Real Sexual Medicine Problems in Pediatric Patients

North American Society for Pediatric and Adolescent Gynecology
2018 Annual Clinical and Research Meeting (ACRM)
April 12-14, 2018
West Palm Beach, FL

Saturday, April 14, 2018 8:00 – 9:00 AM
Plenary 6 – The Alvin Goldfarb Lectureship

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Director, San Diego Sexual Medicine
Director of Sexual Medicine, Alvarado Hospital
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Past-President, International Society for the Study of Women’s Sexual Health
Past-President, Sexual Medicine Society of North America
Editor-in-Chief, Sexual Medicine Reviews
Editor Emeritus, The Journal of Sexual Medicine
Editor Emeritus, International Journal of Impotence Research
Thank you for this honor

dr.irwingoldstein@gmail.com
Learning Objectives:

1. Describe symptoms of persistent genital arousal disorder (PGAD)

2. Examine the clitoris properly in order to rule out clitoral adhesions as a source of pain

3. Recognize congenital neuroproliferative vestibulodynia and describe potential treatment
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Introduction to Sexual Dysfunctions in Pediatric Gynecology

Management of Girls with Genital Pain

Management of Girls with Persistent Genital Arousal Disorder (PGAD) or Orgasm Dysfunction
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International Society for the Study of Women’s Sexual Health (ISSWSH)
“There exist fundamental rights for the individual, including the **right to sexual health** and a capacity to enjoy and control sexual and reproductive behaviour in accordance with a social personal ethic—freedom from fear, shame, guilt, false beliefs and other factors inhibiting sexual response and impairing sexual relationships—freedom from organic disorders, disease and deficiencies that interfere with sexual and reproductive function.”

*World Health Organization, 1994, 1999*
Sexual dysfunctions are usually not exclusively psychologic nor exclusively biologic

Are there many causes of Genital Pain?

1. Altered hormone integrity
2. Increased nerve fiber density - genetic susceptibility leading to elevated levels of nerve growth factor substances
3. An injury to, or irritation of, the pudendal nerves that transmit pain and other sensations
4. Clitorodynia
Case 1

15 yo girl on 18 months of COC
She was prescribed COC because of distressing pain with her menstrual cycles
She can no longer use tampons
She has genital discomfort with tight clothing
She has urgency and frequency; urine cultures and urine analyses are normal
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- Urethral Meatus
- Minor vestibular gland
- Hymen
- Hart’s line
- Minor vestibular glands
- Hart’s line
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**HISTOLOGY**

Hematoxylin-eosin staining: To evaluate inflammation and squamous metaplasia within glandular structures.

- **Vestibular glands - Control**
  - Columnar epithelium of the vestibular glands
  - No chronic inflammatory infiltrate

- **Vestibular glands – Provoked Vestibulodynia**
  - Chronic inflammatory infiltrate
  - Replacement of columnar epithelium by squamous metaplasia

**Negative Internal Controls for AR**

- **Vestibular glands – Control Group**
  - Positive staining AR
  - Negative staining- AR
KEY principle of genital pain management: **undergo magnified assessment of the genito-urinary region via vulvoscopy**, ideally with the subject and the parent/legal guardian visualizing genital anatomy simultaneously with the health care provider.
Hormonally mediated vestibulodynia

The pain began
- While taking hormonal contraceptives or other medications that affect reproductive hormones, such as those for endometriosis, breast cancer, acne, infertility or removal of ovaries.
- While breastfeeding, perimenopause or postmenopause, or during abnormal or missing menstrual cycles.
- Pain is also associated with low calculated free testosterone levels; decreased libido, arousal or energy; or depression.

Congenital neuroproliferative vestibulodynia
- Pain since first tampon insertion or first attempt at intercourse
- Never completely pain-free
- Sensitivity or pain when pushing in on the belly button but none when pressure on the rest of the abdomen. The pain may radiate towards the vagina.

Acquired neuroproliferative vestibulodynia
- The pain began after:
  - A severe allergic reaction to a topical medication
  - A severe yeast infection
- More likely in women with a history of very sensitive skin or irritable or allergic reactions.
- Women may have certain genetic polymorphisms.

Hypertonic pelvic floor dysfunction
- The muscles of the pelvic floor are tight and tender when examined by an experienced doctor or physical therapist; also an abnormal EMG of the pelvic floor muscles.

Vaginitis
- Inflammation that includes the vestibule and vaginal mucosa. The vaginal mucosa typically looks inflamed and there is frequently yellowish discharge.
* Bacterial vaginosis does not cause enough inflammation to cause vestibulodynia.

Desquamative inflammation vaginitis (DIV)
- Thick, yellowish discharge that dries like glue and ruins underwear. The vaginal pH is >5.0 with numerous white blood cells and parabasal cells on wet mount.

Allergic vaginitis
- Semen allergy: swollen and inflamed vagina and vestibule that only occurs when condom is not used during intercourse
- Latex or spermicide allergy: swollen and inflamed vagina and vestibule that only occurs when condoms are not used during intercourse

Candidiasis
- Positive culture for yeast infections that do not respond to three doses of fluconazole.
Combined hormonal contraceptives - oral contraceptives, transdermal patch, vaginal ring - are commonly prescribed medications used by adolescent-aged girls.

Combined hormonal contraceptives are highly associated with vestibulodynia, a suspected common cause of genital pain in adolescent-aged girls.

Not all girls who use combined hormonal contraceptives develop genital pain – but they ALL experience low free testosterone
### Hormonally Mediated Provoked Vestibulodynia

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<table>
<thead>
<tr>
<th>Oral contraceptive use</th>
<th>Cases ($n = 138$)</th>
<th>Controls ($n = 309$)</th>
<th>Relative risk*</th>
<th>95% confidence interval</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Never use</td>
<td>5</td>
<td>4</td>
<td>52</td>
<td>17</td>
</tr>
<tr>
<td>Ever use</td>
<td>133</td>
<td>96</td>
<td>257</td>
<td>83</td>
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<tr>
<td><strong>Current vs. former use†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Former</td>
<td>23</td>
<td>17</td>
<td>68</td>
<td>22</td>
</tr>
<tr>
<td>Current</td>
<td>110</td>
<td>80</td>
<td>189</td>
<td>61</td>
</tr>
<tr>
<td>Duration of use (months)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–11</td>
<td>17</td>
<td>12</td>
<td>32</td>
<td>10</td>
</tr>
<tr>
<td>12 – 23</td>
<td>16</td>
<td>12</td>
<td>36</td>
<td>12</td>
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<td>40</td>
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<td>62</td>
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<td>48 – 71</td>
<td>25</td>
<td>18</td>
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<td>16</td>
</tr>
<tr>
<td>72 – 216</td>
<td>35</td>
<td>25</td>
<td>77</td>
<td>25</td>
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<tr>
<td>Age at first use (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>10 – 15</td>
<td>43</td>
<td>31</td>
<td>69</td>
<td>22</td>
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<tr>
<td>16 – 17</td>
<td>52</td>
<td>38</td>
<td>109</td>
<td>35</td>
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<tr>
<td>18 – 30</td>
<td>38</td>
<td>28</td>
<td>79</td>
<td>26</td>
</tr>
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</table>

*All relative risk estimates were based on never users as the referent category and were adjusted for age (<20, 20–24, 25–29, >29 years), marital status (single; married or common-law spouse; separated, divorced, or widowed), number of years of education (<14, 14–16, >16), body mass index (<20, 20–21, 22–24, >24 kg/m²), age at menarche (<13, 13, >13 years), age at first intercourse (<15, 15–16, >17 years), and lifetime number of sexual partners (1, 2–3, 4–5, >5).

† Refers to use at the time of pain onset for cases and 12 months prior to interview for controls.
Most commonly caused by hormonal contraceptives (may not resolve just by stopping COCs)

Other causes include: hormonal control of endometriosis or hirsutism

Diffuse vestibular tenderness of the entire vestibule
Ostia of glands are frequently erythematous
The vestibule may have a diffuse pallor with superimposed erythema

Low estradiol, low free testosterone, very high SHBG

The Effects of Hormonal Contraceptives on Female Sexuality: A Review

Lara J. Burrow, MD, MiSc,1#,2 Maureen Basho, PhD,1# and Andrew T. Goldstein, MD1#
1#The Center for Vulvar and Vaginal Disorders, Akron, OH, USA; 2Department of Human Science, Georgetown University, Washington, DC, USA; 3The Center for Vulvovaginal Disorders, Washington, DC, USA

Can Oral Contraceptives Cause Vestibulodynia?

Andrew Goldstein, MD1; Lara Burrow, MD,1# and Irwin Goldstein, MD1#
1#The Center for Vulvovaginal Disorders, Washington, DC, USA; 2#The Center for Vulvovaginal Disorders, San Diego, CA, USA

DOI: 10.1111/1743-4002.2020.01885.x
# 9 Blood Tests: Testosterone, SHBG, Dihydrotestosterone, Estradiol, Progesterone, LH, FSH, TSH, prolactin

<table>
<thead>
<tr>
<th>Test</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total testosterone, SHBG, calculated free testosterone (ng/dl)</td>
<td>Use free testosterone calculator (0.6 - 0.8 ng/dl)</td>
</tr>
<tr>
<td>DHT (ng/dl)</td>
<td>Suspicious in lower tertile</td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>Obtain three values in a 28 day cycle</td>
</tr>
<tr>
<td>Progesterone (ng/ml)</td>
<td>Obtain three values in a 28 day cycle</td>
</tr>
<tr>
<td>LH/FSH (mIU/ml)</td>
<td>Obtain three values in a 28 day cycle</td>
</tr>
<tr>
<td>TSH (mIU/L)</td>
<td>Suspicious &gt; 3.0</td>
</tr>
<tr>
<td>Prolactin (ng/ml)</td>
<td>Range established</td>
</tr>
</tbody>
</table>
Hormone-Directed Protein Synthesis

1. Total T in blood; Bound T in blood to SHBG (want SHBG to be LOW as possible)
2. Free T passes thru cell wall into cell cytoplasm
3. Dihydrotestosterone (DHT) synthesized via enzyme - 5 alpha reductase (no 5 alpha reductase in blood)
4. Dihydrotestosterone binds with high affinity to androgen receptor – DHT/AR transcriptional unit
5. DHT/AR transcriptional unit passes thru nuclear membrane – binds to DNA - mRNA
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SHBG = 25 nmol/L

SHBG = 168 nmol/L

Courtesy Dr. I. Goldstein
ANDROGEN BIOSYNTHESIS

DEHYDROEPIANDROSTERONE (DHEA)

3β-HSD

17β-HSD

ANDROSTENEDIONE

ANDROSTENEDIOL

17β-HSD

3β-HSD

TESTOSTERONE (T)

17β-HSD

5α REDUCTASE

DIHYDROTESTOSTERONE (DHT)

CELLULAR RECEPTOR BINDING & PROTEIN EXPRESSION

TESTOSTERONE (T) / DIHYDROTESTOSTERONE (DHT)

ANDROGEN RECEPTOR (AR)

TRANSCRIPTIONAL UNIT

NUCLEUS

DNA

TRANSSCRIPTIONAL ACTIVATION

mRNA

CYTOPLASM

ANDROGEN-DEPENDENT PROTEIN PRODUCTS

ANDROGEN-DEPENDENT PROTEINS AFFECTING GENITOURINARY TISSUES

CLITORIS

VESTIBULE

URETHRAL MEATUS

URETHRA

VAGINA

FEMALE PROSTATE

BLADDER

PELVIC FLOOR

Testosterone levels across the menstrual cycle

Sinha-Hakim et al, JCEM(33) 1998
Three Testosterone-Dependent Organs in the Vestibule

Glans clitoris
Minor Vestibular Glands
Peri-urethral tissue – G-spot
Hormonally Mediated Provoked Vestibulodynia

Treatment:

Stop hormonal contraceptives

Local to vestibule estradiol 0.01%, testosterone 0.1% in methylcellulose BID

Expect no improvement for 6 weeks, 30-40% by 12 weeks
### Case 1

**15 yo girl on 18 months of COC**

She was prescribed COC because of distressing pain with her menstrual cycles.

She can no longer use tampons.

She has genital discomfort with tight clothing.

She has urgency and frequency; urine cultures and urine analyses are normal.

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**15 yo girl on 18 months of COC**

She discontinued the COC and started a LARC- IUD (SKYLA).

She used a topical cream to the vestibule that combined estradiol 0.01% and testosterone 0.1%.

Her urinary symptoms resolved.
**Ulcerative IC** is defined as symptoms of urinary frequency and/or urgency and pelvic pain with documentation of an ulcerative lesion in the bladder on cystoscopic evaluation.

- **(only in 5-10% of the IC cases)**

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**Non ulcerative IC/PBS** as defined by the International Continence Society (ICS) is the complaint of suprapubic pain related to bladder filling accompanied by other symptoms, such as increased daytime and nighttime frequency in the absence of proven urinary infection or other obvious pathology.

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The Vestibule

- Often missed on physical exam and not taught during medical training
- Q-tip testing aids in diagnosis
- Provoked vestibulodynia (PVD)
  - Hormonal changes
  - Inflammation
  - Neurological factors
  - Hypertonic pelvic floor muscles

Provoked Vestibulodynia (PVD)

- Symptoms include provoked pain with sexual intercourse and tampon use or generalized pelvic pain
- Hypertonic pelvic floor muscles and peri-vestibular gland pathology cause LUTS and bladder pain
- Often misdiagnosed as interstitial cystitis/bladder pain syndrome (IC/BPS)
Purpose of the study

- Successful treatment of PVD has been anecdotally observed to resolve IC/BPS patient bladder symptoms.

- Does successful treatment for PVD lead to bladder symptom improvement?

Figure 1. Self-reported improvement in bladder symptoms after treatment for interstitial cystitis (A) or vestibulodynia (B).
What if the reason that 20 years of bladder directed therapy has not found an effective treatment is that the bladder is not the problem in most patients (ulcers excluded)?

It is time to think outside of the bladder!
Are there many causes of Genital Pain?

1. Altered hormone integrity

2. Increased nerve fiber density - genetic susceptibility leading to elevated levels of nerve growth factor substances

3. An injury to, or irritation of, the pudendal nerves that transmit pain and other sensations

4. Clitorodynia
16 yo girl tried tampons at age 12 but could not use them. She has used COC for only 1 week and then stopped due to side effects. She wishes to be sexually active but she has severe entrance genital pain with any sexual activity—she has never had pain-free penetration. She tried to get a ring placed in her umbilicus but it was too painful.
Neuro-Proliferative Vestibulodynia

Adolescent girls may report onset of symptoms after severe or recurrent candidiasis or allergic reaction\(^1,2\)

**Polymorphism in genes coding for IL-1ra, IL-1\(\beta\)\(^2,3\)**

**Decreased INF-\(\alpha\)\(^3\)**

**Elevated TNF, IL-1\(\beta\), IL-6, IL-8, Heparanse\(^3\)**

**Increased mast cells in mucosa\(^4\)**

**Increased inflammation can lead to a proliferation of C-afferent nociceptor\(^4\)**

Neuro-proliferative Vestibulodynia

Primary or congenital neuronal hyperplasia in the primitive urogenital endoderm.

- Umbilical hypersensitivity

Increased density of C-afferent nociceptors in the vestibular mucosa.\(^1,2\)

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Neuro-proliferative Vestibulodynia
Umbilical burning, stinging, hypersensitivity, discomfort is associated in 60% of cases of congenital neuro-proliferative vestibulodynia.

The urachus is endoderm.
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Neuro-proliferative Vestibulodynia

S-100 Immunostain

29-year-old control

Only a few nerve cell bundles are detectable (×25)

Patient with vestibulodynia

Abundant proliferation of nerve fibers (×25)

Involvement of Heparanase in the Pathogenesis of Localized Vulvodynia: Bornstein, Jacob; Cohen, Yitzhak; Zarlat, Doron; Sala, Shira; Ophir, Ella


DOI: 10.1097/pgp.0b013e318140021b

Fig. 1. A x100 Giemsa stain depicting the mast cells subepithelially in a specimen from localized vulvodynia.
Neuro-proliferative Vestibulodynia

Involvement of Heparanase in the Pathogenesis of Localized Vulvodynia.
Bornstein, Jacob; Cohen, Yitzhak; Zarfati, Doron; Sela, Shifra; Ophir, Ella

DOI: 10.1097/pgp.0b013e318140021b

Fig. 2. A x400 (A) and x600 (B). CD117 (C-kit) stain depicting mast cells. They are located subepithelially, among other inflammatory cells, in a specimen from localized vulvodynia.

Fig. 3. Heparanase expression. x400 (A) and x600 (B). Positive cytoplasmatic staining is seen in the subepithelial layer, close to the epithelial basement membrane.
Neuro-proliferative Vestibulodynia

**Table 1. Comparison of semiquantitative scores in localized vulvodynia and controls**

**Fig. 4.** x400 (A) and x600 (B) staining for PGP 9.5. The nerve fibers are seen intruding into the epithelium to more than half its depth.

**Involvement of Heparanase in the Pathogenesis of Localized Vulvodynia.**
Bornstein, Jacob; Cohen, Yitzhak; Zarfati, Doron; Sela, Shifra; Ophir, Ella

DOI: 10.1097/pgp.0b013e318140021b
Surgical Techniques

Vestibular Anesthesia Test for Neuroproliferative Vestibulodynia

Catherine Gagnon, NP, Julie Milton, NP, and Irwin Goldstein, MD
San Diego Sexual Medicine, San Diego, CA, USA

Position of patient for vulvoscopy

Biologic Issues in Neuroproliferative Vestibulodynia
Polymorphisms in genes coding for IL-1 receptor antagonist, and interleukin 1 beta
Decreased interferon-alpha
Elevated tumor necrosis factor, TNF, interleukin-1 beta, interleukin-6, interleukin-8 and heparanase
Increased mast cells limited to the vestibular mucosa (endodermal embryology)
Persistent inflammation leading to proliferation of C-afferent nociceptors

Clitoris
Urethra
Normal minor vestibular glands
Vestibule:
  Lateral border - Hart's line
  Medial border - Hymen
Vagina

Erythematous minor vestibular glands

Normal vestibular histology showing only a few C-afferent nociceptors stained with S100

Abnormal histology showing excess proliferation of C-afferent nociceptors seen in epithelium of vestibule on S100 staining

C-afferent nociceptors extending into epithelium
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Possible steps:

- Amitriptyline 1%/Ketamine .5% cream (Poterucha et al, 2012)
- Cromolyn 5-10% cream (Nyrjesy 2001)
- Montelukast 10 mg po qd (Kander et al 2007)
- Capsaicin 0.025% -0.050% cream to vestibule 20 min/d x 12 weeks (Steinberg A et al 2009)
- Alpha Lipoic Acid 1200mg/d po (Murina et al 2017)

Anticonvulsants
- Gabapentin 100-900mg
- Pregabalin 50-300mg
Case 2

16 yo girl tried tampons at age 12 but could not use them
She has used COC for only 1 week and then stopped due to side effects
She wishes to be sexually active but she has severe entrance genital pain with any sexual activity– she has never had pain-free penetration
She tried to get a ring placed in her umbilicus but it was too painful

16 yo girl could never use tampons at age 12
She had a positive umbilical supersensitivity test
She had a positive vestibular anesthesia test
She tried capsaicin, amitriptyline, interferon, Botox, trigger point injections, PT
At age 18 she underwent complete vestibulectomy with vaginal advancement flap reconstruction – she is now pain-free during penetration
Case 3

17 yo girl could easily use tampons at age 12
She was sexually active at age 16 and had pain-free penetration
She developed severe tonsillitis and was prescribed antibiotics
She developed a severe candidiasis
She applied topical antifungal agent and ever since she has severe entrance pain during penetration

17 yo girl could easily use tampons at age 12
She is doing better with sex therapy, capsaicin, amitriptyline, Botox, trigger point injections and PT
Are there many causes of Genital Pain?

1. Altered hormone integrity
2. Increased nerve fiber density - genetic susceptibility leading to elevated levels of nerve growth factor substances
3. An injury to, or irritation of, the pudendal nerves that transmit pain and other sensations
4. Clitorodynia

Can a girl “hurt” her vulva during bike riding or sports?
15 yo girl was an avid BMX racer since she was a pre-teen
She sustained a bad accident landing with her crotch on the cross bar of the BMX bike
She was taken to the Emergency Room but discharged that day on expectant care
She developed severe pelvic perineal pain while sitting
Physical exam revealed pudendal nerve tenderness at Alcock’s canal
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Ergonomics of 2 Bicycle Saddles
Prof. Dr. Ingo Froböse, Prof. Dr. Luc Bacyens, Kim Tofaute et.al.

Pressure at the Pudendal Area in Women of a Normal Saddle with Gel and of a Saddle with a Hole

Fig. 1 – athletic position - 40°

Fig. 2 – moderate position – 60°
Ultrasonographic and Doppler Findings of Subclinical Clitoral Microtraumatisms in Mountain Bikers and Horseback Riders

Cesare Battaglia, MD, PhD,* Rossella Elena Nappi, MD,† Fulvia Mancini, MD, PhD,* Arianna Ciancioli, MD,* Nicola Persico, MD,* and Paolo Busacchi, MD*

*Department of Obstetrics and Gynaecology, University of Bologna, Bologna, Italy; †Department of Obstetrics and Gynaecology, University of Pavia Research Centre for Reproductive Medicine, Pavia, Italy
Table 5  Regression models of vibratory thresholds and group (bicyclists vs. runners) by genital site*

<table>
<thead>
<tr>
<th>Genital site</th>
<th>Final model</th>
<th>N</th>
<th>Adjusted R²</th>
<th>Beta</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Clitoris</td>
<td>Age</td>
<td>69</td>
<td>0.099</td>
<td>0.026</td>
<td>0.005</td>
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<tr>
<td>Left perineum</td>
<td>Group</td>
<td>67</td>
<td>0.126</td>
<td>1.738</td>
<td>0.002</td>
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<tr>
<td>Right perineum</td>
<td>Group</td>
<td>67</td>
<td>0.085</td>
<td>1.620</td>
<td>0.010</td>
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<tr>
<td>Anterior vagina</td>
<td>Age</td>
<td>70</td>
<td>0.132</td>
<td>0.122</td>
<td>0.001</td>
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<tr>
<td>Posterior vagina</td>
<td>Group</td>
<td>70</td>
<td>0.194</td>
<td>1.653</td>
<td>&lt;0.001</td>
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<tr>
<td>Left labia</td>
<td>Group</td>
<td>68</td>
<td>0.060</td>
<td>0.902</td>
<td>0.025</td>
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<tr>
<td>Right labia</td>
<td>Group</td>
<td>68</td>
<td>0.113</td>
<td>2.010</td>
<td>0.003</td>
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<tr>
<td>Urethra</td>
<td>Age</td>
<td>70</td>
<td>0.212</td>
<td>0.145</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Adjusted for age (linear) and group (dummy)
# Real Sexual Medicine Problems in Pediatric Patients

### Pharmacologic Agents That Decrease Neurotransmission
- Local Anesthesia
- Tricyclic Antidepressants
- Calcium Channel Blocking Agents
- Sodium Channel Blocking Agents
- Anticonvulsant Agents

- **Lidocaine** – topical 1-5%
- **TCA** – Amitriptyline – 25 – 150 mg
  - Nortriptiline – 25 – 100 mg
  - Desipramine – 25 – 300 mg
- **Ca+** – Gabapentin – 100 – 2400 mg
- **Ca+** – Pregabalin – 25 – 300 mg
- **Na+** – Carbemazepine – 100 – 400 mg
- **Na+** – Oxcarbazepine – 150 – 2400 mg
- **Lamotrigine** – 25 – 200 mg

### Opioid Agonist
- Tramadol 25 – 200 mg
- Tapentadol 25 – 400 mg
- Hydrocodone bitartrate and acetaminophen – 5/500
- Oxycodone and Acetaminophen – 2.5/325 – 10/325

### Non-Pharmacologic Strategies That Decrease Neurotransmission
- TENS/Inferential Stimulation
- Sacral Neuromodulation – Interstim
- Pudendal Neuromodulation – Interstim
- Pudendal Nerve Block – local anesthesia and steroid

### Serotonin and Norepinephrine Reuptake Inhibitor
- **SNRI** – Duloxetine – 20 – 120 mg
- SNRI – Venlafaxine – 75 – 225 mg
- SNRI – Desvenlafaxine – 50 – 100 mg
- SRISRPA - Vilazodone – 10 – 40 mg
15 yo girl was an avid BMX racer since she was a pre-teen
She sustained a bad accident landing with her crotch on the cross bar of the BMX bike
She was taken to the Emergency Room but discharged that day on expectant care
She developed severe pelvic perineal pain while sitting
Physical exam revealed pudendal nerve tenderness at Alcock’s canal

15 yo girl was an avid BMX racer since early teens
She underwent several pudendal nerve blocks, uses oral pregabalin, physical therapy and TENS unit with moderate resolution of perineal pain
Are there many causes of Genital Pain?

1. Altered hormone integrity
2. Increased nerve fiber density - genetic susceptibility leading to elevated levels of nerve growth factor substances
3. An injury to, or irritation of, the pudendal nerves that transmit pain and other sensations
4. Clitorodynia
Clitoral Anesthesia Test

Benzocaine 20%
Lidocaine 8%
Tetracaine 8%
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Case 5

8 yo girl was uncomfortable wearing leggings
She was uncomfortable wiping herself after urinating
She was seen by several pediatricians
Her parents were told this was just a phase

Dear Amma,
Thank you for taking me to the Doctor's Office!
My nipple feels a lot better now!
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Introduction to Sexual Dysfunctions in Pediatric Gynecology

Management of Girls with Genital Pain

Management of Girls with Persistent Genital Arousal Disorder (PGAD)
15 year old presents with her mother to better understand treatments for her symptoms of unwanted and unrelenting "feelings down there"

She began experiencing "feelings" around age 6. She recalls beginning to cross her legs to help relieve the "feelings" around age 9

She and her mother have no recollection of any direct injuries to her genital area

She was diagnosed with anxiety disorder in kindergarten. She was diagnosed with ADHD in 2nd grade. She was treated with Stratera for ADHD

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Definition of **PGAD** is characterized by:

- Persistent/recurrent, unwanted/intrusive, distressing feelings of genital arousal or being on the verge of orgasm (genital dysesthesia)
- not associated with concomitant sexual interest, thoughts, or fantasies
- for a minimum of 6 months
PGAD can be lifelong or acquired, generalized or situational, and associated with the following characteristics:

Limited resolution, no resolution, or aggravation of symptoms by sexual activity with or without aversive and/or compromised orgasm or impaired orgasm frequency, intensity, timing, and/or pleasure;

Aggravation of genital symptoms by certain circumstances (sitting, driving, listening to music, general anxiety, stress or nervousness);

Despair, emotional lability, catastrophizing, and/or suicidality;

Inconsistent evidence of genital arousal on physical examination during symptoms (lubrication, swelling of clitoris or labia) (Neurologic vs Vascular)

When PGAD occurs concomitantly with complaints of overactive bladder and/or restless leg syndrome (S2, S3, S4), it can be considered restless genital syndrome.
16 yo avid runner: cross country, marathon, track and field runner since junior high school

As a young teen she masturbated regularly and this was satisfying

Now cannot feel her clitoris, cannot feel a tampon in her vagina, cannot feel urine passing though the “urine passageway”

She now has low back pain with sciatica

She has numbness in her toes
Real Sexual Medicine Problems in Pediatric Patients

Adolescent girls with bothersome and distressing persistent genital arousal disorder or orgasm dysfunction should undergo a thorough biopsychosocial history and physical examination, and laboratory tests.

- Sex Therapy Assessment with Parent or Legal Guardian
- External Pelvic Floor Physical Therapy Assessment
- Medical/Biologic Assessment
  - History and Physical Examination with Vulvoscopy
  - Neuro-genital, Hormonal Testing as needed
Diagnostic efforts should be made to identify **reversible causes of Persistent Genital Arousal Disorder (PGAD)**

**Symptomatic Therapeutic Interventions**

**Modification of Reversible causes**

Psychological problems should be performed through a psychosocial assessment.

Medication-related pathophysiology: A full history of medication use should be performed.

Certain medications negatively affect female sexual functions, such as selective serotonin reuptake inhibitors, antipsychotics, benzodiazepines, and anticonvulsants.
Real Sexual Medicine Problems in Pediatric Patients

Distracting and bothersome genital medical conditions history and physical examination, including diagnostic procedures such as vulvoscopy, cotton swab (Q-tip) testing, and vaginal wet mount and smear testing, should be performed. Pathologies may include: vestibulodynia, vaginitis.

Pelvic floor pathophysiologies pelvic floor physical therapy assessment should be performed.

Endocrine disorders such as low testosterone, low estradiol, low thyroid and elevated prolactin hormones: diagnostic blood testing can be performed to obtain baseline and then post-treatment values. Endocrinopathy states may be classically noted in adolescent age girls on hormonal birth control. The diagnostic blood tests include: total testosterone, sex hormone binding globulin, dihydrotestosterone, luteinizing hormone, follicle stimulating hormone, prolactin, thyroid stimulating hormone, estradiol and progesterone. Calculated free testosterone can be performed using the law of mass action calculator and the values of total testosterone and sex hormone binding globulin.
Neurologic pathophysiologies diagnostic testing can be performed to help localize the sites of neurologic impairment.

Diagnostic neuro-genital tests may be considered, such as quantitative sensory testing, sacral and foot dermatome testing, bulbocavernosus reflex latency testing, vaginal and urethral pelvic afferent nerve testing.
Peripheral Nerves: Autonomic Nerves VERSUS Somatic Nerves
Peripheral Nerves: Sensory Nerves VERSUS Motor Nerves

Somatic
Pudendal

Autonomic nerves
Hypogastric – Sympathetic
Pelvic - Parasympathetic

Sensory afferent innervation
Pudendal nerves – S2, S3, S4 (genital sensation – vibration, hot, cold, touch)
Pelvic nerves - S2, S3, S4 (distension)

Motor efferent innervation
Somatic - Pudendal (pelvic floor)
Hypogastric – Sympathetic (detumescence)
Pelvic – Parasympathetic (vasodilation – erection)

Vagus Nerve – afferent sensory 10th cranial nerve (cervix and likely periurethral anterior vaginal wall female prostate tissue- also the ear)
Rule Out Peripheral Neurologic-Based Sexual Problems

Pudendal nerve (or branches – dorsal/perineal) injury:

- Bicycle/spinning
- Blunt trauma
- Pelvic fracture
- Clitorodynia post-clitoral adhesions with closed compartment balanitis
- Neuro-proliferative vestibulodynia
- High tone pelvic floor dysfunction
Central Nerve Roots (Sacral Spinal Nerve Roots):

Sacral Spinal Nerve Root injuries may cause neurologic sexual dysfunction

Hypofunction VERSUS Hyperfunction

Reduced Genital Sensation

Persistent Genital Arousal Disorder, Genital Pain with Arousal, Genital Itching,
Role of the Cauda Equina

- Spinal Cord
- Conus Medullaris
- T12
- Cauda Equina
- Sacral Spinal Nerve Roots

Diagram shows the spinal cord and cauda equina, highlighting the sacral spinal nerve roots.
1. Neuro-Genital Testing

- Sensory and Reflex testing
- Quantitative Sensory Testing (QST)
- Sacral and Foot Dermatome Testing
- Vaginal and Urethral Pelvic Afferent Nerve Testing (V-PANT, U-PANT)
- Bulbocavernosus Reflex (BCR) Latency Testing

2. Sacral and Lumbar MRI Testing

3. Transforaminal Epidural Spinal Injection (TFESI) Testing
Sacral and Lumbar MRI Testing
Administration of local anesthesia to the sacral/lumbar spine pathology
Real Sexual Medicine Problems in Pediatric Patients

Treatment for adolescent girls with PGAD suspected from neurogenic sexual dysfunction

Disease modification treatment strategies:

*designed to cure the female sexual dysfunction and resolve the underlying pathophysiology(ies)*

Symptomatic therapeutic strategies:

*based on pharmacologic agents used to rebalance brain central nervous system excitatory and inhibitory neurotransmitter imbalances*
# Commonly Used Inhibitory Medications for HYPERFUNCTION

## Symptomatic strategies

1. Varenicline 0.5mg 2-3 times per day
2. Tramadol 50mg 2-3 times per day
3. Clonazepam 0.5mg 2-3 times per day
4. Pregabalin 50mg 3-4 times per day
5. Zolpidem 1mg 3-4 times per day (will be done by compounding pharmacy)
6. Prazosin 1 mg qhs
Case 6

15 year old presents with her mother to better understand treatments for her symptoms of unwanted and unrelenting "feelings down there"

She began experiencing "feelings" around age 6. She recalls beginning to cross her legs to help relieve the "feelings" around age 9

She and her mother have no recollection of any direct injuries to her genital area

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Learning Objectives:

1. Describe symptoms of persistent genital arousal disorder (PGAD)

2. Examine the clitoris properly in order to rule out clitoral adhesions as a source of pain

3. Recognize congenital neuroproliferative vestibulodynia and describe potential treatment