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PERSISTANT SEXUAL AROUSAL SYNDROME

PSAS

Possible Etiologies and Potential Therapies

I am a reproductive endocrinologist in Phoenix, Arizona who specializes in infertility therapy, prolactin disorders, and rare endocrine syndromes. I recently treated a patient with cyclic sexual arousal syndrome who was unable to drive or take public transportation before each menstrual period without intense arousal symptoms, and treated another patient with uncontrollable spontaneous orgasms when on progesterone hormone therapy and during the first trimester of pregnancy. Fortunately, my patients had a good response to therapy or had spontaneous remission after pregnancy, but I am aware that in general, PSAS is considered an essentially untreatable syndrome for most patients, with very few therapies available. While researching my cases I came across the PSAS group at Boston University Medical School, and was then referred to your PSAS support group. As a reproductive endocrinologist, I have some presumptive medical hypothesis for the causes of PSAS which might generate specific therapeutic options. Most of these hypotheses are speculative, but are based on physiologic principles. My emphasis is mostly from an endocrinology perspective. I hope this information will be useful as an initial framework for the evaluation and treatment of PSAS.

Women with PSAS may fit into one (or more) of five diagnostic categories:

1. Pelvic/Sexual Hypersensitivity.
2. Pelvic Congestion Syndrome variant.
3. Neurologic Anomaly (post injury or neurotransmitter related).
4. Endocrine Disorder of Refractory and Resolution phase of the sexual cycle.
5. Tourette's Syndrome variant.

Each category has potential for specific medical therapy, and therefore, may serve as models for women with PSAS who don't respond to current standard therapies. The medical therapies for each diagnostic category are listed below:

1. Pelvic / Sexual Hypersensitivity - characterized by inappropriate and dramatic amplification of normal sexual neurologic sensations into intense and prolonged arousal. Minor pelvic pressures and vibrations unperceived or ignored by most women are somehow immensely magnified into intense sexual arousal in women with PSAS. Women who experience overwhelming sexual excitement or multiple orgasms when driving, riding trains, crossing legs, or after intercourse would fit into this category. Resolution of arousal may require hours or days of masturbation, or may not occur at all because of continued amplification of the ongoing minor pelvic sensations present in all women as part of life. This diagnostic category strongly resembles (and may actually be a subcategory) of interstitial cystitis, now known as *viscerosomatic hyperalgesia*. The technical medical description of the syndrome is "biological up-regulation of sensory processing" due to a barrage of minor neurologic stimuli to the dorsal horn of the spinal cord, followed by spontaneous firing of the dorsal horn neurons to the brain. This produces a greatly exaggerated output of neurological signals that are subsequently very difficult to

suppress. In women with this form of PSAS, minor sensory neurological output from the pelvic organs and clitoris are amplified into a persistent or permanent state of arousal at the brain level. If this diagnostic model of PSAS is correct, then patients may respond to the same medications that are effective for interstitial cystitis and viscerosomatic hyperalgesia. One recommendation would be to use the same three drug therapy that is effective for many women with interstitial cystitis. This consists of initial treatment with amitriptyline, typically for 30 to 60 days, with addition of Neurontin two weeks after the first amitriptyline dose. This is then followed two weeks later by addition of Pentosan polysulfate sodium (Elmiron) as long-term therapy. The amitriptyline is discontinued after 1 to 2 months of use, the Neurontin is discontinued after 6 months of use, and the Elmiron is continued on an indefinite basis. Hopefully, Elmiron would be effective for treatment of pelvic/sexual hypersensitivity disorders, but it probably would not achieve maximum effectiveness until six months into therapy. The other two medications are primarily designed to provide initial relief until the Elmiron takes full effect.

2. Pelvic Congestion Syndrome variant - characterized by large internal varicose-type veins which drain the pelvic and sexual organs, including the uterus, cervix, vagina, vulva, clitoris, and labia. Normally blood is easily and quickly drained from these organs through a small well organized vein system, especially during the resolution phase after orgasm. Some women develop a disorganized dilated vein system (especially if they have a history of endometriosis) which leads to blood congestion of pelvic and sexual organs. Women with PSAS may have a form of pelvic congestion syndrome (old-fashioned name was Allen-Masters Syndrome) with chronically dilated pelvic veins which cannot respond well to neurologic and hormone signals to contract to normal size during the resolution phase of the sexual cycle. Consequently, the pelvic congestion activates the arousal stage continuously. Normally, one to five orgasms is enough to contract the veins and relieve the congestion, but in these PSAS women dozens or even hundreds of orgasms may be required to eventually drain the congestion. Afterwards, easy rapid refill of veins leads to the next episode of persistent intense arousal. Fortunately, this syndrome is easy to diagnose with pelvic ultrasound or laparoscopy. Patients with this variant of PSAS would probably have altered symptoms with a full bladder, and likely would have developed PSAS slowly over several months or years, or after pelvic surgery. No effective therapy is available for pelvic congestion syndrome, but the recent development of a new technique may hold some promise. This involves injection of FlowGel into the pelvic veins by a qualified interventional radiologist. This method is experimental and is done, as far as I know, by only two facilities in the country. It was originally developed for patients with chronic pelvic pain due to pelvic congestion syndrome, and has proven very successful in relieving pain in these patients. I believe that when this procedure is better developed it may also be an option for some women with PSAS.

3. Neurologic Types of PSAS - either due to a neurologic defect caused by a subtle injury, or due to an altered neurotransmitter response. The neuralogic defect of PSAS would develop after an injury such as an episode of meningitis, encephalitis, Reiter's syndrome, or head trauma. The injury may also work at the level of the spinal cord, which contains the direct neurologic feedback circuits controlling clitoral erection, arousal, and resolution. Disruption of the normal neurological functioning of the feedback circuits could theoretically lead to a state of chronic arousal which would be difficult to control or relieve. A much larger amount of sexual stimulation would be needed to neurologically penetrate the affected region to eventually activate the resolution phase of the sexual cycle, and small amounts of microstimulation from everyday activity such as sitting, driving, riding, etc. would maintain or return the state of continuous sexual arousal. The other "altered neurotransmitter response" mechanism could theoretically follow antidepressant or neurologic drug therapy, or for some women PSAS symptoms would increase while on one of these medications. It is well known that some antidepressants, particularly in the SSRI class, have been known to cause priapism in men and multiple spontaneous orgasms in women. The neurologic type of PSAS may be the most difficult to treat. One suggestion is to try the over-the-counter medication NyQuil (used for colds). In many men and women, NyQuil will completely kill arousal for up to 24 hours after each dose. Another suggestion is to increase the

"efficiency" of orgasms by reducing microstimulation and increasing the intensity of macro-stimulated orgasms. The intent is to induce the resolution phase with fewer but more intense orgasms. Another potential treatment is use of a TENS neurostimulation unit, or even a sacral neuromodulator implant, which has been successfully used to block chronic pelvic pain of neurologic or unknown origin. Unfortunately, this method would be very expensive and require surgery.

4. Endocrine Associated PSAS - characterized by minimal or absent refractory phase after orgasm or by chronically elevated sexual arousal due to a hormone related disorder. Women in this category would have PSAS beginning at the time of menopause, or would have increased PSAS symptoms during a specific phase of the menstrual cycle (usually for a few days before the onset of the menstrual period). The three hormones which may play a role in PSAS are progesterone, prolactin, and oxytocin.

A few women appear to be over-sensitive to the arousal effect or to the lowered orgasm threshold effect of *Progesterone*, suffering from PSAS symptoms premenstrually, during early pregnancy, or while on progesterone medication. One of my patients had constant sexual arousal and multiple spontaneous orgasms when treated with progesterone to reduce the risk of a miscarriage in the first trimester of pregnancy, but her PSAS resolved entirely when the progesterone medication was discontinued. Dr. Riley (via Dr. Leiblum's paper) published a case report of a woman with a diagnosis of PSAS who had uncontrollable arousal and masturbation for a few days before each menstrual period, but no symptoms of PSAS during the rest of her menstrual cycle. The premenstrual phase is the time when natural progesterone levels reach their peak, followed by a steep decline. Several other types of premenstrual dysphoria are well known, and all seem to be related to the progesterone level. Fortunately, control of progesterone levels and progesterone cycling is medically relatively easy. If this type of PSAS is related to progesterone physiology, a number of treatment options would be available including noncyclic oral contraceptives, late follicular phase estrogen patches to reduce luteal progesterone production, or even progesterone receptor blockers such as RU-486.

Another hormone, *Prolactin*, has recently been shown to maintain the refractory and relief phase after orgasm. Men have a larger release of prolactin after orgasm, which seems to reduce arousal, erection, and orgasmic capacity for several hours after orgasm (i.e. the "refractory phase"). Women typically have a delayed or lowered prolactin release with much smaller and shorter refractory phases and therefore are capable of multiple orgasms, but usually achieve relief and resolution after one to five orgasms. A prolactin release disorder could play a role in some women with PSAS. An absence or deficiency of prolactin would lead to continued sexual arousal with minimal or no relief after each orgasm. These women may have a very short refractory period lasting for a few seconds to a minute or so, followed immediately by another rapid build up of sexual arousal. If minimal or no prolactin surge is released from the pituitary at the time of orgasm, or if the prolactin hormone receptors are absent from pelvic organs or brain centers, then these women would have no relief or resolution of pelvic congestion. This potential cause of PSAS is speculative, but would likely respond to prolactin based therapy. Some medications will dramatically increase the release of prolactin from the pituitary gland - an example is Domperidome which is normally used as an antinausea drug. Whether these medications will also increase the prolactin surge after orgasm is uncertain, but if so they would be useful in the treatment of PSAS. Researchers are currently developing more powerful drugs to specifically enhance or block prolactin receptors in different tissues, and when commercially available these new medications could be even more effective.

Oxytocin is the other hormone released in large quantities from the pituitary gland at the time of orgasm, causing contraction of tiny muscle cells in the breast and generating a sense of relaxation or calmness in the brain. It is conceivable that an absent or diminished surge of oxytocin would minimize or prevent resolution of pelvic congestion, or the subjective feeling of relief. Women with oxytocin deficiency may experience very short refractory periods after each orgasm followed by a rapid return of intense

sexual arousal requiring another orgasm for relief. Hundreds of orgasms may be needed to eventually release enough oxytocin to diminish the state of prolonged sexual arousal. Diagnosis of this potential cause of PSAS would be difficult because oxytocin is hard to measure by standard laboratory tests. However, it would probably be a treatable syndrome. An oxytocin nasal spray would substitute for a pituitary surge of this hormone to "hammer down" chronic sexual arousal. Unfortunately, the commercial version of this product (Syntocin nasal spray) is no longer manufactured or available. A good compounding pharmacy may be able to mix a substitute, but this would have to be used under the supervision of an endocrinologist because of the possibility of an antidiuretic and low sodium level side effect.

5. Tourette's Syndrome variant of PSAS - would be characterized by persistent sexual arousal associated with ticks, compulsive masturbation, intrusive thoughts, and usually a family history of Tourette's syndrome or similar disorder. Technically this would not be a true variant of PSAS, but instead would be classified as a type of obsessive compulsive disorder with similar symptoms. Standard Tourette's therapy by a qualified neurologist would be appropriate.

I would like to emphasize that most of the information provided above is speculative. The intent is to develop some ideas for treating a syndrome that currently has few therapeutic options. It is unknown which, if any, of the diagnosis categories listed is an accurate representation of PSAS. It is possible that many women have a sub-clinical version of PSAS, with the capacity for multiple orgasms, after which arousal can be ignored or turned off. A few of these women may develop a hypersensitive response to normal sexual function which then progresses to PSAS.

As a matter of medical opinion, I would be opposed to clitorectomy as a PSAS therapy - the underlying chronic arousal may continue unchanged, but a potential trigger for stimulation relief would be permanently removed. This may result in "the worst of both worlds" situation; continuous arousal with diminished or absent ability for orgasm. Whether neurological blocks such as prudendal block would generate a similar situation or would result in effective relief is yet to be seen, but this therapy is outside of my field of expertise.

Hopefully the information provided in this outline will be useful for exploring some treatment options for a relatively untreatable syndrome. I recommend that the response to any trial of medical therapy be recorded in a symptom diary, as this information will be useful in narrowing down a diagnostic category and hopefully a more effective treatment. Upon request, I can refer patients with PSAS to physicians around the country who specialize in diagnosis and treatment of pelvic congestion syndrome, viscerosomatic hyperalgesia, interstitial cystitis, "neurotransmitter" neurology, reproductive endocrinology, and Tourette's neurology. I can be contacted at hrcraigmd@yahoo.com. Use the term "PSAS" in the title line, the email filter will probably not allow the words orgasm, etc in the title to go through, but OK to use any terms in the message itself.

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