare diction, interpretation, and musical style, among other layers of nuance a performer strives to add to their craft. Once the singer arrives on the job, rehearsing a role can typically range from two to three weeks. This includes six to nine hours of rehearsal daily, parsed out in three-hour chunks with hour-long breaks. The week leading up to performances, rehearsals drop to approximately three to five hours per day. On performance day, the performer will generally rest the voice leading up to the event, which can range from two to four hours in length. Based on these estimations, the singer in preparation mode might train the instrument intensively up to seventeen hours per week. In rehearsal mode, general voice use could extend beyond a forty-hour work week. Performance mode raises the intensity of voice use to its highest level of functioning, but the time element drops dramatically to around six hours per week.

Female classical singers in particular are phonating at incredibly high frequencies compared to the rest of the singing population. Not only that, but the high frequencies are paired with high levels of subglottal air pressure and subsequently extended closure phases of

the vocal folds in order to create a sound that travels over a 100-piece orchestra to fill a 3,800-seat opera house, such as the Metropolitan Opera house, without amplification. Imagine the delicate balance taking place at the laryngeal level, but with what dynamic energy the laryngeal muscles have to be working in order to maintain such high frequencies for long periods and at such high decibel levels.

The vocal athlete undertakes years of physical training to hone their craft. Individually customized voice lessons and coachings focus specifically on their strengths and weaknesses, building the instrument's power, endurance, agility, and flexibility. A classical singer may study voice for ten plus years leading up to launching a professional career, and continue to study and coach privately throughout the entirety of that career. Classical vocal performers must keep a meticulous practice regimen to maintain and build vocal quality and efficiency.

> Vocal training can greatly enhance vocal efficiency. It has been noted that the larynges of trained singers age less rapidly. Trained singers can also compensate for many variations in physiologic or environmental conditions and can often produce a normal-sounding voice in the presence of laryngeal pathology, such as edema or nodules. The study of vocal mechanism in gifted or exceptional singers or speakers can demonstrate the range of human capacity and identify specific strategies to improve vocal efficiency in patients with inadequate phonation.[2]

This intensive physical training sculpts, defines, and strengthens the vocal musculature of the singer, similar to any athlete building other muscles of the body to boost their physical performance. Increased muscle tone and development not only enhances execution of skill, but also slows the aging process. Renowned otolaryngologist, head and neck surgeon, professional

[2] Gayle E. Woodson, "Research in Laryngology," in *Diagnosis and Treatment of Voice Disorders*, 3rd edition, ed. John S. Rubin, Robert Thayer Sataloff, and Gwen S. Korovin (San Diego: Plural Publishing, Inc., 2006), 146.

singer, and voice teacher Robert Thayer Sataloff says, "…the speaking voice changes expected with age in normal individuals do not appear to be as prominent (if they occur at all) in professional voice users."[3] Predictable vocal function decline and atrophy within the general population are not prevalent in active, trained singers.

Muscle definition and tone are indicative of increased blood flow to the active musculature. When a muscle is active, blood flow is amplified to bring more oxygen to the highly metabolic part of the body. "Muscles having strong oxidative metabolisms are dependent on blood flow for efficient function. Athletically trained muscles will have higher oxidative metabolisms."[4] A higher level of vascularity is the body's natural response to increased activity, and is a benefit to the working muscles, providing the amount of oxygen and fuel that the active muscles need to work effectively and efficiently. In a study of seventeen volleyball players, researchers aimed to quantify change in tendon vascularity due to intense activity of the musculotendinous unity. Tendons were imaged using Doppler sonography. Researchers found that moderate athletic exercise significantly improved the detection of tendon blood flow. Investigators determined that further examination into how much activity is required to see the maximum vascularity is needed, and from that research, a standardized protocol to image tendon vessels could be established.[5]

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[3] Robert Thayer Sataloff, "Molecular and Cellular Structure of Vocal Fold Tissue: Response," in *Vocal Fold Physiology: Frontiers in Basic Science*, ed. Ingo R. Titze (San Diego, Singular Publishing Group, 1993), 28.
[4] Donald S. Cooper, Lloyd D. Partridge, Fariborz Alipour-Haghighi, "Muscle Energetics, Vocal Efficiency, and Laryngeal Biomechanics," in *Vocal Fold Physiology*, 47.
[5] Jill L. Cook et al, "Is Vascularity More Evident After Exercise? Implications for Tendon Imaging," *American Journal of Roentgenology,* Volume 185 (2005): 1138-1140.

Just as a physician in sports medicine would supervise the prevention, management and rehabilitation of exercise related injuries in elite sports athletes, the professional classical singer must maintain a good relationship with their otolaryngologist in order to prevent or treat vocal pathologies that can arise throughout their careers. Two leading experts in the field of otolaryngology, Sataloff and Jean Abitbol, have researched and published extensively on vocal health and performance medicine. In his text *Professional Voice: The Science and Art of Clinical Care,* Sataloff states:

> The arts-medicine specialist is trained to recognize subtle differences in the supranormal to near-perfect range in which the professional performer's body must operate. To really understand performers, physicians must either be performers themselves or work closely with performers. In voice, this means a laryngologist working with a singing teacher, voice coach, voice trainer, voice scientist, speech-language pathologist, and often other professionals.[6]

Abitbol also supports the team approach when it comes to treating classical singers. He further explains the importance of listening to the singer's perception of their own voice. Due to the nuanced nature of a singer's fine motor control over their instrument, they will be more attuned to slight deviances of sound and quality. "When artists complain of a vocal problem, most of the time they are right. Which means that if I can't detect a pathology of the vocal cords, it doesn't mean that there isn't one, it simply means that I haven't found it."[7] Both doctors believe in a very communicative and supportive relationship between singer and doctor, in order to establish the best possible care for the top vocal athletes.

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[6] Sataloff, Mary Hawkshaw, "Performing Arts-Medicine and the Professional Voice User: Risks of Nonvoice Performance," in *Professional Voice: The Science and Art of Clinical Care*, 2nd edition, ed. by Sataloff (San Diego, Singular Publishing Group, 1997), 359.

[7] Jean Abitbol, *Odyssey of the Voice* (San Diego, Plural Publishing, 2006), 218.

When considering the years of physical training, the extensive vocal exercise regimens, the vocal load, and extreme physical benchmarks this population must maintain to be the best in their profession, classical singers truly are vocal Olympians. For all the display of strength and dexterity, the classical voice is a very sophisticated instrument dependent upon the intricate synchronization of breath pressure and detailed muscle coordination. Bearing in mind this delicate balance, female classical singers must also contend with the effects of hormones on the instrument. The next chapter will investigate this phenomenon.

Chapter 2: Female Hormonal Cycle in Singers

Much research has been done over the last forty to fifty years regarding the female hormonal cycle and its effects on the singing voice, yet there is still much to be discovered. Hormone levels vary wildly from woman to woman, as does each singer's individual instrument and vocal fold physiology. Some women suffer from premenstrual syndrome (PMS) whereas others do not. "There is no such phenomenon as an average period."[8] The following is a chart showing average hormone levels of estrogen and progesterone for men in comparison to women in the follicular phase[9] (first half of the cycle) and the luteal phase (second half) of the menstrual cycle. The range of estrogen in the follicular phase is wide, but the levels of estrogen and progesterone in the luteal phase have quite a large range.

Table 1: Base sex hormone concentrations:[10]

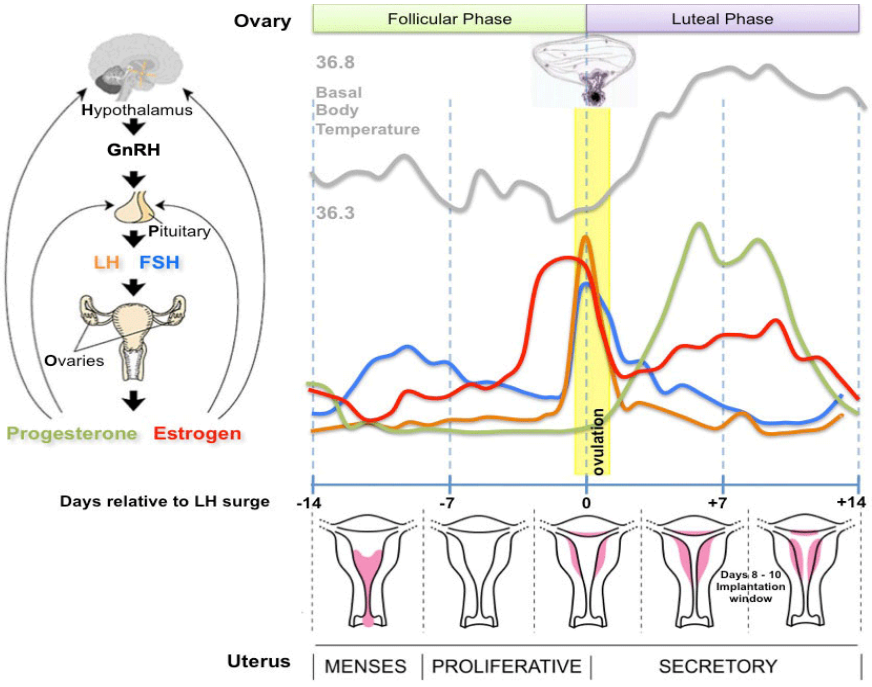
Hormone	**Male**	**Female follicular phase**	**Female luteal phase**
Estrogen ($pmol \cdot L^{-1}$)	22.0-88.1	36.7-183.5	440.4-1376.2
Progesterone ($pmol \cdot L^{-1}$)	<1.90	0.32-4.74	7.9-88.5

While there is no such thing as an average period experience, the average length of period is around 28 days (see Fig. 1). Day 1 is counted when menses actually begin. This is instigated by dramatic drop in levels of progesterone and estrogen. The uterus sheds its

[8] Dorothy Baldwin, *Understanding Female Sexual Health* (New York, Hippocrene Books, 1993), 58.
[9] Many of the discipline specific terms used in this text are defined in Appendix A.
[10] Nigel A.S. Taylor and Herbert Groeller, ed., *Physiological Bases of Human Performance during Work and Exercise* (London, Churchill Livingstone Elsevier, 2008), 214.

thickened lining, and there is "vasoconstriction of endometrial vessels, endometrial collapse, and epithelial desquamation" or peeling of the outermost layer of tissue.[11] Menses usually last around five days. The end of menses brings about the follicular phase in which follicles in the ovary mature, and estrogen levels begin to rise leading up to ovulation. During this phase (Days 5-13), a hormone secreted by the anterior pituitary gland called Follicular Stimulating Hormone (FSH) stimulates estrogen levels to rise. By Days 13-15, the estrogen level has peaked, which stimulates the anterior pituitary gland to release a sudden surge of Lutein Hormone (LH). This sudden surge of LH causes ovulation, the release of the egg from the ovary.

Figure 1. Menstrual cycle[12]



[11] Ofer Amir and Tal Biron-Shental, "The impact of hormonal fluctuations on female vocal folds," *Current Opinion in Otolaryngology and head and Neck Surgery,* Volume 12 (2004): 181.

[12] Mark Hill, University of New South Wales Embryology website, https://embryology.med.unsw.edu.au/embryology/index.php/File:Menstrual_cycle.png, accessed May 23, 2019.

Ovulation kicks off the second half of the menstrual cycle, the luteal phase, in which the uterus lining thickens to prepare for possible pregnancy. During Days 16-23 estrogen drops to around mid-level and plateaus, but can also fluctuate a bit. Progesterone level rises dramatically and peaks toward the end of this phase. Days 24-28 are the pre-menstrual days (still luteal phase). Progesterone and estrogen levels begin to drop. It is during this time that PMS symptoms can be experienced. When progesterone and estrogen have reached baseline levels, menses are instigated and the cycle begins again.[13]

The rapid drop of progesterone and estrogen in the pre-menstrual days can bring signs and symptoms of PMS. "Estrogen and progesterone affect all female-specific tissue, keeping it moist and plumped up. They stimulate the breasts to swell, cervical mucus to increase, the uterus lining to thicken, and so on."[14] The female body prepares for a possible pregnancy, but when progesterone levels fall, it is an etiology of premenstrual tension.[15]

The most common PMS symptom is fluid retention, the physiology and etiology of which will be discussed in detail later in this chapter. This fluid retention may lead to not only physical symptoms, but also emotional symptoms.

> In women the most common cause of generalized swelling (edema) is premenstrual fluid retention. The addition of several pounds of water which occurs gradually during the two- to ten-day length of time before menses may cause a variety of symptoms including swollen legs, breast fullness, pelvic ache, headache, nervousness, irritability, insomnia, and loss of concentration. These symptoms peak in intensity just before menses and [typically] cease abruptly after the onset of bleeding. Both the physical and emotional symptoms of PMS

[13] Baldwin, *Female Sexual Health*, 46.
[14] Ibid., 47.
[15] Taylor, *Human Performance*, 50.

> appear to have some biochemical basis related to the high level of hormones in the second half of the menstrual cycle, when the estrogen level is higher. Research indicates that an important factor is the ability of estrogen to partially block salt and water excretion by the kidneys. As a result, the body retains fluid. Some women experience congestion of the pelvic veins and feel this congestion as a dull, low abdominal aching pressure.[16]

The high levels of progesterone and estrogen ahead of the pre-menstrual days, followed by the rapid drop of those hormones during the pre-menstrual days may also lead to another PMS symptom. Digestive issues can occur due to vasodilatation of the blood vessels in smooth muscle. With the loss of tonicity of the esophagus, a bout or recurrence of gastric reflux can transpire.[17]

Another prevalent symptom of PMS is painful menstruation, even though it does not occur during the pre-menstrual days. Dysmenorrhea is the medical term for painful menstrual cramps caused by uterine contractions. Hormones produced in abundance during menstruation are prostaglandins. They are made by the uterus and other body tissues. Prostaglandins control the contractions of blood vessels and smooth muscle in the uterus and digestive tract.[18] "Women with primary dysmenorrhea tend to be extra-sensitive to prostaglandins. The uterus contracts too strongly and cramping pains are felt. Because prostaglandin constricts the blood vessels, it can upset blood flow and cause the headaches, hot and cold flushes, diarrhea, and nausea of dysmenorrhea."[19] Prostaglandins are produced in large quantities as the uterus lining

[16] Bruce D. Shephard and Carroll A. Shephard, ed., *The Complete Guide to Women's Health, Third Revised Edition* (New York, Plume, 1997), 477.
[17] J. Abitbol, *Odyssey of the Voice*, 221.
[18] Baldwin, *Female Sexual Health*, 49.
[19] Ibid., 49.

thickens in the days leading up to menses. When the uterine lining breaks down during menstruation, the large amounts of prostaglandins are released and can circulate in the blood stream, causing headaches, and sometimes severe gastric distress. It is for this reason that the most effective treatment of dysmenorrhea is prostaglandin inhibitors such as Ibuprofen. "Although menstrual cramps are widely believed to be due to an imbalance between estrogen and progesterone prior to menstruation, it is clear that the pain is prostaglandin-mediated."[20] Taken a few days ahead of menses, this can reduce prostaglandin levels and prevent them from circulating in the blood.[21]

For female classical singers, PMS symptoms can extend beyond those common to most women to affect the vocal folds as well. Laryngopathia premenstrualis is a medical term describing vocal dysfunction characterized by decreased vocal efficiency ahead of menses. This symptom may not be noticed at all by a non-singer; however, for the highly functioning manner in which female classical singers use their vocal apparatus, these changes in the voice will not go unnoticed. It is a very common condition that is usually more apparent to the singer than to the listener. The etiologies are physiological, anatomic, and psychological alterations secondary to endocrine changes.[22] These symptoms were medically observed in singers as early as 1974, as noted here by Leo Van Gelder in an article in the *Journal of Communication Disorders*; a time

[20] Sataloff, Kate A. Emerich, and Cheryl A. Hoover, "Endocrine Dysfunction," in *Vocal Health and Pedagogy*, ed. by Sataloff (San Diego, Singular Publishing Group, 1998), 169.
[21] Baldwin, *Female Sexual Health*, 51.
[22] Sataloff, "Care of the Professional Voice," in *Performing Arts Medicine, Second Edition*, ed. Sataloff (San Diego, Singular Publishing Group, 1998), 152.

when many European opera houses allowed 'grace days' of rest for female singers ahead of their menses.

> It is mainly singers who complain of voice changes just before and during menstruation. The voice varies from dull and colorless to raucous and hoarse. In some cases, there is some hyperemia [an excess of blood in the vessels supplying an organ or other part of the body], edema or even hemorrhage of the vocal cords. It is also possible that forced singing may cause small hematomas [a solid swelling of clotted blood within the tissues] of the vocal cords to extend.[23]

It is of interest to compare and contrast the differences in the female voice at ovulation to signs of laryngopathia premenstrualis ahead of menses. During the follicular (ovulatory) phase, estrogen is high and progesterone is low. Abitbol, et al. conducted fascinating research connecting physiological changes of cervical mucosa to similar changes in laryngeal mucosa. "Estrogens cause thickening of the endometrial mucosa and an increase in the secretions of the endocervical glandular cells. A similar hormonal effect is noted in the laryngeal mucosa, with an increased secretion of the glandular cells above and below the vocal fold edges."[24] High levels of estrogen cause cervical and laryngeal mucus to become thin, watery, stretchable, and abundant.[25] The perceived aural effects, as well as visual effects as seen by laryngoscope, on the voice were noted by Jean Abitbol.

> The estrogens secreted by the ovaries have different implications for the larynx. They result in a slight thickening of the cordal mucous membrane, which creates greater vibratory amplitude. The voice acquires a good timbre. The desquamation of superficial cells is reduced, accompanied by a decrease in the

[23] Leo Van Gelder, "Psychosomatic Aspects of Endocrine Disorders of the Voice," *Journal of Communication Disorders*, Volume 7 (1974): 258.
[24] J. Abitbol, Patrick Abitbol, and Béatrice Abitbol, "Sex hormones and the female voice," *Journal of Voice*, Volume 13, Issue 3 (1999): 435.
[25] Amir and Biron-Shental, *Current Opinion in Otolaryngology,* 180.

> need to clear one's throat and in the amount of laryngeal mucous fluid. The lipid cells under the cordal mucous membrane are stimulated. The voice becomes more supple.[26]

That supple voice quality can change drastically when the combination of high levels of estrogen and progesterone are at work on the body, followed by a rapid decline to baseline levels.

Similar to the most common of PMS symptoms, vocal fold edema is the most prevalent of laryngopathia premenstrualis symptoms, due to increased vascularity (blood volume) and fluid retention. Swelling increases stiffness of the vocal folds and compromises flexibility of the mucosal wave. According to Sataloff, "The human voice is extremely sensitive to endocrinologic changes. Many of these are reflected in alterations of fluid content of the lamina propria just beneath the laryngeal mucosa. This causes alterations in the bulk and shape of the vocal folds and results in voice change."[27] In the chapter entitled "Endocrine Dysfunction" in Sataloff's text *Vocal Health and Pedagogy*, the authors explore not only the hormones' affect on fluid retention in the vocal folds, but also its affect on the vascularity of the tissue of the vocal tract.

> The premenstrual estrogen/progesterone combined activity causes vasodilatation by relaxing smooth muscles, thereby increasing blood volume. These changes result in engorgement of vocal fold blood vessels, and vocal fold edema. In addition, polysaccharides break down into smaller molecules in the vocal folds and bind water, increasing fluid accumulation. Aldosterone contributes to cyclical salt and water retention as well. Vasodilatation also causes changes in nasal patency, self-perception, and possibly concentration.[28]

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[26] J. Abitbol, *Odyssey of the Voice*, 214.
[27] Sataloff, "Care of the Professional Voice," *Performing Arts Medicine*, 152.
[28] Sataloff, Emerich, and Hoover, "Endocrine Dysfunction," *Vocal Health and Pedagogy,* 169.

Physiological changes of the vocal fold vasculature during the premenstrual days appear to contribute to vocal fold edema as much as fluid retention. It could be considered that perhaps change in vocal fold vascularity is the *etiology* of fluid retention that leads to vocal fold edema. The connections between vocal fold vasculature and the menstrual cycle will be further explored in later chapters.

Fluid *within* the vocal fold tissue is not the only fluid that is affected by these hormonal shifts. Mucus covering the vocal fold mucosa that is used to lubricate the folds during phonation also undergoes a change in texture, thereby affecting the efficiency of the mucosal wave and influencing the sound of the voice. High levels of progesterone decrease glandular activity. This has an antiproliferative effect on the vocal fold mucosa; mucus secretions become more viscous, more acidic, dryer, and opaquer as a result.[29]Lubrication of the vocal folds is lost and the need to clear one's throat can be overwhelming.

To summarize the signs of laryngopathia premenstrualis, Jean Abitbol states, "During the premenstrual period, the dryness of the vocal folds, the increase in the acidity level (often exacerbated by an esophageal reflux common at this time), the reduced tonicity of the laryngeal muscle, edema of the vocal folds, and venous dilatation of the microvarices all combine to cause a vocal premenstrual syndrome."[30] These symptoms are presented due to the relationship between high levels of both estrogen and progesterone. Edema presents in the interstitial tissues and in Reinke's space, the virtual space located between the vocal muscle

[29] Amir and Biron-Shental, *Current Opinion in Otolaryngology*, 180.
[30] J. Abitbol, P. Abitbol, and B. Abitbol, "Sex hormones and the female voice," 435.

and the free edge of the vocal fold that allows the sliding of the mucosa over the muscle and vocal ligament during the mucosal wave. Increased episodes of gastroesophageal reflux are present. This acid reflux may cause a posterior laryngitis with edema of the posterior third of the vocal folds and reduced mobility of the cricoarytenoid joints. Dilatation of the microvarices may be complicated by small ruptures leading to a hematoma. This explains why vocal professionals should abstain from taking aspirin or other blood thinners, especially at this time. This combination of dryness, reflux, capillary fragility, and edema can cause not only posterior laryngitis, but also a host of other problems that will be explored later in this document.

The resulting symptoms of dysphonia due to this premenstrual vocal syndrome can appear minor (or altogether nonexistent) to a non-singer, but are extremely noticeable to a professional voice user. However, research performed on non-singing female subjects has shown an overall lowered fundamental frequency. "When the level of estrogens declines sharply after the 21st day of the intermenstrual interval a breakdown of these molecules into smaller units occurs; these units are also water-binding. Together with increased permeability of small blood vessels this increases the vibrating mass of the vocal cords, which results in a lowering of pitch and in huskiness."[31] Loss of upper register is commonly experienced. This includes not only a loss of high tones, but can also consist of loss of control of the upper register. Female singers complain of inability to perform a *messa di voce* or sing pianissimo in that area of the voice; the low tones are rarely affected. Other widespread complaints include

[31] Friedrich S. Brodnitz, "Hormones and the Human Voice," *The NATS Bulletin*, Volume 47, Issue 2 (1971): 186-187.

vocal fatigue, slight hoarseness, slower response time of the instrument, and muffled voice, "loss of certain high harmonics, with a more metallic and huskier voice."[32]

> Most of the voice-related negative effects of hormonal changes associated with the menstrual cycle occur in the pre- or early-menstrual days. Excess loading of the vocal folds with fluid changes their mass and thus may affect vibratory behavior. This is usually not problematic for the average speaker but may present a problem for the professional singer. Submucosal hemorrhages in the larynx are not uncommon. Diuretics should be avoided because they do not free the protein-bound submucosal fluid and may have irritating drying effects on airway tissues. There are no drugs available to counteract the normal physiological effects of the menstrual period or pregnancy, and voice therapy is of no value in these cases.[33]

Dysphonia due to changes in vocal fold physiology unfortunately is not the only concern regarding the female classical singer's instrument. Compromised breath support is commonplace to singers suffering from PMS symptoms. This can be attributed to menstrual cramping, back pain, diarrhea, and also the loss of tone in all striated muscles due to venous dilatation. Loss of muscle tone can affect the vocal muscles, the abdominal muscular belt, as well as the intercostal muscles, resulting in reduced pulmonary power.[34] "Muscle cramping associated with menstruation causes pain and compromises abdominal contraction. This undermines support and makes singing or projected speech (acting and public speaking) difficult and potentially dangerous. Dysmenorrhea is also associated with diarrhea and low back pain, which further impair support."[35] When one considers the necessity of the elite vocal

[32] J. Abitbol, P. Abitbol, and B. Abitbol, "Sex hormones and the female voice," 435.
[33] Raymond H. Colton, Janina K. Casper, and Rebecca Leonard, *Understanding Voice Problems: A Physiological Perspective for Diagnosis and Treatment, Fourth Edition* (Baltimore, Lippincott Williams & Wilkins, 2011), 324.
[34] J. Abitbol, P. Abitbol, and B. Abitbol, "Sex hormones and the female voice," 438.
[35] Sataloff, Emerich, and Hoover, "Endocrine Dysfunction," *Vocal Health and Pedagogy,* 169.

athlete to have complete use of their faculties in order to support their rigorous level of vocal fold activity, being vocally compromised can be detrimental to a high-level performing career.

There are many research studies supportive of the signs and symptoms of laryngopathia premenstrualis in the literature. The most ground-breaking was done by Jean Abitbol, et al., published in the *Journal of Voice* in 1989.[36] Researchers studied 38 female subjects, aged 21-40 years; all were professional voice users not taking hormonal contraceptives. Twenty-two of the 38 subjects presented with vocal premenstrual syndromes: hoarse voice and increase of voice fatigue as measured by Dynamic Vocal Exploration (DVE). DVE is a trifold method of observation and measurement: spectrograph (acoustic), stroboscopy (visual), and EGG (glottographic). Researchers determined that voice changes from estrogen and progesterone secretion are associated with water retention, edema of the interstitial tissue, and venous dilatation.

Jean Abitbol, et al. followed up this study with another one published in the *Journal of Voice* ten years later.[37] Researchers studied 97 female voice professionals, aged 23-36, over the course of three complete menstrual cycles. All subjects chosen presented with premenstrual dysphonia. The vocal folds viewed via DVE during the premenstrual period showed congestion, microvarices on the superior surface of both vocal folds, edema of the posterior third of the vocal folds, posterior chink, and a loss of its vibratory amplitude. All 97 women showed signs of vocal muscle atrophy, reduction in the thickness of the mucosa and reduced mobility in the cricoarytenoid joint. This study also confirms physiologic effects of hormones on the vocal folds,

[36] J. Abitbol, et al., "Does a Hormonal Vocal Cord Cycle Exist in Women? Study of Vocal Premenstrual Syndrome in Voice Performers by Videostroboscopy-Glottography and Cytology on 38 Women," *Journal of Voice*, Volume 3, Issue 2 (1989): 157-162.
[37] J. Abitbol, P. Abitbol, and B. Abitbol, "Sex hormones and the female voice," 424-446.

concordant with hormone testing, visually confirmed vascular changes of the vocal folds, and premenstrual dysphonia as experienced by the subjects and confirmed via acoustic measurements. The results determined by this study are trifold: 1) **mucosal** (in all 97 subjects) – edema of vocal mucosa and thickened and diminished glandular secretion (reduced supraglottic and subglottic secretions led to dryness of the larynx) resulting in impairment of amplitude, 2) **vascular** (in 71 subjects) – premenstrual dilatation of microvarices with reactionary edema, submucosal vocal fold hematoma in 13 subjects, vocal fatigue, and associated posterior chink, and 3) **muscular** (in 59 subjects) – decreased muscular tone, diminished power of contraction of the vocal muscle resulting in decreased range.

In 2001, Sung Won Chae, et al. published an acoustic study in the *Journal of Voice* on 28 women (non-singers), aged 21-30 years.[38] Researchers studied the subjects for two menstrual cycles, taking acoustic measurements mid-cycle (around ovulation) and two to three days before menstruation. Subjects reported normal cycles and were not taking birth control pills. In subjects presenting with PMS symptoms, jitter (perturbation in frequency) was significantly increased during the premenstrual phase in comparison to the follicular phase. Vocal fold edema produces an increase in jitter value and decrease in fundamental frequency of the speaking voice.

[38] Sung Won Chae, et al., "Clinical Analysis of Voice Change as a Parameter of Premenstrual Syndrome," *Journal of Voice*, Volume 15, Issue 2 (2001): 278-283.

Another study published in the *Journal of Voice* in 2007 was conducted by Maree Ryan on twenty-two female classical singers and 6 male singers as a control group.[39] Singers took record of their basal body temperature, moods, level of fatigue, and perceived vocal quality in a daily journal. Singers took audio recording of part of an aria at three points in their cycle: premenstrual, ovulatory, and luteal phases. Fatigue was lowest on Day 1 of menses, and perceived vocal quality was lowered from Day 24 – Day 4 of next cycle. Most factors of vocal quality affected were pitch, range, vocal fatigue, and vocal control.

There are many more scientific studies yielding results supportive of the presence of laryngopathia premenstrualis in premenstrual women. The following are two quite comprehensive literature reviews for reference. Filipa Lã has conducted a great deal of research on human subjects exploring the effects of pregnancy and hormonal birth control on the female classical singing voice. Her literature review was published in *Research Studies in Music Education* in 2005.[40] Dhanshree Gunjawate, et al. recently published a very inclusive literature review in the *Journal of Voice* in 2017, "The Effect of Menstrual Cycle on Singing Voice: A Systematic Review."[41]

The signs and symptoms of premenstrual vocal syndrome are present and objectively measured, but the larynx does not secrete sex hormones; neither does its neighbor, the thyroid. What makes it such a hotspot of hormonal activity? "All hormonal activity needs a

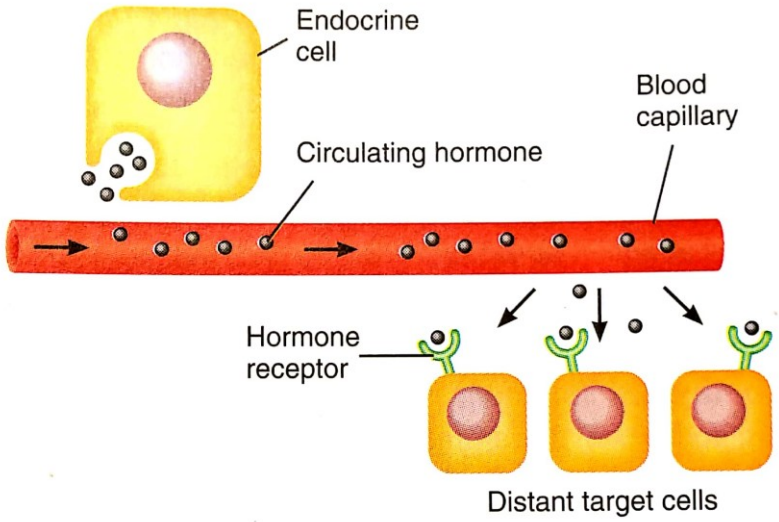
[39] Maree Ryan and Dianna T. Kenny, "Perceived Effects of the Menstrual Cycle on Young Female Singers in the Western Classical Tradition," *Journal of Voice*, Volume 23, Issue 1 (2009): 99-108.
[40] Filipa Lã and Jane W. Davidson, "Investigating the Relationship Between Sexual Hormones and Female Western Classical Singing," *Research Studies in Music Education*, Volume 24 (2005): 75-87.
[41] Dhanshree R. Gunjawate, et al., "The Effect of Menstrual Cycle on Singing Voice: A Systematic Review," *Journal of Voice,* Volume 31, Issue 2 (2017): 188-194.

target organ or target cells with specific receptors."[42] The larynx is a target organ for sex hormones containing receptors specific to each sex hormone.

It is helpful at this point to know a few basic principles about endocrinology and how hormones travel in the blood to reach their respective destination points in the target organs. (See Figure 2.)

> Most water-soluble hormone molecules circulate in the watery blood plasma in a "free" form (not attached to other molecules), but most lipid-soluble hormone molecules are bound to transport proteins. In general, 0.1-10% of the molecules of a lipid-soluble hormone are not bound to a transport protein. This free fraction diffuses out of capillaries, binds to receptors, and triggers responses. As free hormone molecules leave the blood and bind to their receptors, transport proteins release new ones to replenish the free fraction.[43]

Figure 2. Hormone circulation[44]

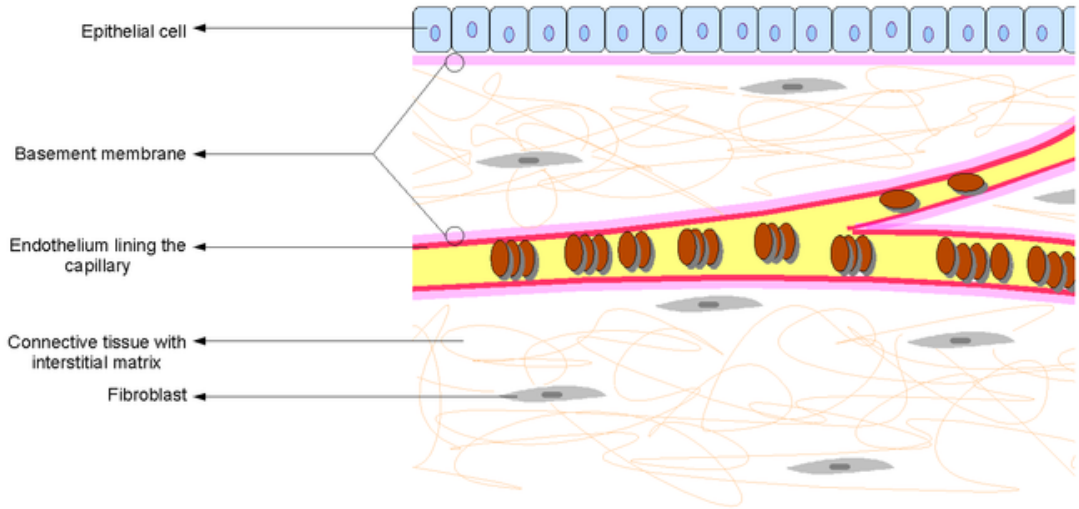


[42] J. Abitbol, *The Female Voice,* PDF e-book, (San Diego: Plural Publishing, 2019), 71.
[43] Gerard J. Tortora and Bran Derrickson, *Principles of Anatomy and Physiology,* 12th edition (Hoboken, NJ, John Wiley & Sons, Inc., 2009), 646.
[44] Tortora and Derrickson, *Anatomy and Physiology,* 645.

Estrogen and progesterone are both lipid-soluble hormones. Both hormones are secreted by the ovaries and enter the blood stream searching for target cells within target organs. They travel to their respective receptor cells in the vocal fold mucosa by moving through the permeable capillary walls into the interstitial fluid (also known as interstitial space). This interstitial fluid is a conduit between the capillaries and the body tissue and cells. It is the medium through which oxygen, carbon dioxide, hormones, salt, sugar, neurotransmitters, fatty acid, and water may all travel.[45] The vocal fold mucosa ground substances have a very high viscosity of aqueous solution. That solution includes a large proportion of extracellular interstitial spaces which provide viscoelasticity to the tissue and "are key components for structural maintenance and viscoelasticity of the superficial layer of the lamina propria of vocal fold mucosa as vibrating tissue." [46] The figure below shows the interstitial fluid in relation to the capillaries, epithelium, and connective tissue.

[45] Mark A. Creager, et al., *Vascular Medicine: A Companion to Braunwald's Heart Disease* (New York, Saunders Elsevier, 2006), 845.
[46] Kiminori Sato, "Functional Fine Structures of the Human Vocal Fold Mucosa," *Diagnosis and Treatment of Voice Disorders*, 3rd edition, ed. John S. Rubin, Robert T. Sataloff, and Gwen S. Korovin, (San Diego: Plural Publishing, Inc., 2006), 50.

Figure 3. Interstitial space[47]



Interstitial fluid "is largely an ultrafiltrate of blood. Its rate of production reflects the balance between factors that favor filtration out of capillaries and those that favor reabsorption."[48] Nutrients necessary to the tissue cellular matrix travel via the bloodstream, through capillary walls, to reach the interstitial space. Excess interstitial fluid and waste pass into the lymph stream and become lymph. Creager, et al. describe the relationship between interstitial fluid and the lymphatic system.

> The volume and the composition of the interstitial fluid are kept in balance by the lymphatic system. The functions of that system include (1) transport of excess fluid, protein, and waste products from the interstitial space to the blood

[47] Lumen: Boundless Anatomy and Physiology website, https://courses.lumenlearning.com/boundless-ap/chapter/body-fluids/, accessed on May 25, 2019. This work is licensed under the Creative Commons Attribution-ShareAlike 4.0 International License. To view a copy of this license, visit http://creativecommons.org/licenses/by-sa/4.0/ or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA.

[48] Creager, et al., *Vascular Medicine*, 845.

> stream; (2) distribution of immune cells and substances from the lymphoid tissues to the systemic circulation; (3) filtration and removal of foreign material from the interstitial fluid; and (4) in the viscera, to promote the absorption of lipids from the intestinal lumen.[49]

These principles relative to endocrinology and hormone transport in the blood become important when focusing on the larynx as a hormone target organ containing estrogen and progesterone receptors.

There are many research studies supportive of the presence of sex hormone receptors in the vocal folds. The 1989 study by Jean Abitbol, et al. was previously reviewed in regards to the presence of laryngopathia premenstrualis in twenty-two of the 38 female subjects. The most fascinating facet of this study are the vocal fold and cervical smears taken of those twenty-two subjects. Vocal fold smears were taken at ovulation and premenstrual phase for two consecutive cycles. Cervical smears were taken from nine of the 38 women on the same day their vocal fold smears were performed. Scientists could visually not tell the smears apart; they appeared *identical*. All twenty-two subjects had luteal deficiency as confirmed by vocal fold smear. Luteal deficiency means the female body does not produce enough progesterone to maintain a pregnancy if one should occur, which indicates a hormonal imbalance. In all nine subjects, cervical smears were identical to vocal fold smears at *both* points of the cycle. Discussing his research study, Jean Abitbol states,

> By 1982, receptors for estrogen hormones had been identified on the vocal cords and in the uterus. These separate objective findings were confirmed by J. Abitbol et al. in 1986 and 2004 by comparative studies of smears taken from the

[49] Ibid., 845.

> vocal cords and the cervix of the uterus, during the same day of the menstrual cycle. Given that both have the same type of mucous membrane, it is only logical that they should have the same cyclical impact. This is consistent with the observation that the voice can change with the menstrual cycle.[50]

Scott-Robert Newman, et al. from the University of Utah Health Sciences Center published their study on deceased human subjects in the *Journal of Voice* in 2000.[51] Researchers performed immunohistochemical staining of the vocal folds of 42 males and females, aged 2mo – 82 years. They found hormone receptors in the nucleus and cytoplasm of cells in the vocal folds. There were statistically significant differences in gender and age distribution. Researchers evaluated the overlying epithelium, lamina propria, and glandular tissue: androgen, estrogen, and progesterone receptors were identified within the human vocal fold tissue: epithelial cells, glandular cells, and fibroblasts. Newman, et al. state, "Hormonal activity is a likely contributor to the normal homeostasis in the lamina propria and understanding its role may help us understand conditions in which homeostatic balance has been disrupted.[52] The action of hormones on voice or the effect of withdrawal of hormones on voice is a complex issue that depends not only on serum concentration of hormones, but also on concentration of hormone receptors and the cellular biology once the receptors have been activated."[53]

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[50] J. Abitbol, *Odyssey of the Voice*, 215.
[51] Scott-Robert Newman, et al., "Preliminary Report on Hormone Receptors in the Human Vocal Fold," *Journal of Voice*, Volume 14, Issue 1 (2000): 72-81.
[52] Ibid., 73.
[53] Ibid., 80.

In 2013, Jan W. Brunings, et al. performed immunohistochemical staining of surgically excised benign vocal fold lesions of 37 female patients, aged 18-78 years. [54] Researchers examined surgically excised lesions of the vocal folds, including polyps, cysts, granulomas, nodules, laryngoceles, and Reinke's space edema. They found the estrogen and progesterone receptor staining were mainly in fibroblasts next to small vessels and more prominent in specimen from laryngeal edema. Brunings, et al. state, "Our results though, only showed estrogen receptor and progesterone receptor expression in edema and laryngocele tissue. Because the goal in these types of surgery is minimal damage surgery, it was not possible to harvest great amounts of tissue for histopathological studies."[55] Research indicated that estrogen and progesterone receptors are expressed in the larynx of the female human vocal fold in conjunction with edema.

In a study published in the *Journal of Voice* in 2016, Tolga Kirgezen, et al., took immunohistochemical staining of the vocal folds of 42 deceased male (21) and female (21) subjects.[56] Researchers examined androgen, estrogen, and progesterone receptors in the epithelium, superficial layer of the lamina propria, vocal ligament, and macula flava of the vocal folds, and found most sex hormone receptors within the macula flava and the vocal ligament. Maculae flavae are located at the anterior and posterior edges of the membranous parts of the bilateral vocal folds. "The maculae flavae play a necessary role in the extracellular matrix to

[54] Jan W. Brunings, et al., "The Expression of Estrogen and Progesterone Receptors in the Human Larynx," *Journal of Voice,* Volume 27, Issue 3 (2013): 376-380.
[55] Ibid., 379.
[56] Tolga Kirgezen, et al., "Sex Hormone Receptor Expression in the Human Vocal Fold Subunits," *Journal of Voice*, Volume 31, Issue 4 (2016): 476-482.

provide the viscoelastic characteristics of an adult's vocal fold lamina propria.[57] Therefore, these areas may affect the development of the vocal folds as well as the gender-related variations observed in the vocal folds."[58]

The million-dollar question is, what does this mean for female classical singers? The answer is – edema. *Imbalance* in forces (hormone levels) governing fluid transfer from blood capillaries to the interstitial space, and from lymphatic capillaries to interstitial space, give rise to the formation of edema.

> ESTROGEN increases CAPILLARY PERMEABILITY and allows the passage of INTERCAPILLARY FLUIDS to the INSTERSTITIAL SPACE. PROGESTERONE decreases CAPILLARY PERMEABILITY, thus trapping the extracellular fluid out of the capillaries and causing TISSUE CONGESTION [edema]. This congestion is quite apparent in the breasts, in the lower abdominal and pelvic tissues, as well as in the VOCAL FOLDS, where it causes PREMENSTRUAL DYSPHONIA.[59]

The dysphonic symptoms of laryngopathia premenstrualis felt by female classical singers and not necessarily seen by their otolaryngologists are caused by an imbalance of estrogen and progesterone during the premenstrual days. This imbalance affects the vocal folds at the cellular level between the blood and the interstitial fluid to create edema that stiffens the vocal folds, not allowing the expected lengthening to reach the uppermost pitches in the singer's range, loss of flexibility, slow response time, and a thicker, huskier, possibly hoarse quality to the voice. Jean Abitbol summarizes the process neatly in *Odyssey of the Voice*:

[57] Ibid., 476.
[58] Ibid., 481.
[59] J. Abitbol, *The Female Voice*, 98. Capitalization added by Monzón for emphasis.

> Progesterone also brings on a slight decrease in the muscle tone of the vocal cords, and it diminishes, and may even inhibit, the permeability of capillaries. This causes the extravascular fluid, that is, fluid outside the blood vessels, to stagnate in the tissues of the vocal cords, bringing on an edema of the vocal cords, which remain swollen during the week prior to menses. It is thanks to the estrogens that the intravascular fluid is transferred to the extravascular spaces in the surrounding tissues. Then, when progesterone is secreted, if the balance between the two hormones is satisfactory, the interstitial fluid will be well distributed. The edema of the vocal cords will be minimal. If, on the contrary, this is not the case, the progesterone will prevent the return of the interstitial fluid to the vessels, causing an edema to form. The progesterone in this instance closes the door of the capillaries and prevents them from draining the tissues. This imbalance between estrogens and progesterone causes a cyclical edema in the last week of the menstrual cycle, caused by, the accumulation of interstitial fluid in the vocal cords.[60]

It has been established up to this point that imbalance in the levels of estrogen and progesterone ahead of menses leads to edema of the vocal folds, due to the presence of estrogen and progesterone receptors in the vocal folds, making the larynx a target organ for hormonal activity. This edema results in premenstrual dysphonia for many female classical singers, the elite of vocal athletes. Their elite vocal status is evidenced by the physical demands placed upon their instruments, and the nuance necessary to execute those musical demands. What happens to the active muscles of athletes when exercised frequently? The physiology of these muscles will be explored at the vascular level in the following chapter.

[60] J. Abitbol, *Odyssey of the Voice*, 216.

Chapter 3: Increased Vascularity

Increased vascularity is a coveted look in the world of bodybuilding, with bulging veins prominent over the entire torso and limbs. A simple search on the Internet yields many articles boasting Six Ways to Boost Vascularity, or How to Get More Vascular in Four Easy Steps, et cetera. The medical definition of vascularity is the quality or state of being vascular, which is defined by Merriam-Webster Dictionary as: supplied with or containing ducts and especially blood vessels.[61] What does it mean to be "vascular" or have "increased vascularity", and why is that important to singers? To answer the former question, increased vascularity is the amplified existence of veins in the tissue. The latter question remains to be answered, more research is necessary, but based on anatomical evidence, one can speculate and hypothesize. That is where new research begins, is it not? "Anatomic evidence can only *suggest* function; therefore, any description of laryngeal function based on anatomy must be *speculative*."[62]

Due to the vocal athlete's advanced level of laryngeal function, it poses the question: will a classical singer's vocal folds have increased vascularity, similar to the limbs of an Olympian runner? Exercise has been proven to increase capillarity in active muscles, and it is an interesting notion to consider increased blood flow to the classical singer's main muscles and tissues of phonation and how it affects performance. Furthermore, how does this affect the premenstrual classical singer? But first, a few basic principles of vascularity and blood flow will be considered.

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[61] Vascular definition, Merriam-Webster Medical Dictionary website, https://www.merriam-webster.com/dictionary/vascular#medicalDictionary, accessed on May 25, 2019.

[62] Ira Sanders, "The Microanatomy of the Vocal Fold Musculature," *Diagnosis and Treatment of Voice Disorders,* 63.

Regarding blood flow regulation, the circulatory system is closed; blood is incompressible. Blood volume cannot change rapidly. Therefore, sudden constriction of a blood vessel in one area of the body must always be accompanied by opposite dilation of another part of the circulatory system. However, if constriction is sustained, total blood volume changes can occur slowly with the interstitial fluid, or by changes in fluid excretion by the kidneys.[63]

Blood viscosity, the thickness of the blood, does not remain constant. It depends mostly on the ratio of plasma (fluid) volume to red blood cells. Blood viscosity can change depending on a number of factors, including dehydration or polycythemia (an unusually high number of red blood cells), even body temperature. Any condition that increases the viscosity of blood thus increases blood pressure. The higher the viscosity of the blood, the higher the vascular resistance.[64]

Arterioles are small arterial branches that lead to capillaries. These vessels have a great capacity to regulate blood flow and change their vascular resistance by decreasing and increasing their diameters. The walls of the arterioles are very muscular. They respond to hormonal, nervous, and local control mechanisms that can "constrict so intensely as to almost completely block blood flow, or dilate the vessels to increase blood flow as much as twenty times normal."[65] Arterioles are generally vascular compliant. The more easily a vessel can be distended by pressure, the greater the level of vascular compliance.

[63] John E. Hall, and Thomas A. Adair, *Physiology* (Philadelphia, Lippincott-Raven Publishers, 1998), 87.
[64] Tortora and Derrickson, *Anatomy and Physiology,* 773.
[65] Hall and Adair, *Physiology*, 91.

Vascular resistance is related to how hard the heart has to work to circulate the blood through the body; it is the opposition to blood flow due to friction between the walls of blood vessels and the blood itself. This resistance depends on total length of the blood vessel, blood viscosity, and the size of the blood vessel lumen.[66] "If the viscosity is increased (determined principally by the concentration of red blood cells) the vascular resistance increases as well. If the radius of the blood vessel is decreased (vasoconstriction), then the vascular resistance increases as well."[67]

The last principle of vascularity to examine is hormonal regulation of the circulation; there are hormones that can influence circulatory function, two of which are relative to this discussion: prostaglandins and vasopressin. Keep in mind, prostaglandins are produced in abundance during menstruation. They have important intracellular effects, but some travel through the blood stream. Some are active in the uterus and endometrial tissue as vasoconstrictors, and some are active in the smooth muscle tissue of the digestive tract as vasodilators, both of which are at work during menstruation.[68] Women with dysmenorrhea may be sensitive to or have excess amounts of prostaglandins. Vasopressin is an antidiuretic hormone and is one of the most powerful vasoconstrictors in the body. It is released by the posterior pituitary in response to decreased blood volume (as occurs in hemorrhage) or dehydration.[69]

[66] Tortora and Derrickson, *Anatomy and Physiology,* 773.
[67] Hall and Adair, *Physiology,* 88-89.
[68] Ibid., 93.
[69] Ibid.

With the basic vascularity principles relative to this dialogue reviewed, exploration of tissue vascularity relative to exercise and activity will now be examined. It could be said that classical singers have strong vocal folds; maintaining high frequencies at high amplitudes with high sub-glottal pressure would require strength of tissue. The training regimen and performance schedule that professional classical singers sustain is a form of weight training for the voice. Weight training makes muscles bigger (hypertrophic). Large muscles directly correspond to muscle strength. According to the authors of *Vocal Exercise Physiology*, there are "several factors that lead to muscle hypertrophy: an increase in contractile proteins [that form myofybrils], an increase in *capillary density* [vascularity], an increase in the number and size of the myofybrils [which form cross sections of striated muscle], and an increase in the amount of connective tissue surrounding the muscle fibers."[70] According to the same authors, "Hypertrophy is hormonally determined."[71] These hormonal disturbances must be equalized for the body to return to pre-exercise levels.[72] In the fast-twitch muscle fibers, if the principle of overload is applied, hypertrophy can be developed in any muscle. Strength of the muscles involved in vocal performance can be increased in singers and voice patients if a proper overload is used.[73]

The purpose of warming up tissues ahead of exercise is to dilate capillary beds and augment blood flow to the working muscles. The warm-up will increase body temperature,

[70] Keith G. Saxon and Carole M. Schneider, *Vocal Exercise Physiology* (San Diego, Singular Publishing Group, Inc., 1995), 118.
[71] Ibid.
[72] Ibid., 70.
[73] Ibid., 119.

assisting blood flow as well, and decrease the number of injuries to the working muscles.[74]The purpose of cooling down the tissues after intense activity is to return the blood to the heart and avoid blood pooling in the extremities. Oxygenation during the cool-down returns the body to homeostasis.[75] The local tissues of active musculature autoregulate their own blood flow, which is also of benefit to the active muscles. "This is beneficial to the tissue because it allows the rate of tissue delivery of oxygen and nutrients and removal of waste products to parallel the rate of tissue activity."[76] Precise means of local blood flow autoregulation are still unknown.

> In many tissues, autoregulation appears to be linked to oxygen delivery or release from the tissues of metabolic waste products, such as adenosine and carbon dioxide, that cause vasodilation. For example, in metabolically active tissues, rapid utilization of oxygen tends to reduce oxygen tension in vascular smooth muscle. This, in turn, dilates the arterioles, increases blood flow, and causes more oxygen delivery to the active tissues. At the same time, a high rate of metabolism causes increased formation of vasodilatory metabolites that also increase blood flow. The higher rate of blood flow removes the waste products of metabolism, restoring their tissue levels toward normal.[77]

Exercise physiology is the study of how the body reacts to physical activity, including muscle oxygenation and metabolism, circulation, and fatigue. Exercise increases the tissue's metabolic demand for oxygenation. It requires cardiovascular modifications that elevate muscle blood flow. This includes increased muscle vascular conductance and cardiac output for active tissue, and decreased vascular conductance in resting tissues.[78] Training not only elevates oxygen consumption and extraction changes, but also increases the amount of hemoglobin in

[74] Ibid., 69.
[75] Ibid., 70.
[76] Hall and Adair, *Physiology*, 91.
[77] Ibid.
[78] N. Taylor and Groeller, *Human Performance,* 9-10.

the blood as well as overall blood volume. This elevation in hemoglobin and blood volume allows the athlete to work for a longer period of time without fatigue.[79] The thyroarytenoid muscle, which forms the body of the vocal fold, is a very fatigue-resistant muscle. The following comparison is a fascinating example of how highly oxidative and fatigue-resistant the human vocal fold is.

> In considering the hypothesis that specialization of the oxidative system is one basis of fatigue-resistance in laryngeal muscle, it is useful to provide a specific comparison. If we compare the leg muscles of untrained and trained men, it is found that in the trained men, the mitochondria and lipid droplets, which are characteristic for highly oxidative fibers, are enormously extended by athletic training. Human vocal is muscle has, at least in part, a content of mitochondria comparable to a leg muscle of a highly trained athlete. Some studies indicate that this intensity of oxidative metabolism is found particularly in the medial or vocalis portion of the thyroarytenoid muscle.[80]

Another hallmark of active, hypertrophic muscles is increased capillary density. "Aerobic and anaerobic training increase the capillary density in the skeletal muscle. When you train, therefore, more blood capillaries surround the muscle fiber. More capillaries mean that the muscle itself can get bigger, which, in turn, means enhanced oxygen delivery and waste-product removal."[81] This increased vascularity is of *benefit* to the active athlete, and is as nature intended. Active muscles need to be oxygenated and waste must be removed to achieve efficient function. This benefit can turn to detriment when hormonal imbalances occur that can upset the delicate equilibrium of fluid in the tissues.

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[79] Saxon and Schneider, *Vocal Exercise Physiology*, 112.
[80] Cooper, Partridge, and Alipour-Haghighi, *Vocal Fold Physiology*, 47-48.
[81] Ibid., 112.

Capillary density increases by a process called angiogenesis, the growth of new blood vessels to active tissue. “Physiologic angiogenesis is a tightly regulated process of vascular growth and is normally restricted to ovulation, menstruation, development of the embryo and placenta, and wound healing.”[82] Mechanisms that initiate angiogenesis are largely unknown. Decreased levels of oxygen within the tissue and increased metabolic activity of a tissue both seem to initiate angiogenesis. Changes in metabolic activity lead to proportional changes in angiogenesis and, hence, proportional changes in capillarity. Oxygen plays a pivotal role in this regulation. These factors are critical for survival of vascular networks and for structural adaptations of vessel walls.[83]

Angiogenesis is a mechanism for long-term blood flow regulation. This regulation occurs through changes in tissue vascularity and growth of new blood vessels. With chronic increases in blood pressure, the walls of the blood vessels become thicker and more muscular, leading to increases in vascular resistance. Angiogenesis is a possible response to that increase in vascular resistance.

> If a tissue becomes chronically overactive and therefore requires an increased supply of nutrients and increased removal of waste products of metabolism, the blood supply usually increases within a few weeks to match the needs of the tissues. One mechanism by which this occurs is the growth of new, parallel blood vessels in the tissues, which decreases vascular resistance and increases blood flow.[84]

[82] Creager, et al., *Vascular Medicine*, 969.
[83] Hall and Adair, *Physiology*, 93-94.
[84] Hall and Adair, *Physiology*, 94.

There has been an increase in recent research regarding the vascularity of the vocal folds. Mucosal blood vessels of the vocal fold margin enter from the anterior or posterior end of the membranous vocal fold, run roughly parallel to the vibratory edge, and are normally very small. Few vessels enter into the mucosa perpendicularly or directly from the underlying muscle. This vessel arrangement is also advantageous to vibration.[85] The medial area of thyroarytenoid muscle is richly supplied with capillaries and mitochondria for oxygenation. "In the human vocal folds in particular, the existence of a medial region of the [thyroarytenoid] muscle in which mitochondria and capillaries are denser than in the rest suggests a special role for the periphery which would depend on continuity of blood flow."[86] Capillary diameter is at the high end of normal in the laryngeal musculature. Capillary length per cross sectional area of the laryngeal musculature was found to be twice that of the thyrohyoid (an external laryngeal muscle, more typical skeletal muscle).[87] This indicates an exceptionally high capillary density in the laryngeal musculature. Flow and transportation of fluids (blood and interstitial fluid) should be considered when investigating the vascular structure of the vocal folds. "The ground substance of the lamina propria contains fluid and interstitial matrix. Under normal conditions, the fluid is limited, but tissue injury and inflammation cause accumulation of free fluid, primarily from capillaries."[88] This accumulation results in edema within the lamina propria, the vibratory cover of the vocal folds, which then results in stiffness and compromised vocal quality.

[85] Steven D. Gray, Minoru Hirano, and Kiminori Sato, "Molecular and Cellular Structure of Vocal Fold Tissue," *Vocal Fold Physiology: Frontiers in Basic Science*, ed. Titze (San Diego, Singular Publishing Group, Inc., 1993), 2.
[86] Cooper, Partridge, and Alipour-Haghighi*, Vocal Fold Physiology,* 85.
[87] Ibid., 43-44.
[88] Gray, Hirano, Sato, *Vocal Fold Physiology,* 11.

The text *Vocal Fold Physiology: Frontiers in Basic Science* was published over twenty-five years ago, but contains a profound dive into the structure and function of the human vocal folds by many of the most ground-breaking and headlining voice scientists of the time period, such as editor and voice scientist Ingo Titze, otolaryngologist Sataloff, voice scientist and otolaryngologist Minoru Hirano, who discovered and described the layered structure of the vocal folds. In response chapter content, the following are interesting excerpts from question and answer sessions among the voice researchers reflecting on the role vascularity plays in vocal fold function:

> Dr. Scherer: "Would you please discuss the scenario of a high pitch held for a long time wherein the cricothyroid and thyroarytenoid are strongly contracted? Please discuss this in terms of metabolism, circulation, and fatigue."
>
> Dr. Donald S. Cooper: "Both muscles have strong oxidative metabolisms, which therefore are dependent on blood flow for efficient function. The human thyroarytenoid muscle, which would be involved in the tensor mechanism of phonation, contains many more mitochondria than does the cricothyroid, and is especially well vascularized. The fluid pressures within the thyroarytenoid would be the sum of pressures from longitudinal tension of the vocal fold, pressures from thyroarytenoid's own activity, and intramuscular pressures from propagation into the fold of collision pressures. Regions of the muscle where fluid pressures [are high] may not recover from fatigue until the pressure drops.[89]
>
> Titze: "What do we know about the transport properties of fluids through the epithelium? Does irrigation on the inside on the folds have any relation to irrigation on the outside, or are they totally independent?"
>
> Hirano: "Basically, the fluids of the inside of the vocal fold come from the blood vessels while those of the outside of the vocal fold come from glands. Under special conditions, fluids might move in and out through the epithelium."[90]

[89] Cooper, Partridge, and Alipour-Haghighi*, Vocal Fold Physiology,* 83.
[90] Gray, Hirano, Sato, *Vocal Fold Physiology*, 24.

Further connection can be established, moving from examining vascularity of the vocal folds to exploring vascularity in relation to the menstrual cycle. Oxygenation of the vocal folds is improved during the follicular phase (first half) of the menstrual cycle due to estrogen improving permeability of the blood vessels and capillaries, which are abundant in the vocal folds.[91] However, when progesterone and estrogen are both present and imbalanced, all pulmonary bets are off. In the luteal phase (second half) of the menstrual cycle, the pulmonary response changes and there are subjective and objective limitations to exercise:

> The menstrual cycle can modulate the ventilatory response to exercise through changes in circulating progesterone and estrogen. Progesterone administration results in hyperventilation at rest and exercise, as well as increasing the resting ventilatory response to hypoxia [absence of enough O2 in tissues to sustain bodily function] and hypercapnia [abnormally high CO2 levels in blood].[92]

The menstrual cycle also affect change in blood viscosity. "A pronounced elevation of blood viscosity factors [thickened blood] which would be indicative of serious cardiovascular disorder in a male, can be entirely normal in a young menstruating female."[93] Changes in blood viscosity due to menstruation result in higher viscosity ahead of menses and lower viscosity after blood loss during menses. In a study of menstruating women observed by scientists in the mid-20th century, blood viscosity was highest a few days before the onset of the menstrual period. Viscosity decreased rapidly during the menstrual period, then plateaued, remaining relatively steady.[94] Blood viscosity factors vary greatly during the female hormonal cycle.

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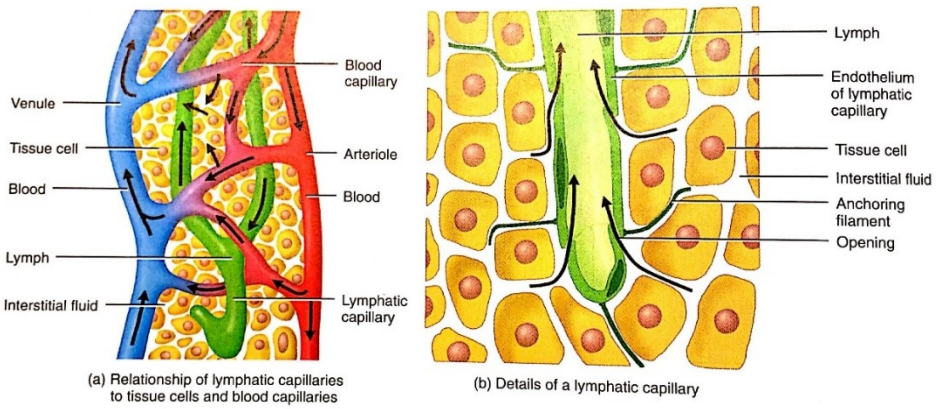
[91] J. Abitbol, *Odyssey of the Voice,* 215.
[92] N. Taylor and Groeller, *Human Performance,* 44-45.
[93] Leopold Dintenfass, *Blood Viscosity, Hyperviscosity and Hyperviscosaemia* (Boston, MTP Press Limited, 1985), 6.
[94] Ibid., 36-37.

Vascular constriction and capillary ischemia [inadequate blood supply] of healthy women have been reported within the menstrual cycle.[95] Take into account, the higher the viscosity of the blood, the higher the vascular resistance. The higher the vascular resistance, friction between the red blood cells and the capillary walls is elevated, thereby putting pressure on the walls of already fragile capillaries.

One of the primary functions of the lymphatic system is to drain excess interstitial fluid (which causes tissue swelling) from tissue spaces and return it to the blood.

> Edema develops when the production of interstitial fluid (lymph) exceeds its transport through the lymphatic system. Thus, an overproduction of lymph or a decreased ability to remove fluid from the interstitium may result in edema. Conditions associated with overproduction of lymph include elevated venous pressures, increased capillary permeability, and hypoproteinemia. Elevated hydrostatic pressure [vascular resistance] in the veins results in increased filtration of plasma from venules and blood capillaries. Conversely, local inflammation increases capillary permeability, accelerating the loss of protein and fluid to the interstitium despite a normal capillary hydrostatic pressure.[96]

Figure 4. Interstitial fluid entering the lymphatic system[97]



[95] Ibid., 40-41.
[96] Creager, et al., *Vascular Medicine*, 845.
[97] Tortora and Derrickson, *Anatomy and Physiology, 834.*

Overproduction of interstitial fluid/lymph results in edema. Typically, edema is not [visually] noticeable in tissues until interstitial fluid volume has ascended to 30% above standard. Swelling can result from either surplus filtration or insufficient reabsorption. Two situations may cause excess filtration: "increased capillary blood pressure causes more fluid to be filtered from capillaries, and increased permeability of capillaries raises interstitial fluid osmotic pressure."[98]

In conclusion, imbalance of progesterone and estrogen in combination with increased vascularity of the vocal folds can give rise to vocal fold stiffness and loss of flexibility due to increased mass of the vocal fold cover, or edema. This edema is due to estrogen increasing capillary permeability, and progesterone decreasing capillary permeability and trapping the excess interstitial fluid in the interstitial space too rapidly for it to be absorbed into the lymphatic system. The fluid retention that gives rise to edema results in reduced mucosal wave and symptoms of premenstrual dysphonia. These factors and others may set about a chain reaction that can add a heightened risk of vocal injury for female classical singers.

[98] Ibid., 772.

Chapter 4: Increased Risk of Vocal Pathology

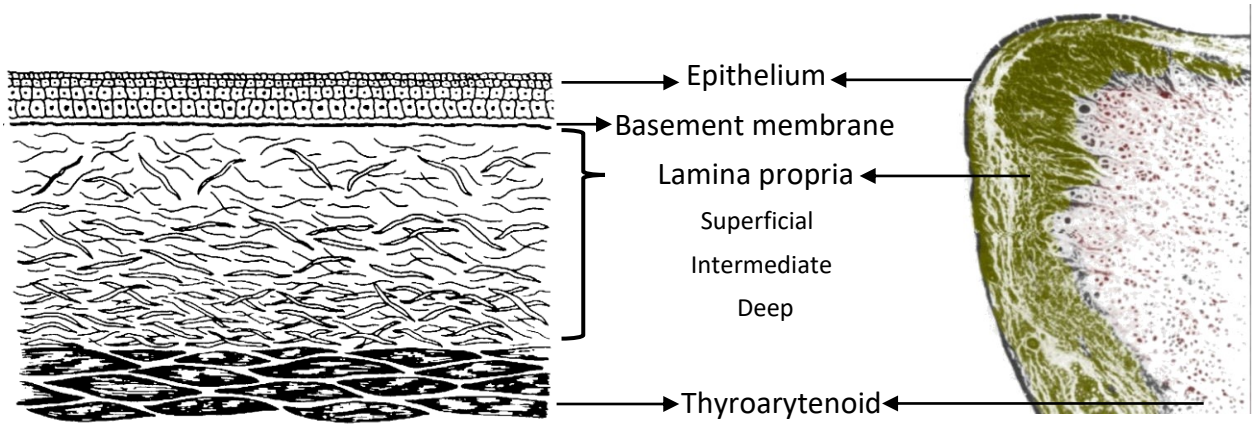
Modern-day athletes train rigorously to prepare the body for their respective sport and to protect their tissues from injury and damage. The modern-day vocal athlete does the same. If the voice is not prepared for the upcoming role and increasingly saturated performance calendars classical singers find necessary to maintain a lucrative career, the instrument can suffer strain and injury. Physiological voice changes respective to the female hormonal cycle have been discussed in detail. Vascular changes to the voice particular to physical exertion and the female hormonal cycle have been deliberated in detail. Increased vascularity of the vocal structure during premenstrual days could give rise to more extreme cases of these physiological changes of the tissues, presenting an increased risk of vocal pathology. Combined with a classical singer's increased sensitivity to those changes and need for exacting action of the vocal folds, the performer can become quite compromised.

Vocal fold anatomy is beautifully and intricately structured so as to maintain extended oscillation while remaining fatigue and injury resistant. However, just as some people are more prone to dental cavities than others, some vocal folds are more sensitive to physiological changes that can affect physical outcomes. "The intricacy of the transition between the epithelium and superficial layer of the lamina propria is an individual trait. If there is a difference in the density of anchoring fibers, this might affect vibratory ease, efficiency, regularity, and vocal fold resilience."[99] This area of transition to which Sataloff refers is critical to the occurrence of an efficient mucosal wave. Voice scientist Minoru Hirano's pioneering

[99] Sataloff, "Molecular and Cellular Structure of Vocal Fold Tissues: Response," *Vocal Fold Physiology*, 27.

body-cover theory describes the layered structure of the vocal folds; this anatomy allows the cover to move independently from the body (mucosal wave). (See Figure 5.)

Figure 5. Layered structure of the vocal folds[100]



The outermost layer is called the epithelium, made up of strong and flexible interlocking stratified squamous cells. The basement membrane connects the epithelium to the lamina propria, which is also the individualized area of "transition" Sataloff discusses above. In the chapter of *Vocal Fold Physiology* entitled "Molecular and Cellular Structure of Vocal Fold Tissue," Gray, Hirano, and Sato state, "Investigations of benign vocal fold disease have indicated that the basement membrane zone may be predisposed to vocal injury during great vibratory stress."[101] The remainder of the vocal fold cover is the lamina propria: the superficial layer, the intermediate layer, and finally the deep layer. Each layer gets more viscous moving deeper

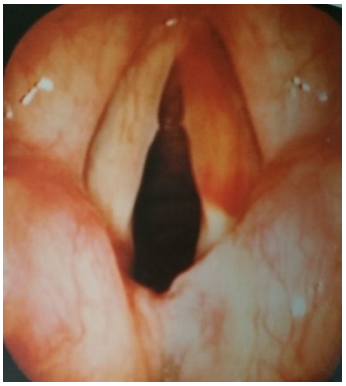
[100] Scott McCoy, *Your Voice: An Inside View,* Second edition (Delaware, OH, Inside View Press, 2012), 103. Permission to use this image granted by Scott McCoy, May 30, 2019.
[101] Gray, Hirano, and Sato, *Vocal Fold Physiology,* 10-11.

toward the body of the vocal folds, the thyroarytenoid muscle. Both the body and the cover are highly vascular, perhaps more so in active classical singers. "Vessels in the vocal fold mucosa are related to voice disorders. Fragility of and alteration in the permeability of the vessels are causes of edema of the superficial layer of the lamina propria (Reinke's space), which may become Reinke's edema. Hemorrhage of vessels is one etiology of vocal fold polyps."[102]

A common vocal injury in the premenstrual classical singer is the submucosal hemorrhage.[103] A hemorrhage occurs when blood escapes a ruptured blood vessel, and the etiology is typically an acute traumatic episode. "The most common presenting symptom of vocal fold hemorrhage is sudden change in vocal quality. The sudden onset of symptoms is evident because blood dissects in the submucosal plane, altering the vibratory motion of the vocal fold."[104]

Figure 6. Vocal fold hemorrhage (A) and microvarices (B)[105]

A.



B.

[102] Sato, "Functional Fine Structures of the Human Vocal Fold Mucosa," *Diagnosis and Treatment of Voice Disorders*, 52.
[103] Sataloff, "Care of the Professional Voice," *Performing Arts Medicine*, 152.
[104] Joseph R. Spiegel, et al., "Vocal Fold Hemorrhage," *Professional Voice: The Science and Art of Clinical Care,* Second Edition, ed. Sataloff (San Diego, Singular Publishing Group, 1997), 541.
[105] Jean and Patrick Abitbol, "The Larynx: A Hormonal Target," *Diagnosis and Treatment of Voice Disorders*, 401-402.

There are many factors and combinations of factors that contribute to the increased fragility of the vocal fold vessels, many of which were previously explored in preceding chapters of this document. Other prevalent vascular voice disorders are varices and ectasias. An ectasia is a dilation of a small vessel; a varix is a "prominent, distended, lengthened, and tortuous blood vessel on the surface of the vocal fold."[106] In a study by Pi-Tang Lin, et al., published in the *Journal of Voice* in 1991,[107] researchers found that of thirty women who experienced vocal fold hemorrhage, eight subjects had hormonal imbalances caused by either abnormal menstrual cycles, use of hormone supplements, or use of birth control pills. When the cause of the hormonal imbalance was cleared, the body was brought back into equilibrium, and the hemorrhage healed on its own.

There are other voice disorders that may befall professional voice users, such as nodules, cysts, muscle tension dysphonia, granulomas, and even the human papilloma virus. These pathologies are not relevant to the vascularity of the premenstrual voice, and are often caused by voice misuse or abuse and improper vocal hygiene, however, those actions can also be factors that contribute to the risk of injury facing the classical singer suffering laryngopathia premenstrualis. Vocal pathologies that are fed by blood vessels in the vocal folds, including hemorrhages, varices, ectasias, and polyps are likely the most prevalent vocal injuries caused by hormonal imbalances in the premenstrual classical singer.

[106] Colton, Casper, and Leonard, *Understanding Voice Problems*, 175.
[107] Pi-Tang Lin, Jordan C. Stern, and Wilbur J. Gould, "Risk Factors and Management of Vocal Cord Hemorrhages: An Experience with 44 Cases," *Journal of Voice*, Volume 5, Issue 1 (1991): 74-77.

The female classical singer may encounter other dangers other than increased vascularity and hormonal imbalance putting her at risk for vocal injury. It is pertinent to educate all female singers and their teachers and coaches regarding the various factors that may contribute to development of a vocal pathology in the days leading up to menses. At the core of many vocal sins is insufficient vocal hygiene education among singers. Vocal misuse, abuse, and overuse can add further pressure to blood vessels that are already pressurized and fragile.

An element of vocal hygiene that should be prioritized by singers is hydration. All singers should ingest enough water to *systemically* hydrate the vocal folds. Rachel Gates, author of *The Owner's Manual to the Voice*, suggests drinking enough water to keep urine pale.[108] The body will be giving preference to hydrating the major organs to maintain life; the level of hydration of the vocal folds does not fall into that category.

> In the premenstrual period, decreased estrogen and progesterone levels are associated with altered pituitary activity. An increase in circulating antidiuretic hormone results in fluid retention in Reinke's space as well as in other tissues. The fluid retained in the vocal fold during inflammation and hormonal fluid shifts is bound, not free water. Diuretics do not remobilize this fluid effectively and dehydrate the singer, resulting in decreased lubrication and thickened secretions and persistently edematous vocal folds.[109]

Recall that vasopressin is an antidiuretic hormone released as the body's response to dehydration. Blood viscosity is also affected if the body is not properly hydrated. Certain

[108] Rachel Gates, L. Arick Forrest, and Kerrie Obert, *The Owner's Manual to the Voice* (New York, Oxford University Press, 2013), 37.
[109] Sataloff, Mary Hawkshaw, and Deborah Caputo Rosen, "Medications: Effects and Side Effects in Professional Voice Users." *Professional Voice: The Science and Art of Clinical Care*, Second Edition, ed. Sataloff (San Diego: Singular Publishing Group, 1997), 458.

medications directed at premenstrual and menstrual symptoms contain diuretics such as antihistamines and caffeine to combat bloating. These medications will affect the body's level of hydration, as well as a host of other medications that can be drying to the voice.

Gastric reflux can affect any singer and can exacerbate laryngopathia premenstrualis. Women enduring symptoms of PMS might also experience loss of tonicity of esophagus smooth muscle due to vasodilation of that vasculature. As previously stated, this is an action of the estrogen/progesterone combination during the premenstrual days. Laryngopharyngeal reflux (LPR) is also known as "silent reflux," as it is rarely accompanied by heart burn and is not as severe as gastroesophageal reflux disease (GERD). However, both LPR and GERD involve relaxation of the esophageal sphincter. This allows stomach acid to spill back into the larynx, thereby irritating the vocal folds and surrounding mucosa, which could already be swollen and fragile due to other premenstrual vocal syndrome symptoms. Proper vocal hygiene can educate a singer on ways to avoid LPR.

Another element of vocal hygiene that is vital to all professional voice users is managing vocal load. The first chapter mentioned the typical vocal load facing the actively performing classical singer. Voice use for choral and vocal music educators can border on overwhelming overuse if not guarded carefully. Putting that much pressure on an already pressurized instrument can be a dangerous road to navigate and should be traversed with caution. Leaving hormonal imbalance out of the equation entirely and just focusing on the occupational hazard

of vocal misuse and abuse facing these music educators, teachers represent twenty percent of voice clinic loads.[110] That is an alarming statistic.

> Submucosal vocal fold hemorrhage appears to be a more prevalent injury than previously recognized. It is more commonly reported in professional voice users, especially singers, due to their extreme vocal demands [and extreme sensitivity to changes in their instrument]. The diagnosis of vocal fold hemorrhage requires a high index of suspicion. Patients can present with sudden or progressive changes in vocal quality and may not be able to discern a specific event that led to the voice change.[111]

Vocal hygiene, specifically healthy voice use and vocal load should be an integral part of a vocal musician's curriculum.

The final component of vocal hygiene most relevant to vascularity of the voice and the menstrual cycle of classical singers is the affect certain medications can have on the instruments. When discussing hydration, it was mentioned that some medications aimed at alleviating PMS symptoms contain diuretics such as caffeine and antihistamines. Singers should be aware of medications that have side effects of dryness. More pressing concerns, however, are certain pain medications that thin the blood, or affect clotting, as they may increase the risk of vocal fold hemorrhage.[112] Non-steroidal anti-inflammatory medications (NSAIDs) are wonderfully effective in treating pain and reducing inflammation. If given enough time to work out of the system before heavy voice use, it is unnecessary to avoid taking NSAIDs. However, a word of warning: the combination of capillary fragility with such drugs and other premenstrual

[110] The National Center for Voice and Speech website, http://www.ncvs.org/research_tools.html, accessed on May 27, 2019.
[111] Spiegel, et al., "Vocal Fold Hemorrhage," *Professional Voice*, 552.
[112] Ibid., 550.

physiological changes may put a professional voice user at unacceptable jeopardy of vocal fold hemorrhage. Medications that impair coagulation should be avoided when excess voice use cannot be circumvented.[113]

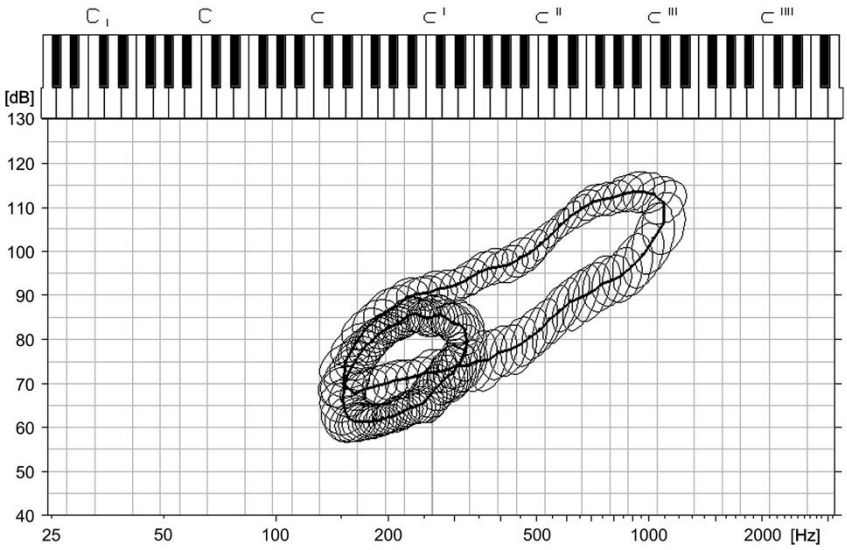
> Anecdotally, premenstrual and early menstrual hormonal changes have been associated with an increased risk of vocal fold hemorrhage. This is presumed to be due to increased capillary fragility. The use of anticoagulants such as aspirin and ibuprofen for premenstrual cramps increases the risk of hemorrhage. Physicians and voice professionals must be familiar with these risk factors, and must be particularly careful to advise professional voice users on simultaneous multiple risk factors such as premenstrual hormonal changes, aspirin use, and singing with impaired support technique owing to the pain of menstrual cramps. Submucosal vocal fold hemorrhage usually follows trauma. In the authors' opinion, it is more likely to occur following ingestion of aspirin and other anticoagulants and in women prior to menses, although that was not proven definitively (or studied specifically) in the research.[114]

Outside the scope of vocal hygiene, but of specific applicability to female classical singers, is the consideration of friction. There are higher levels of collision forces at work in the female voice in general, but this is especially true for the female classical singer. The average fundamental frequency range of speech for a man is 100-120 Hertz (Hz), which is doubled for a woman at 200-220 Hz. Keep in mind, the frequency is the amount of times the vocal folds collide *per second*; creating friction, and thereby phonation. Frequency variability on average is 25-30 Hz for connected speech. Obviously, the normal singing range and tessitura of mezzos and sopranos will extend way beyond these numbers. A voice range profile (VRP) measures minimum and maximum frequency and amplitude throughout a singer's range, and varies greatly dependent upon the singer's Fach. In a research study done by Lamarche, et al.,

[113] Sataloff, Emerich, and Hoover, "Endocrine Dysfunction," *Vocal Health and Pedagogy,* 169.
[114] Spiegel, et al., "Vocal Fold Hemorrhage," *Professional Voice*, 551-552.

scientists took VRP measurements of speech and singing for thirty female opera singers (sixteen sopranos, eight mezzos, six contraltos).[115] The figure below shows the average VRP contours including covariation ellipses for all thirty singers.

Figure 7: Average VRP contours for thirty female opera singers[116]



The difference in the highest singing frequencies and the highest speaking frequencies are estimated at over 750 Hz. That is a variance of more than 750 vocal fold collisions per second of sound. If one takes into consideration capillary fragility, increased vascularity, and high levels of edema resulting in stiffness of the vocal folds, smashing the compromised vocal folds against each other at not only high frequencies but also extended duration is a recipe for disaster.

[115] Anick Lamarche, Sten Ternström, and Peter Pabon, "The Singer's Voice Range Profile: Female Professional Opera Soloists," *Journal of Voice*, Volume 24, Issue 4 (2008): 410-426.
[116] Ibid., 418.

> Not all hemorrhages resolve completely. In some cases, the hematoma within the layers of the vocal fold organizes and fibroses, resulting in scar and permanent dysphonia. In others, hemorrhage may be followed by persistent, enlarged, varicose vessels. In some patients, particularly professional singers, the increased bulk and engorgement of these vessels associated with heavy voice use produces subtle but disturbing changes. This is especially true in high sopranos. In addition, in a small number of patients, recurrent vocal fold hemorrhage may occur from repeated traumatic rupture of a varicose vessel, generally on the superior or leading surface of the vocal folds.[117]

Additionally, ponder the amount of muscle force, full vocal fold closure, and subglottal pressure necessary to maintain these pitches as a full *forte*. Connected speech has an average amplitude of 70 decibels (dB) with an amplitude variability of 10 dB. According to Lamarche, et al., the average amplitude of the thirty singers in his study was around 90 dB, which he considered to be *mezzoforte*, with an amplitude variability of around 60 dB.[118] A fun fact: amplitude is logarithmic. Large changes in amplitude are indicated by relatively small numerical changes. Adding only 3 dB will *double* the amplitude. Singing at higher amplitudes brings more vocal fold mass to meet at the midline, creating a larger surface area upon which these forces of friction occur. For example, a lyric soprano repeatedly practicing her C6 at 1,046.50 Hz at an amplitude of 115 dB the day before expected menses will put a risky amount of stress on vocal folds that may be otherwise compromised.

There are precautions a female classical singer can take in order to prevent possible pathologies and reduce her symptoms of larygopathia premenstrualis, which will also reduce her PMS symptoms. Hydration is first and foremost. Singers can drink eight to ten glasses per

[117] Spiegel, et al., "Vocal Fold Hemorrhage," *Professional Voice*, 553.
[118] Ibid., 412.

day, use caution with over-the-counter and prescription medications that are drying, and limit intake of caffeine and alcohol. Systemic hydration will help maintain fluid levels in the lamina propria necessary to a healthy mucosal wave, thereby reducing stiffness of the vocal folds. It can also prevent blood from becoming too viscous, and prevent excess vasoconstriction due to the body's release of vasopressin in response to dehydration. In order to preserve hydration levels, a singer can also reduce sodium intake. "The body retains water to dilute dietary salt, so restriction of salt is one of the most important steps in reducing fluid retention."[119] This will allow the fluid levels to be free throughout the body, rather than bound to sodium which can increase edema due to fluid retention.

Exercise can do a great deal to alleviate symptoms of PMS and premenstrual vocal syndrome. Exercise can regulate hormones, lower stress, reduce inflammation, aid sleep, and help to maintain healthy weight. Activity can relieve not only vascular congestion but also emotional tension in many women.[120] Exercise prior to menstruation can be beneficial to singing. Airway resistance is decreased due to vasoconstriction of nasal mucosal vasculature, and blood flow is increased to the airway (nose, mouth, pharynx, larynx).

> The nasal dilatory muscles, and presumably the skeletal muscles of pharyngeal and laryngeal regions, contract in phase with, but slightly preceding, inspiratory muscle recruitment, and this drive to the upper airway muscles is increased with increasing ventilation, resulting in decreased resistance and a less collapsible airway. Therefore, the work required to overcome flow resistance during exercise is minimized by adjustments occurring in the upper airway that decrease flow resistance.[121]

[119] Shephard and Shephard, *Complete Guide to Women's Health,* 477.
[120] Ibid.
[121] N. Taylor and Groeller, *Human Performance*, 35-36.

It can be difficult to do, but when able, a singer should schedule performances and auditions around her menstrual cycle. European opera houses no longer allow "grace days" of vocal rest for female singers ahead of their periods, and American opera houses never have. When cancellations cannot be made, perhaps vocal load can be adjusted to minimize friction to swollen and sensitive vocal folds.

For severe cases of premenstrual vocal syndrome, hormone treatments can be considered. Hormonal birth control has been shown to regulate hormone levels. "The endocrinologist who understands arts-medicine concerns can help with diagnosis and stabilizing serum hormone concentrations in women prone to cyclical vocal fold hemorrhage."[122] There is increasingly more research done on the effects of hormonal birth control on the singing voice. Side effects of such medications should be taken into account before beginning treatment.

Jean Abitbol has had fascinating results with natural remedies in his patients with premenstrual voice syndrome. His therapies are individualized for each woman, and have yielded many positive outcomes. Abitbol prescribes his treatment for ten days per month: eight days before onset of menses, and two days once menstruation has begun. His remedies include vitamins A, B6, B5, C and E, as well as minerals magnesium, calcium, iron, zinc, phosphorus, and copper. "These remedies are combined with vascular therapy and antiedema drugs, such as bromelaines from pineapples; prostaglandin inhibitors, such as mefenamic acid; and with antireflux treatment. Also, during this period, we suggest the following diet; low protein,

[122] Sataloff, Emerich, and Hoover, "Endocrine Dysfunction," *Vocal Health and Pedagogy,* 167.

vegetables (carrots), fibers, olive oil, and no alcohol."[123] Considering the conceivable pitfalls of putting additional hormones into the body, a natural approach is often preferred when possible.

The female classical singer may face increased risk of vocal pathology due to hormonal imbalance, increased vascularity of the vocal folds, and many other contributing factors. Elements complicating this heightened risk include dehydration, certain medications, gastric reflux, poor vocal hygiene, vocal misuse and abuse, as well as high levels of friction from normal use associated with being an elite vocal performer. A female classical singer suffering from laryngopathia premenstrualis is very sensitive to the physiological changes taking place in her body, and should take all precautions available to her to reduce symptoms and prevent vocal injury.

It is unlikely that the vocal athlete will ever possess as much societal (or monetary) value as the sports athlete. Yet, exploration of voice science and voice care continues to expand. Revolutionary research into the vascularity of the voice is now underway, allowing doctors to recognize laryngeal cancers at an early stage. This investigation is relevant to hormonal changes in the voice, and will be explored in the final chapter of this document.

[123] J. Abitbol and P. Abitbol, "The Larynx: A Hormonal Target," *Diagnosis and Treatment of Voice Disorders,* 403.

Chapter 5: Further Investigations

A few of the most prevalent areas of advanced voice science research focus on biomechanics of the voice, patient care, an interdisciplinary team approach, and the larynx as a hormone target organ. Sataloff and John Rubin co-author the chapter entitled "Voice: New Horizons," in Sataloff's *Professional Voice: The Science and Art of Clinical Care*.[124] In it, they discuss each of these areas (and others) and their importance. The authors recognize the value of interdisciplinary collaboration across many fields that results in relevant voice research and new clinical approaches and techniques. They identify patient care to be the driving force behind more and more academic institutions developing voice centers; patient care is exposing voice scientists and clinicians to the numerous challenges in voice care and research.

Advances in endocrinological research regarding the larynx as a hormone target organ are reaching new heights. "Additional clarification of the nature and location of hormone receptors and of end-organ mechanisms of response to hormonal manipulations (such as premenstrual changes) may offer ways of blocking adverse effects when hormonal fluctuation or dysfunction is inevitable, and possibly produce methods of reversing hormone-related voice changes."[125]

> The numerous proteins in the basement membrane and their normal ability to combine with antigens and other substances [such as hormones] also raise compelling questions about pathogenesis and therapy. We attribute many voice problems to "fluid collection" in the superficial layers of the lamina propria, for example. These include laryngopathia premenstrualis, allergy, hypothyroidism,

[124] John S. Rubin and Robert T. Sataloff, "Voice: New Horizons," *Professional Voice: The Science and Art of Clinical Care*, Second Edition, ed. Sataloff (San Diego: Singular Publishing Group, 1997), 801-808.
[125] Ibid., 802.

> and others. It seems likely that various substances combine with proteins in the basement membrane, altering its function and permeability, and resulting in symptoms. This possibility is particularly exciting. If it turns out to be accurate, it then raises the prospect of developing blocking substances that can be attached therapeutically to basement membrane proteins to fill their receptors and prevent the vocal effects of conditions such as allergy and laryngopathia premenstrualis. This would be a major therapeutic advance, especially for professional voice users.[126]

Rubin and Sataloff encourage further investigation into muscle physiology, including the fatigue resistance of the laryngeal muscles and their metabolic requirements, as well as the functional implications and the relationship between fast and slow twitch muscle fibers present in the vocal folds. Another fascinating area of laryngeal biomechanics to be explored is the applicability of sports medicine studies in exercise physiology to laryngeal habilitation and rehabilitation.[127] Sataloff states, "Since the ultrastructure of the vocal fold is not unique, for the most part, what more can we learn from researchers in other fields who have worked on similar cells and muscles? From the practical standpoint of the voice trainer or speech-language pathologist, how should our knowledge of laryngeal muscle structure guide the selection of vocal exercise tasks, as similar studies have guided other athletic practice?"[128] Imagine the possible fruits of collaborative labor from such experts in the fields of endocrinology, kinesiology, exercise physiology, cytology, otolaryngology, speech-language pathology, and vocology regarding the hormonally cyclical female voice?

[126] Sataloff, "Molecular and Cellular Structure of Vocal Fold Tissue: Response," in *Vocal Fold Physiology*, 27.
[127] Rubin and Robert T. Sataloff, "Voice: New Horizons," *Professional Voice*, 803.
[128] Sataloff, "Molecular and Cellular Structure of Vocal Fold Tissue: Response," in *Vocal Fold Physiology*, 26-27.

A prime example of this kind of cutting-edge research is a study by Hagit Shoffel-Havakuk, et al., published in 2018 by the *Journal of Voice*, entitled "Menstrual Cycle, Vocal Performance, and Laryngeal Vascular Appearance: An Observational Study on 17 Subjects."[129] Researchers observed seventeen female subjects, aged 23-43, none of whom were professional voice users or taking hormonal birth control. Researchers were able to prove increased vascularity during the subjects' pre-menstrual days and how it affected vocal fold function. All observations and measurements were taken at two points in the subjects' menstrual cycle: the early days when progesterone was at its projected lowest level, and a few days before menses were expected to begin, when progesterone was at its projected peak. The scientists had the subjects fill out a Voice Handicap Index (VHI) to measure the patient's perception of their own voice quality. They took acoustic measurements of jitter (frequency perturbation) and shimmer (amplitude perturbation). Serum hormone levels were tested: at pre-ovulation – progesterone is lower, post-ovulation – progesterone is higher. Researchers found higher progesterone levels to coincide with increased vascularization of the vocal folds and surrounding tissues. The researchers were able to identify this increased vascularity by laryngeal endoscopy using narrow band imaging (NBI).

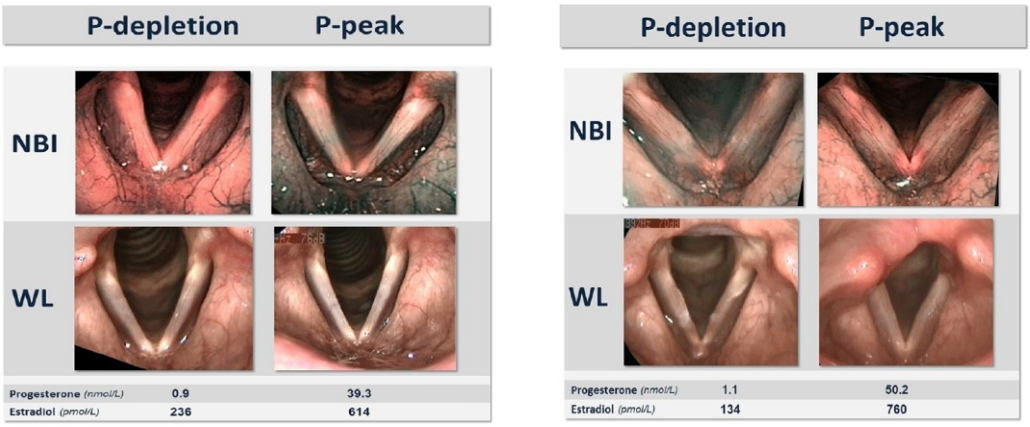
Laryngeal endoscopy typically provides views using white light (WL) technology, or stroboscopy to view the mucosal wave. The NBI is an exciting technology that is recent to the field of otolaryngology. It filters the white light into specific wavelengths that are absorbed by hemoglobin, granting a penetrative and precise view of the submucosal micro-venous

[129] Hagit Shoffel-Havakuk, et al., "Menstrual Cycle, Vocal Performance, and Laryngeal Vascular Appearance: An Observational Study on 17 Subjects," *Journal of Voice*, Volume 32, Issue 2 (2018): 226-233.

dilatation, which enhances the visibility of blood vessels below the surface. This infiltratory view of the vocal folds has allowed otolaryngologists to identify cancerous tissue at much earlier stages than what was previously done. Malignant cancer is vascularly fed; witnessing changes to that vascularity has led to earlier cancer diagnoses and receipt of treatment in patients.

In Shoffel-Havakuk's study, the images taken via laryngeal endoscopy of the vocal folds using WL were compared to images taken using NBI. The NBI images clearly reveal vascularity changes at premenstrual points of the cycle. The images below are of two different subjects.

Figure 8. NBI and WL images showing vascular changes at progesterone peak and depletion[130]



The vascularity of the vocal folds is more prominent in the NBI images than in the WL images; the bluish hue is more pronounced in the vascularized tissue. In conclusion, the vascular congestion of laryngeal tissue correlates with elevated progesterone levels in the days leading

[130] Ibid., 230.

up to menses, thereby supporting the existence of the premenstrual vocal syndrome.[131] This study did not recruit subjects already suffering with PMS symptoms, indicating imbalanced levels of estrogen and progesterone. Shoffel-Havakuk, et al. suggest further studies of this nature with singers experiencing premenstrual dysphonia to determine whether the vascular congestion is indeed associated with premenstrual dysphonia.[132]

The Ohio State University Voice and Swallowing Disorders Clinic has submitted a proposed research study to the OSU Institutional Review Board for approval that intends to do just as Shoffel-Havakuk, et al. suggest. We are seeking an *n* of twenty female classical singers, non-smokers, aged 18-45, with relatively regular menstrual cycles who experience symptoms of PMS and premenstrual dysphonia. Subjects will be excluded if they are: taking hormonal birth control within the past three months, breastfeeding, pregnant, three months post-partum, have a history of any of the following: pulmonary illness, laryngeal surgery, or neurological disease.

Using NBI, this study aims to evaluate vascularity of the vocal folds in relation to peak and baseline progesterone and estrogen levels during different phases of the menstrual cycle in professional classical singers BEFORE and AFTER active use. The increased demand placed on the vocal folds by these vocal athletes also increases the likelihood of intensified vascularity present in the vocal folds and surrounding tissues. Capturing NBI images before and after twenty to thirty minutes of rigorous singing will expectantly support that theory. According to

[131] Ibid., 232.
[132] Ibid.

the Shoffel-Havakuk study, the changes in vascularity were subtle yet easy to detect with NBI, but showed no significant effect on self-perception and acoustic measurements of the voice in non-singers. However, the subjects in her study were non-singers with no voice complaints. The OSU study will measure singers' own perception of their voices using the Singing Voice Handicap Index (SVHI) with the intent of yielding more forthcoming results. Pregnancy will be ruled out at each visit with a urine pregnancy test. Serum hormone levels will be measured via blood draw at both appointments, pre-ovulation, and just ahead of expected menses. Data collected will be sent to our statistician who will perform statistical analysis on the de-identified data.

Professional singers use their voices to their full extent regarding pitch, amplitude, subglottal pressure, and fine motor skills. They are more aware of the changing subtleties of their instruments and therefore more likely to observe the premenstrual changes. Add to that the increased level of vascularity due to high level demands placed upon the vocal folds of classical singers, and it warrants further research to support the careers of professional voice users. Outcomes of this research may assist female singers who suffer from laryngopathia premenstrualis in preventing of further vocal pathologies due to increased vascularity of the vocal folds and hormonal imbalance. It can also encourage further exploration into alleviating symptoms of premenstrual dysphonia in female classical singers.

Classical singers are the Olympians of vocal performers. Many female classical singers feel vocally compromised ahead of menses. Hormonal changes in addition to augmented vascularity can increase likelihood of injury to the voice. Having concrete knowledge of possible

vascular changes at the laryngeal level at the premenstrual point in the cycle in comparison to the middle of the cycle can greatly prepare singers for managing these changes and improve patient care for singers facing these physiological challenges.

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Appendix A: Terms and Definitions

Angiogenesis – the growth of new blood vessels to active tissue

Desquamation – the peeling of the outermost layer of tissue

Dysmenorrhea – painful menstrual cramps caused by uterine contractions

Follicular phase – proliferative phase, the first half of the menstrual cycle in which follicles in the ovary mature, and estrogen levels begin to rise leading up to ovulation

Hematoma – a solid swelling of clotted blood within the tissues

Hypercapnia – abnormally high CO2 levels in blood

Hyperemia – an excess of blood in the vessels supplying an organ or other part of the body

Hypoxia – absence of enough O2 in tissues to sustain bodily function

Interstitial fluid – the thin layer of fluid surrounding cells within the body, serving as a conduit between the capillaries and the body tissue and cells

Ischemia – inadequate blood supply

Laryngopathia premenstrualis – describing vocal dysfunction characterized by decreased vocal efficiency ahead of menses

Luteal insufficiency/deficiency – occurs when the female body does not produce enough progesterone to maintain a pregnancy if one should occur

Luteal phase – secretory phase, the second half of the menstrual cycle in which the endometrium of the uterus thickens in preparation for pregnancy, and sloughs off in the absence of pregnancy

Polycythemia – an unusually high number of red blood cells

Vasoconstriction – occurs when the radius of a blood vessel is decreased

Vasodilatation – occurs when the radius of a blood vessel is increased