Hormone Mediated and Neuro-Proliferative Vestibulodynia – Diagnosis and Treatment

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Disclosures

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Objectives

Characterize subset of women who will benefit from the surgical treatment of dyspareunia

Analyze blood tests to understand the relevance of values to vestibular health and vestibulodynia

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Symptoms versus Diagnosis

Hormone-Mediated Vestibulodynia

Neuro-proliferative Vestibulodynia

SYMPTOM VERSUS DIAGNOSIS

Vulvodynia is a "*symptom*" literally meaning pain (dynia) in the vulvar region (vulvo) and is used to describe the symptoms of chronic or recurrent pain or discomfort in the vulvar region

The nature of the vulvodynia pain may vary widely from woman to woman - and can be associated with such symptoms of burning, stinging, irritation, or rawness - and can be present at various times, such as during or after penetration, or with certain clothing, or in certain positions

Patients and health care providers should not consider the "*symptom*" vulvodynia as a "*diagnosis*" and then provide universal treatments

SYMPTOM VERSUS DIAGNOSIS

PSYCHOLOGIC CAUSES:

Vulvodynia can be due to primary psychologic causes, such as aversion disorders

Vulvodynia can be due to associated with secondary psychologic causes, such as poor self-esteem, embarrassment, humiliation and frustration from having sex only to please the partner

SYMPTOM VERSUS DIAGNOSIS

PELVIC FLOOR CAUSES:

Vulvodynia can be due to primary high tone pelvic floor dysfunction, such as vaginismus

Vulvodynia can be due to secondary high tone pelvic floor dysfunction from an underlying medical/biologic condition

Medical or biologic causes vulvodynia:

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. Abnormal response of tissues to Candida infection, or recognized allergies or non-specific allergies
5. Dermatologic conditions: lichen sclerosus or lichen planus
6. Vulvar granuloma fissuratum
7. Peri-urethral glans pathology
8. Desquamative Inflammatory Vaginitis
9. Bartholin cyst
10. Clitorodynia
11. Pelvic Congestion Syndrome
12. Endometriosis
13. Pelvic Organ Prolapse
14. Interstitial Cystitis
15. Referral from Hip Disease
16. Partner Issues – Peyronie’s disease, piercings
17. High tone pelvic floor dysfunction

Vestibulodynia

The pain is confined to the vestibule: it (generally) stops outside of Hart's line and there is (generally) no pain inside the vagina.

The pain is throughout the entire vestibule. (If the pain is significantly worse in the back part of the vestibule consider a dual diagnosis, and follow the next decision tree the right as well)

The pain is much worse at 4,6, & 8 o'clock position of the vestibule (and there is minimal or no pain on either side of the urethra.)

There may be tenderness when deep pressure is applied to the perineum

The pain is mainly in the vestibule but there is irritation, redness, and (possibly fissures) on the perineum or in the grooves between the labia minora and majora.

Ulcers or erosions that may be confined to the vestibule but may also occur on the labia and perineum .

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 sex

--- 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 irritant 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

Lichen planus

Ulceration in the vestibule that can have "fern-like" or violet borders. The erosions can extend into the vagina and can also affect the mouth. Very significant scarring of the vulva and vagina possible.

Lichen Sclerosus

Ulcerations in the vestibule and labia but not in the vagina. Thick, white, itchy skin with very significant scarring.

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

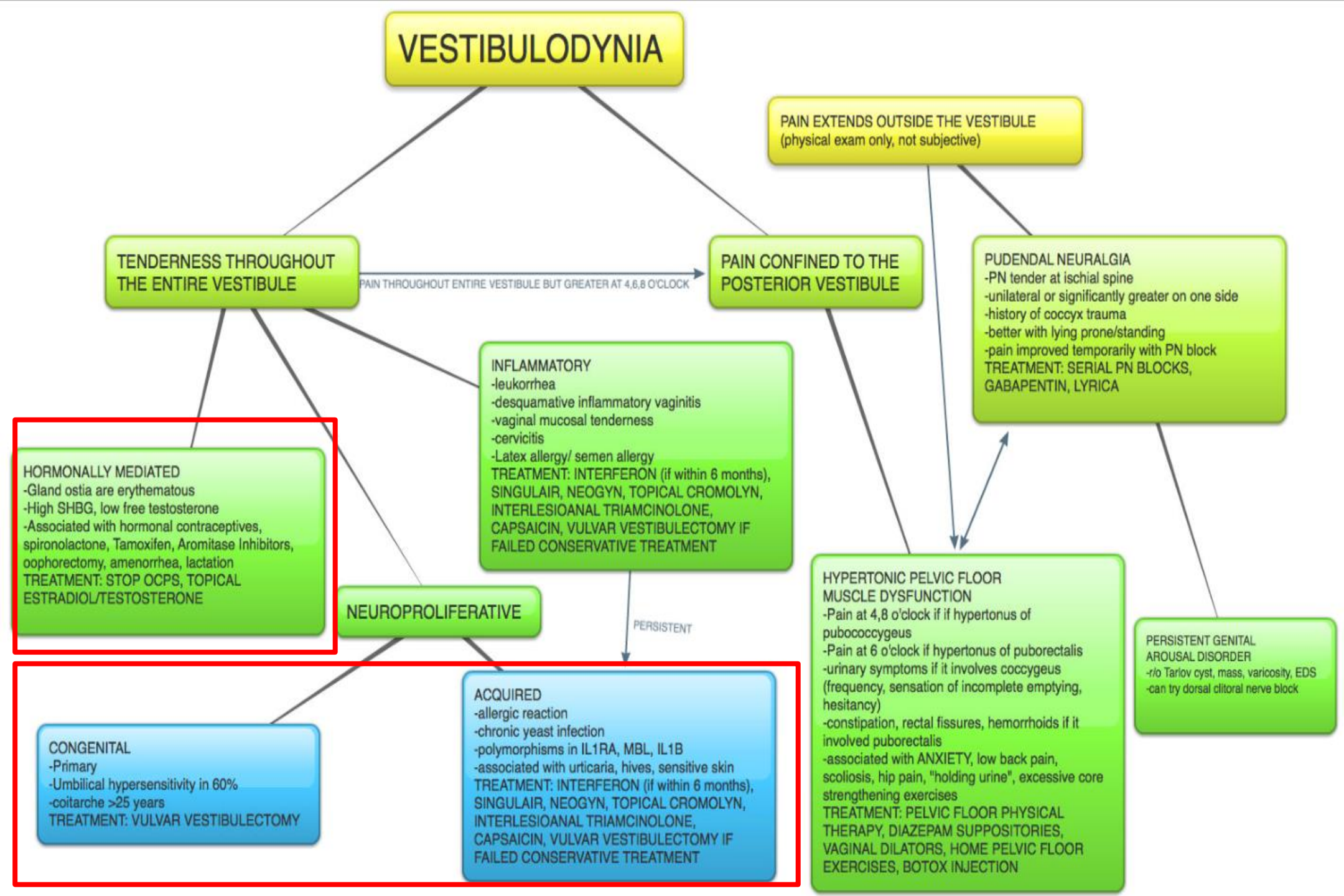
Allergic vaginitis

--- 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.


VESTIBULODYNIA
PAIN EXTENDS OUTSIDE THE VESTIBULE
(physical exam only, not subjective)
TENDERNESS THROUGHOUT THE ENTIRE VESTIBULE
PAIN THROUGHOUT ENTIRE VESTIBULE BUT GREATER AT 4,6,8 O'CLOCK
PAIN CONFINED TO THE POSTERIOR VESTIBULE
PUDENDAL NEURALGIA
-PN tender at ischial spine
-unilateral or significantly greater on one side
-history of coccyx trauma
-better with lying prone/standing
-pain improved temporarily with PN block
TREATMENT: SERIAL PN BLOCKS, GABAPENTIN, LYRICA
INFLAMMATORY
-leukorrhea
-desquamative inflammatory vaginitis
-vaginal mucosal tenderness
-cervicitis
-Latex allergy/ semen allergy
TREATMENT: INTERFERON (if within 6 months), SINGULAIR, NEOGYN, TOPICAL CROMOLYN, INTERLESIOANAL TRIAMCINOLONE, CAPSAICIN, VULVAR VESTIBULECTOMY IF FAILED CONSERVATIVE TREATMENT
HORMONALLY MEDIATED
-Gland ostia are erythematous
-High SHBG, low free testosterone
-Associated with hormonal contraceptives, spironolactone, Tamoxifen, Aromitase Inhibitors, oophorectomy, amenorrhea, lactation
TREATMENT: STOP OCPS, TOPICAL ESTRADIOL/TESTOSTERONE
NEUROPROLIFERATIVE
PERSISTENT
HYPERTONIC PELVIC FLOOR MUSCLE DYSFUNCTION
-Pain at 4,8 o'clock if if hypertonus of pubococcygeus
-Pain at 6 o'clock if hypertonus of puborectalis
-urinary symptoms if it involves coccygeus (frequency, sensation of incomplete emptying, hesitancy)
-constipation, rectal fissures, hemorrhoids if it involved puborectalis
-associated with ANXIETY, low back pain, scoliosis, hip pain, "holding urine", excessive core strengthening exercises
TREATMENT: PELVIC FLOOR PHYSICAL THERAPY, DIAZEPAM SUPPOSITORIES, VAGINAL DILATORS, HOME PELVIC FLOOR EXERCISES, BOTOX INJECTION
PERSISTENT GENITAL AROUSAL DISORDER
-r/o Tarlov cyst, mass, varicosity, EDS
-can try dorsal clitoral nerve block
CONGENITAL
-Primary
-Umbilical hypersensitivity in 60%
-coitarche >25 years
TREATMENT: VULVAR VESTIBULECTOMY
ACQUIRED
-allergic reaction
-chronic yeast infection
-polymorphisms in IL1RA, MBL, IL1B
-associated with urticaria, hives, sensitive skin
TREATMENT: INTERFERON (if within 6 months), SINGULAIR, NEOGYN, TOPICAL CROMOLYN, INTERLESIOANAL TRIAMCINOLONE, CAPSAICIN, VULVAR VESTIBULECTOMY IF FAILED CONSERVATIVE TREATMENT

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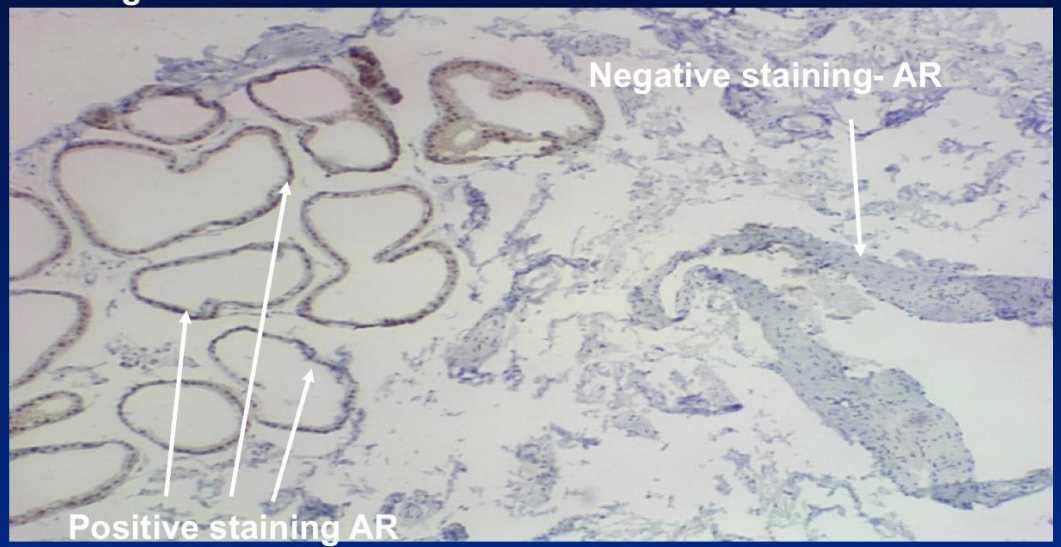
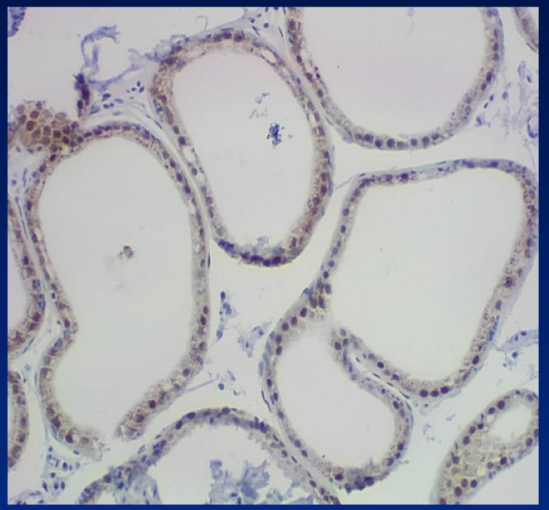
Hormonally Mediated Provoked Vestibulodynia

Negative Internal Controls for AR



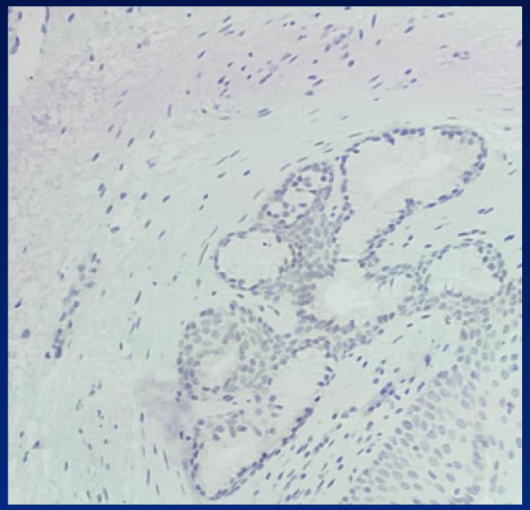
Vestibular glands – Control Group

Without Provoked Vestibulodynia



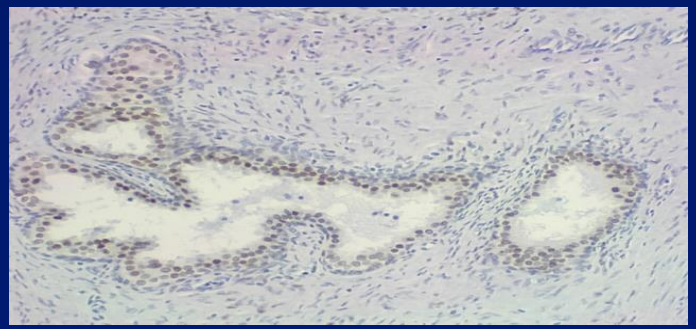
Vestibular glands – Positive cellular nuclei staining with anti-androgen receptor (AR)

With Provoked Vestibulodynia



Vestibular glands – Negative cellular nuclei staining with anti-androgen receptor (AR)

Positive External Controls for AR

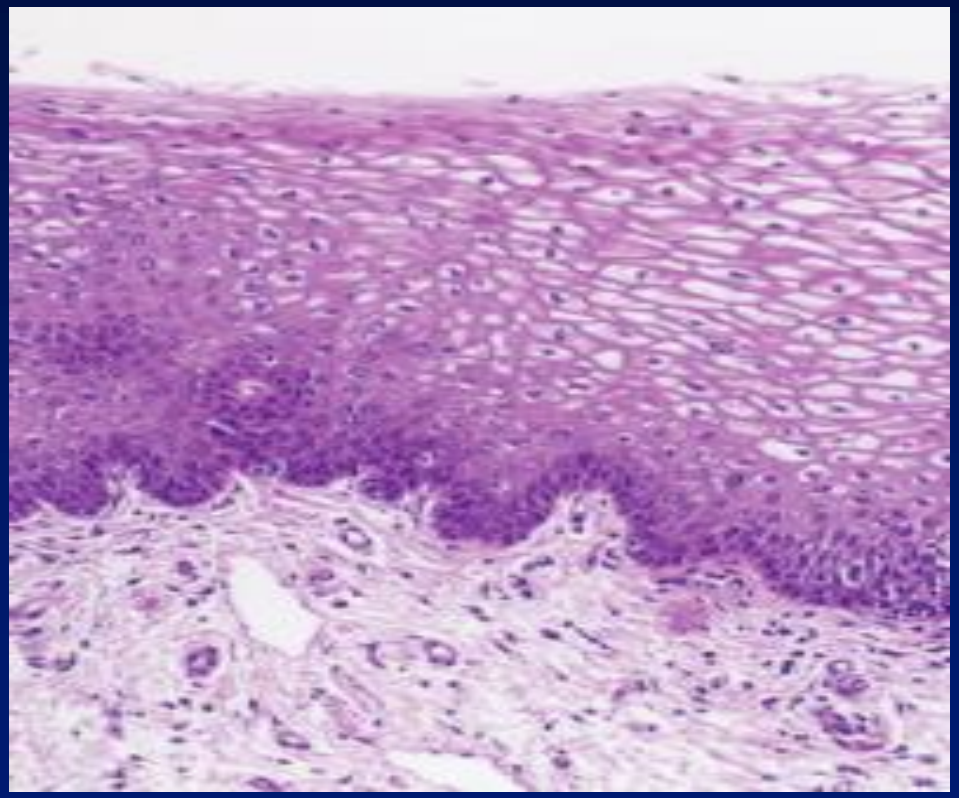


Prostate cancer sections

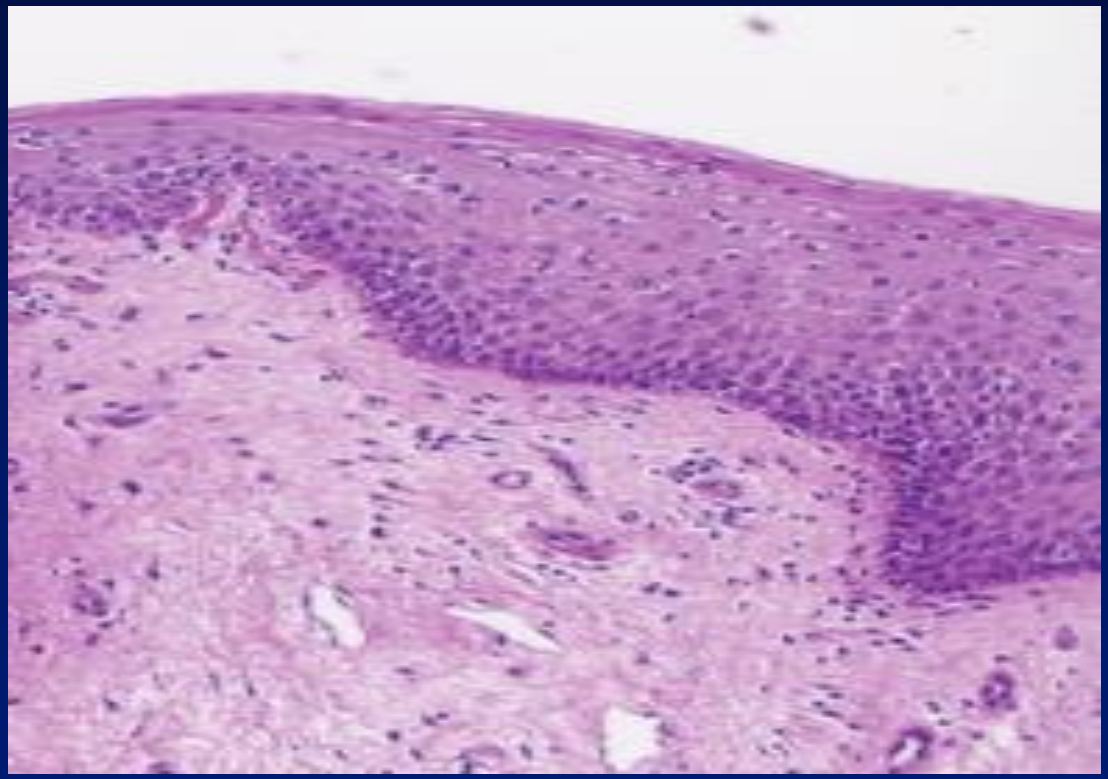
Hormonally Mediated Provoked Vestibulodynia

Women on OCP have altered morphological pattern with low and sparse dermal papillae

Might affect interlocking function of dermal papillae making epithelium more sensitive to stress (i.e., mechanical strain)



Normal Vestibular Epithelium[2]



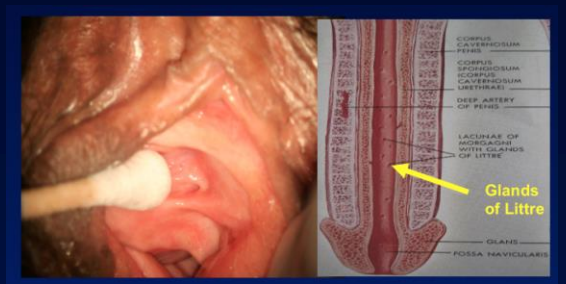
Vestibular Epithelium of Women on OCPs[2]

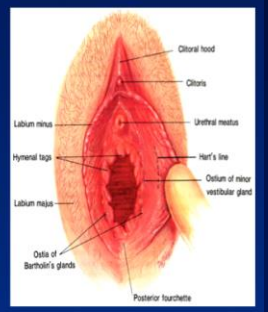
Johannesson U et al *Br J Dermatol. 2007, 157: 487-493)*

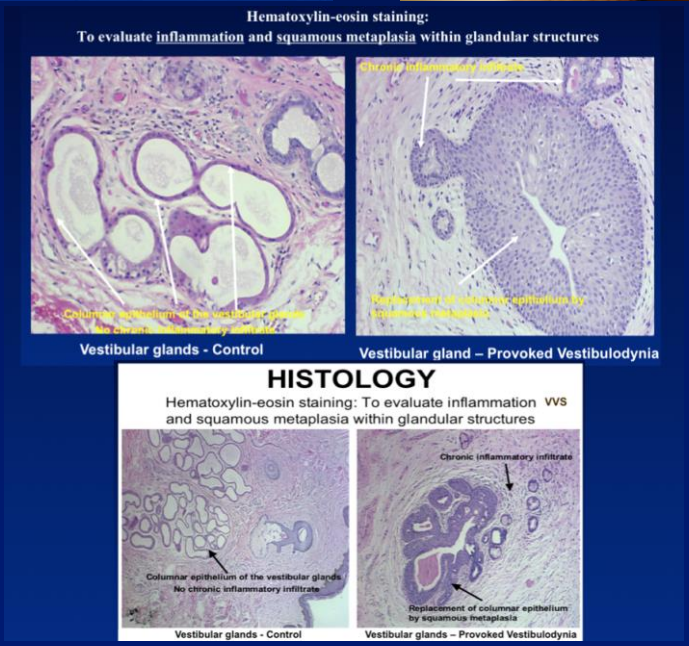
Hormonally Mediated Provoked Vestibulodynia

Associated with :

1. hormonal contraceptives (may not resolve just by stopping OCPs.)
2. menopause
3. oophorectomy
4. hormonal control of endometriosis or hirsutism, breast-feeding
5. infertility treatments
6. treatment of breast cancer



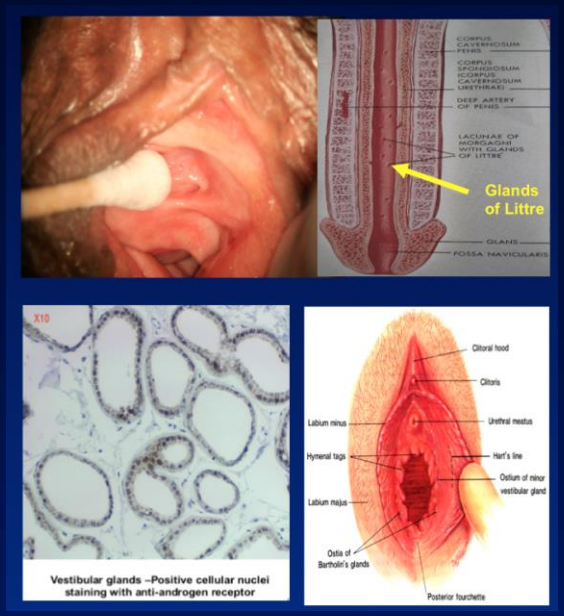


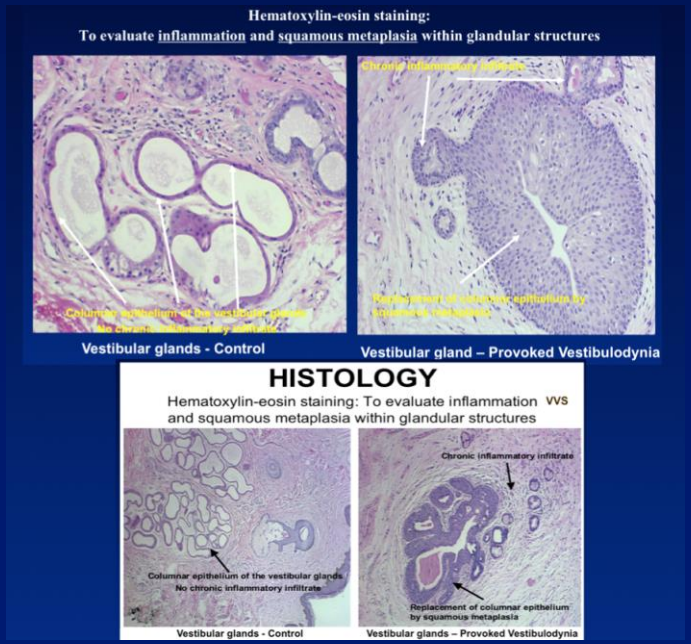


Burrows LJ, Goldstein AT. Vulvodynia. *J Sex Med 2008;5:5-15.*

Hormonally Mediated Provoked Vestibulodynia

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





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Use of Oral Contraceptive Pills and Vulvar Vestibulitis: A Case-Control Study

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Vulvar vestibulitis is characterized by superficial pain during intercourse. Exploratory studies have suggested that oral contraceptives (OCs) could be associated with occurrence of vulvar vestibulitis. This 1995–1998 case-control study in Québec, Canada, sought to reassess this association. Included were 138 women with vulvar vestibulitis whose symptoms had appeared in the previous 2 years and 309 age-matched controls who were consulting their physicians for reasons other than gynecologic problems or contraception. Cases and controls were interviewed to obtain a detailed history of OC use and information on potential confounding factors. Relative risks were estimated by using logistic regression. The authors found that 4 percent of cases had never used OCs compared with 17 percent of controls. The relative risk of vulvar vestibulitis was 6.6 (95 percent confidence interval: 2.5, 17.4) for ever users compared with never users. When OCs were first used before age 16 years, the relative risk of vulvar vestibulitis reached 9.3 (95 percent confidence interval: 3.2, 27.2) and increased with duration of OC use up to 2–4 years. The relative risk was higher when the pill used was of high progestogenic, high androgenic, and low estrogenic potency. The possibility that OC use may contribute to the occurrence of vulvar vestibulitis needs to be evaluated carefully. *Am J Epidemiol* 2002;156:254–61.

case-control studies; contraceptives, oral; dyspareunia; pain; vulvar diseases; vulvitis

Oral contraceptive use	Cases (n = 138)		Controls (n = 309)		Relative risk*	95% confidence interval
	No.	%	No.	%		
Never use	5	4	52	17	1.0	
Ever use	133	96	257	83	6.6	2.5, 17.4
Current vs. former use†						
Former	23	17	68	22	4.3	1.4, 12.7
Current	110	80	189	61	7.1	2.7, 18.9
Duration of use (months)						
1–11	17	12	32	10	5.9	1.9, 18.1
12 – 23	16	12	36	12	4.7	1.5, 14.3
24 – 47	40	29	62	20	7.9	2.8, 22.3
48 – 71	25	18	50	16	7.3	2.4, 21.7
72 – 216	35	25	77	25	6.9	2.3, 21.1
Age at first use (years)						
10 – 15	43	31	69	22	9.3	3.2, 27.2
16 – 17	52	38	109	35	6.2	2.3, 17.0
18 – 30	38	28	79	26	5.4	1.9, 15.2

* 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/m^2), 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.

Bouchard et al.Am J Epidemiol vol 156, No 3, 2002

Clitoral Vascularization and Sexual Behavior in Young Patients Treated with Drospirenone–Ethinyl Estradiol or Contraceptive Vaginal Ring: A Prospective, Randomized, Pilot Study

J Sex Med 2014;11:471–480

Cesare Battaglia, MD, PhD,* Elena Morotti, MD,† Nicola Persico, MD, PhD,* Bruno Battaglia, MS,* Paolo Busacchi, MD,* Paolo Casadio, MD,* Roberto Paradisi, MD,* and Stefano Venturoli, MD*

Table 1 Physical, clinical, and hormonal profile before and after the treatment with Yasmin (group I; n = 21) or NuvaRing (group II; n = 19)

				P value	
Variable	Group	Baseline (a)	6 months (b)	a vs. b	I vs. II at 6 months
Age (years)	I	26.1 ± 2.7			
	II	27.0 ± 1.9			
BMI (kg/m^2)	I	20.8 ± 2.2	21.1 ± 1.0		
	II	22.0 ± 1.5	22.2 ± 0.9		
Estradiol (pmol/L)	I	199 ± 57	110 ± 49	0.01	
	II	222 ± 104	197 ± 112		0.003
Androstenedione (nmol/L)	I	9.9 ± 2.7	8.1 ± 2.4		
	II	9.3 ± 1.5	8.8 ± 1.6		
Testosterone (nmol/L)	I	1.9 ± 0.6	1.3 ± 0.4	0.007	
	II	2.1 ± 0.9	1.6 ± 0.5	0.011	
SHBG (nmol/L)	I	53 ± 15	171 ± 11	<0.001	
	II	55 ± 13	162 ± 17	<0.001	
FAI (%)	I	3.6 ± 2.0	0.6 ± 0.3	<0.001	
	II	4.0 ± 1.9	1.1 ± 0.3	<0.001	0.026
FEI (%)	I	4.0 ± 2.1	0.6 ± 0.3	<0.001	
	II	4.0 ± 2.0	1.5 ± 0.3	<0.001	<0.0001

BMI = body mass index; FAI = Free Androgen Index; FEI = Free Estrogen Index

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Table 2 Ultrasonographic, Doppler follow measures monitoring before and after the treatment with Yasmin (group I; n = 21) or NuvaRing (group II; n = 19)

				P value	
Variable	Group	Baseline (a)	6 months (b)	a vs. b	I vs. II at 6 months
Clitoral Volume (mL)	I	0.85 ± 0.09	0.65 ± 0.13	0.050	
	II	0.98 ± 0.32	0.75 ± 0.15	0.039	

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Table 3 Behavioral profile indices before and after the treatment with Yasmin (group I; n = 21) or NuvaRing (group II; n = 19)

				P value	
Variable	Group	Baseline (a)	6 months (b)	a vs. b	I vs. II at 6 months
MFSQ Sex (score)	I	51.2 ± 5.0	42.0 ± 8.9	0.001	
	II	54.1 ± 4.4	47.5 ± 10.3	0.001	0.037
Intercourse/week (n)	I	2.6 ± 0.6	1.8 ± 0.8	0.036	
	II	2.7 ± 1.2	2.5 ± 1.1		0.050
Orgasmic Frequency (score)	I	6.0 ± 1.4	4.2 ± 1.3	0.019	
	II	6.1 ± 0.9	5.4 ± 1.4		0.050
Orgasmic Intensity (score)	I	6.0 ± 1.1	5.5 ± 1.3		
	II	6.6 ± 0.5	5.7 ± 2.5		
Pain During Intercourse (score)	I	6.6 ± 0.3	3.0 ± 0.5	0.011	
	II	6.7 ± 0.5	5.6 ± 1.0		0.003
BDI (score)	I	6.8 ± 3.3	6.7 ± 5.0		
	II	6.2 ± 5.2	6.5 ± 4.4		

BDI = Beck's Depression Inventory; MFSQ = two-factor McCoy Female Sexuality Questionnaire

Hormonal Contraception and Female Pain, Orgasm and Sexual Pleasure

J Sex Med 2014;11:462–470

Nicole K. Smith, PhD, MPH,* Kristen N. Jozkowski, PhD,† and Stephanie A. Sanders, PhD‡,§

Table 1 Participant characteristics (n = 1,101)

		Contraceptive method status		
	Total sample % (n)	Nonhormonal % (n)	Hormonal % (n)	Significance
Characteristics	100 (1,101)	51.4 (566)	48.6 (535)	*P*
Age				
18–24	52.4 (577)	38.7 (219)	66.9 (358)	$P < 0.001$
25–34	34.3 (378)	40.5 (229)	27.9 (149)	
35–44	11.1 (122)	17.3 (98)	4.5 (24)	
45–51	2.2 (24)	3.5 (20)	0.7 (4)	
Race/ethnicity				
White/European American	81.6 (898)	79.7 (451)	84.1 (450)	$P = 0.270$
Black/African American	4.5 (49)	5.5 (31)	3.4 (18)	
Latina/Hispanic	6.4 (70)	6.9 (39)	5.8 (31)	
American Indian or Native Alaskan	2.9 (32)	3.9 (22)	1.9 (10)	
Asian/Asian American	4.0 (44)	3.4 (19)	4.1 (22)	
Native Hawaiian/Pacific Islander	0.7 (8)	0.7 (4)	0.7 (4)	
Relationship status				
Single	45.6 (497)	35.6 (199)	56.0 (298)	$P < 0.001$
Married	26.5 (289)	35.2 (197)	17.3 (92)	
Living with partner	22.4 (244)	22.2 (124)	22.6 (120)	
Separate/divorced	5.3 (58)	6.8 (38)	3.8 (20)	
Exclusivity status				
Exclusive relationship	81.0 (890)	76.6 (433)	85.6 (457)	$P = 0.038$
Nonexclusive relationship	18.8 (207)	23.0 (130)	14.4 (77)	
No relationship	0.0 (0)	0.0 (0)	0.0 (0)	
Education level				
High school graduate or less	14.5 (148)	15.1 (85)	11.7 (63)	$P = 0.121$
Trade/business School	2.3 (25)	2.5 (14)	2.1 (11)	
Some college	44.0 (484)	40.5 (229)	47.7 (255)	
Completed college	26.4 (290)	26.2 (148)	26.5 (142)	
Graduate school	13.9 (153)	15.8 (89)	12.0 (64)	
Children in the home				
Yes	27.8 (267)	39.5 (195)	15.5 (72)	$P < 0.001$
No	72.2 (692)	60.5 (299)	84.5 (393)	

Hormonal Contraception and Female Pain, Orgasm and Sexual Pleasure

J Sex Med 2014;11:462–470

Nicole K. Smith, PhD, MPH,* Kristen N. Jozkowski, PhD,† and Stephanie A. Sanders, PhD‡,§

Table 2 Contraceptive method use (n = 1,101)

Type of method	% (n)
Hormonal method	48.6 (535)
Combined hormonal pill	72.1 (386)
Progestin-only pill	5.6 (30)
Hormonal patch	3.7 (20)
Vaginal ring	13.3 (71)
Birth control shot	5.2 (28)
Nonhormonal	51.4 (566)
Male condoms	60.9 (345)
Female condoms	0.4 (2)
Diaphragm/cap/shield	1.9 (11)
Copper IUD	12.0 (68)
Fertility awareness/Natural FP	10.6 (60)
Withdrawal	26.1 (148)
Vasectomy	0.0 (0)
Tubal ligation	6.0 (34)

Participants could be included in the nonhormonal method categories more than once
IUD, intrauterine device; FP, family planning

Table 3 Mean differences in sexual function measures based on contraceptive method

	Total M (SD)	Hormonal M (SD)	Nonhormonal M (SD)	*t* (d.f.)
Frequency of sex	9.86 (9.41)	8.90 (8.84)	10.83 (9.91)	3.88** (1,151)
Initiating sex	0.55 (0.99)	0.46 (1.01)	0.59 (1.24)	NS
Pain	0.13 (0.33)	0.21 (0.19)	0.06 (0.21)	−3.43** (1,148)
Arousal	0.78 (64)	0.67 (0.50)	0.86 (0.69)	2.58* (1,148)
Satisfaction	1.30 (1.97)	1.30 (2.85)	1.32 (1.41)	NS
Drier vagina	0.18 (0.26)	0.29 (0.24)	0.08 (0.24)	−3.48** (1,145)
Orgasm	1.07 (1.74)	0.88 (1.00)	1.18 (2.00)	1.82* (1,153)
Pleasure	0.69 (1.20)	0.68 (0.30)	0.70 (2.1)	NS
Lubricant use	0.25 (0.611)	0.31 (0.47)	0.19 (0.69)	−1.63* (1,150)

*$P < 0.05$, **$P < 0.01$
d.f., degrees of freedom; M, mean; SD, standard deviation

Sexual Behavior and Oral Contraception: A Pilot Study

J Sex Med 2012;9:550–557

Cesare Battaglia, MD, PhD,* Bruno Battaglia, MS,* Fulvia Mancini, MD, PhD,† Paolo Busacchi, MD,* Maria Chiara Paganotto, MD,* Elena Morotti, MS,* and Stefano Venturoli, MD*

Table 1 Hormonal and biochemical profile before and after 3-month treatment with an oral contraceptive containing 30 µg ethinylestradiol and 3 mg drospirenone in 21 young, healthy women without sexual problems

	Normal range	Baseline (N = 21)	After 3 months (N = 21)	Significance ($P < 0.05$)
Estradiol (pmol/L)	45–350	187 ± 86	81 ± 44	0.021
Testosterone (nmol/L)	0.70–2.70	1.2 ± 0.2	1.0 ± 0.7	0.477
Androstenedione (nmol/L)	1.0–11.5	8.4 ± 1.1	7.8 ± 0.8	0.124
SHBG (nmol/L)	30–120	56 ± 29	115 ± 44	0.029
FAI (%)		2.1 ± 0.7	0.8 ± 0.7	0.011
FEI (%)		0.32 ± 0.02	0.06 ± 0.05	<0.001

FAI = free androgen index; FEI = free estrogen index; SHBG = sex hormone binding globulin

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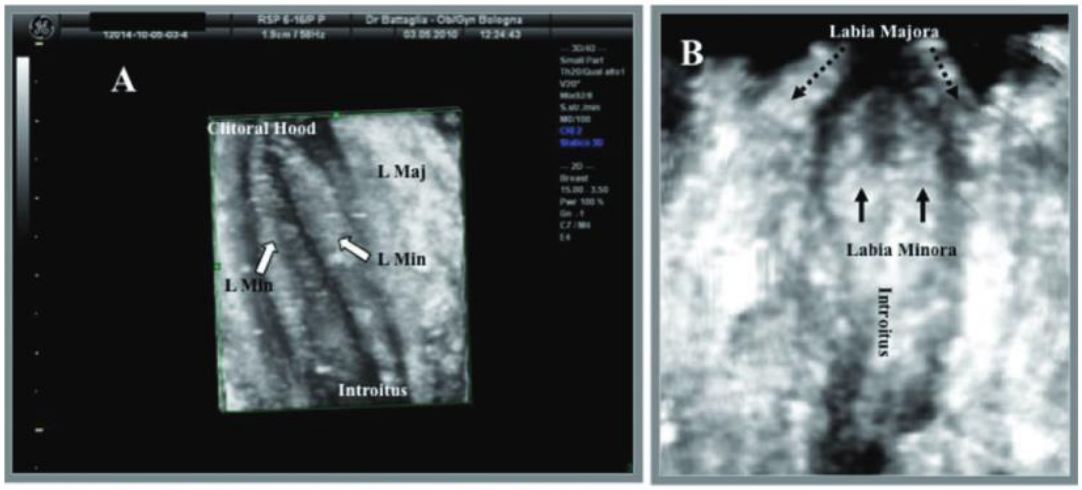
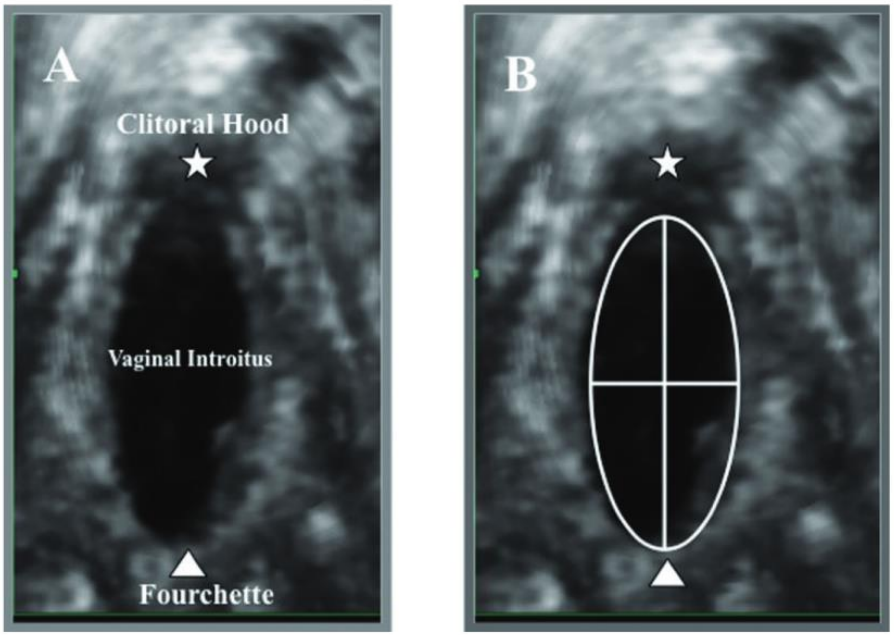
Table 2 Ultrasonographic and Doppler indices before and after 3-month treatment with an oral contraceptive containing 30 μg ethinylestradiol and 3 mg drospirenone in 21 young, healthy women without sexual problems

	Baseline (N = 21)	After 3 months (N = 21)	Significance ($P < 0.05$)
Labium minus thickness (mm)	4.5 ± 0.4	3.9 ± 0.4	0.001
Vaginal introitus area (cm^2)	1.04 ± 0.23	0.81 ± 0.21	0.044





Sexual Behavior and Oral Contraception: A Pilot Study

J Sex Med 2012;9:550–557

Cesare Battaglia, MD, PhD,* Bruno Battaglia, MS,* Fulvia Mancini, MD, PhD,† Paolo Busacchi, MD,* Maria Chiara Paganotto, MD,* Elena Morotti, MS,* and Stefano Venturoli, MD*

Table 3 Behavioral profile indices before and after 3-month treatment with an oral contraceptive containing 30 μg ethinylestradiol and 3 mg drospirenone in 21 young, healthy women without sexual problems

	Baseline (N = 21)	After 3 months (N = 21)	Significance ($P < 0.05$)
MFSQ sex (score)	49.6 ± 8.6	45.9 ± 8.4	0.033
Intercourse/week (N)	2.6 ± 1.3	1.5 ± 1.0	0.047
Orgasmic frequency (score)	6.1 ± 0.7	4.5 ± 0.6	0.005
Orgasmic intensity (score)	6.0 ± 1.1	5.3 ± 1.4	0.248
Pain during intercourse (score)	6.6 ± 0.6	3.0 ± 0.5	<0.001

MFSQ = McCoy Female Sexuality Questionnaire

Table 1 Demographic data

	All participants	
Participants (after screening for unserious responders)	Number 1,086	Percentage 100.0
Contraception in past 6 month		
Yes	945	87.0
No	141	13.0
Method of contraception in past 6 month(multiple answers possible)		
Oral contraceptives (OC) total	752	69.2
Contraceptive implant	8	0.7
Intrauterine methods	19	1.7
Vaginal contraceptive ring	78	7.2
Condoms	243	22.4
Fertility awareness	17	1.6
Other contraception	8	0.7
Sexually active in the past 4 weeks		
Yes	1,057	97.3
No	29	2.7
Age (years)		
<25	856	78.8
≥25 and <35	223	20.5
>35	7	0.6
Stable relationship		
Yes	869	80.0
Mean duration	3.2 (std 2.6) years	
No	217	20.0
Pregnancy		
No pregnancy	1,046	96.3
One pregnancy	29	2.7
More than one pregnancy	11	1.0
Pregnant in the last 2 years		
Yes	26	2.4
No	1,060	97.6
Active wish for children		
Yes	37	3.4
No	1,049	96.6
Smoking		
Yes	131	12.1
Mean number of cigarettes/day	8.7 (std 6.8) cigarettes / day	
No	955	87.9

Prevalence of Sexual Dysfunction and Impact of Contraception in Female German Medical Students

J Sex Med 2010;7:2139–2148

Christian W. Wallwiener, MD,* Lisa-Maria Wallwiener, MD,† Harald Seeger, PhD,* Alfred O. Mück, MD, PhD,* Johannes Bitzer, MD,‡ and Markus Wallwiener, MD§

The method of contraception and smoking were factors with significant effect on the total FSFI score whereby hormonal contraception was associated with lower total FSFI scores and lower desire and arousal scores than no contraception and non-hormonal contraception only. Other variables such as stress, pregnancy, smoking, relationship and wish for children had an important impact on sexual function as expected according to earlier studies.

The contraception method has a significant effect on the sexual functioning score and women using contraception, especially hormonal contraception, had lower sexual functioning scores

OCP USERS = FOUR VULVOSCOPIC FINDINGS

Clitoral atrophy

Provoked vestibulodynia

Labial resorption

Limited robust peri-urethral tissue

UNUSUAL LOCATIONS OF +’ve Q-TIP TESTING

Hormonally Mediated Provoked Vestibulodynia

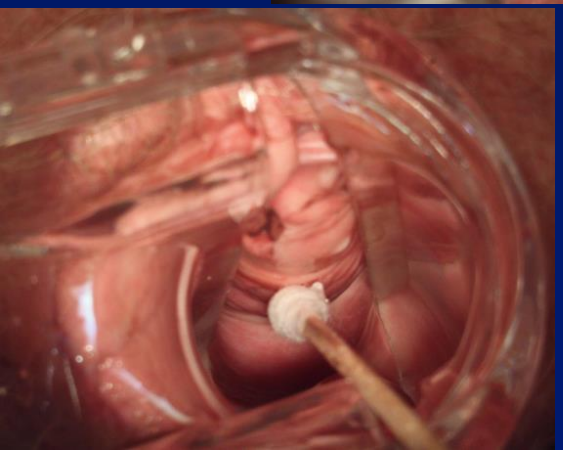
Treatment:

- **Stop hormonal contraceptives**
- **Systemic testosterone – ideal calculated free testosterone 0.8 ng/dl**
- **Local to vestibule estradiol 0.02%/testosterone 0.1% in methylcellulose BID**
- **Expect no improvement for 6 weeks, 30-40% by 12 weeks**

Burrows LJ, Goldstein AT. Vulvodynia. *J Sex Med 2008;5:5-15.*

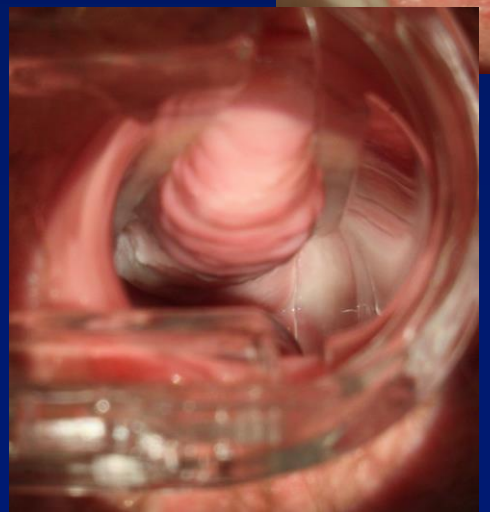
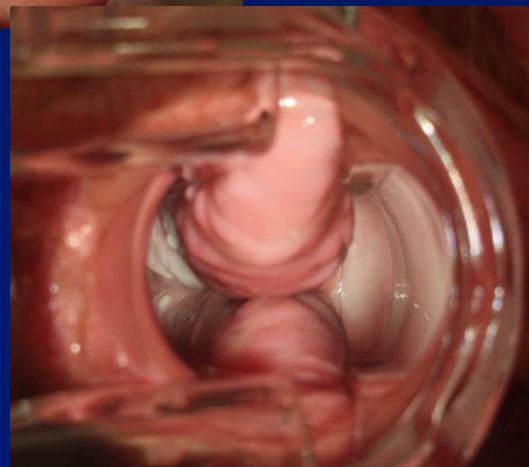
Vulvoscopy 10/5/12




Vulvoscopy 1/18/13



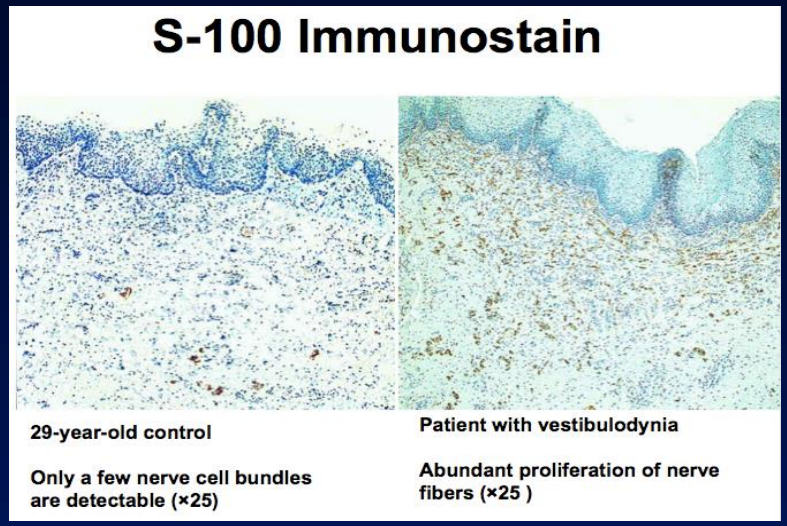




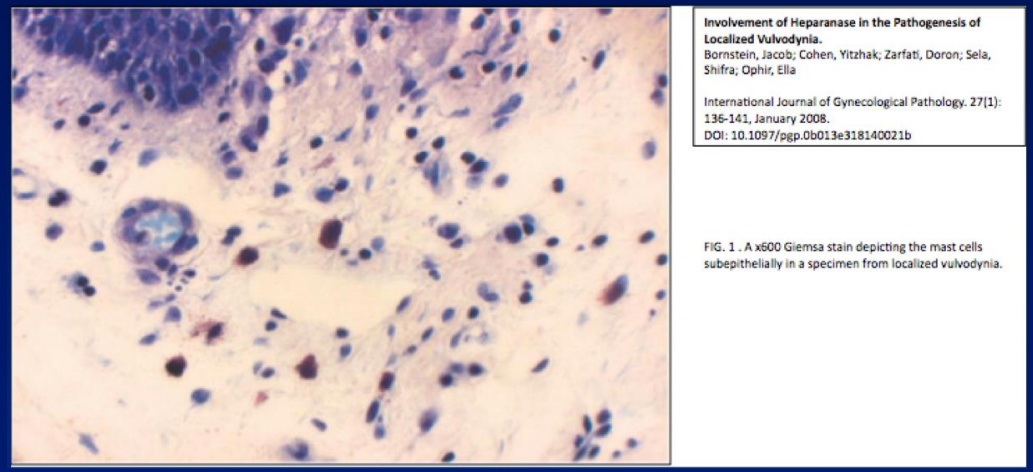
Medical or biologic causes vulvodynia:

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. Abnormal response of tissues to Candida infection, or recognized allergies or non-specific allergies
5. Dermatologic conditions: lichen sclerosus or lichen planus
6. Vulvar granuloma fissuratum
7. Peri-urethral glans pathology
8. Desquamative Inflammatory Vaginitis
9. Bartholin cyst
10. Clitorodynia
11. Pelvic Congestion Syndrome
12. Endometriosis
13. Pelvic Organ Prolapse
14. Interstitial Cystitis
15. Referral from Hip Disease
16. Partner Issues – Peyronie's disease, piercings
17. High tone pelvic floor dysfunction

Acquired Neuro-Proliferative Vestibulodynia

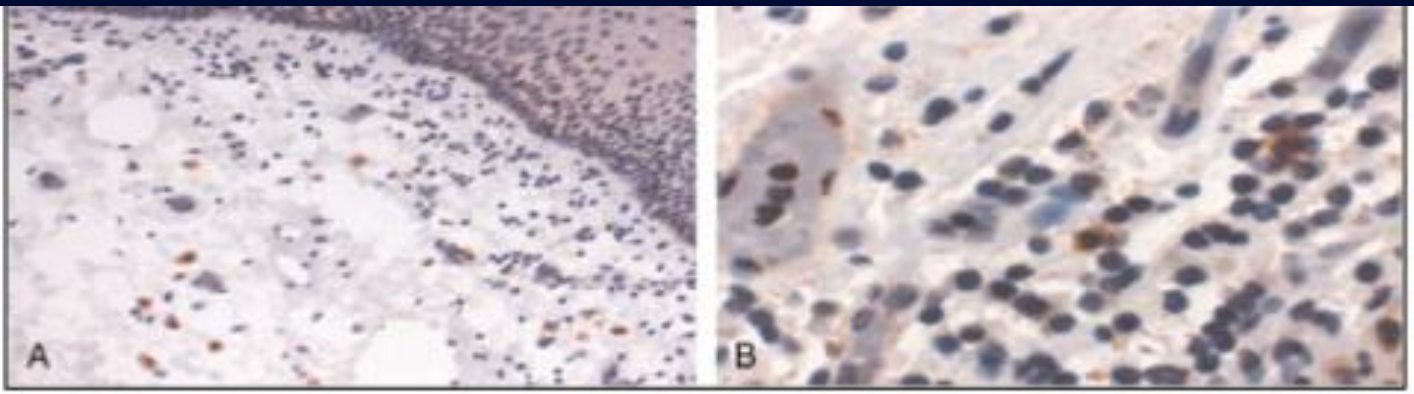
- Women reports onset of symptoms after severe or recurrent candidiasis or allergic reaction[1,2]
- Polymorphism in genes coding for IL-1ra, IL-1β[2,3]
- Decreased INF-α[3]
- Elevated TNF, IL-1β, IL-6, IL-8, Heparanse[3]
- Increased mast cells in mucosa[4]
- Persistent inflammation can lead to a proliferation of C-afferent nociceptor[4]





1. Harlow BL Ann Epidemiol. 2009 Nov;19(11):771-77
2. Witkin SS Am J Obstet Gynecol. 2002 Mar;186(3):361-4.
3. Foster Am J Obstet Gynecol. 2007 Apr;196(4):346.e1-8
4. Bornstein J Int J Gynecol Pathol. 2008 Jan;27(1):136-41.

Neuroproliferative Vestibulodynia



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

International Journal of Gynecological Pathology. 27(1): 136-141, January 2008.
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.

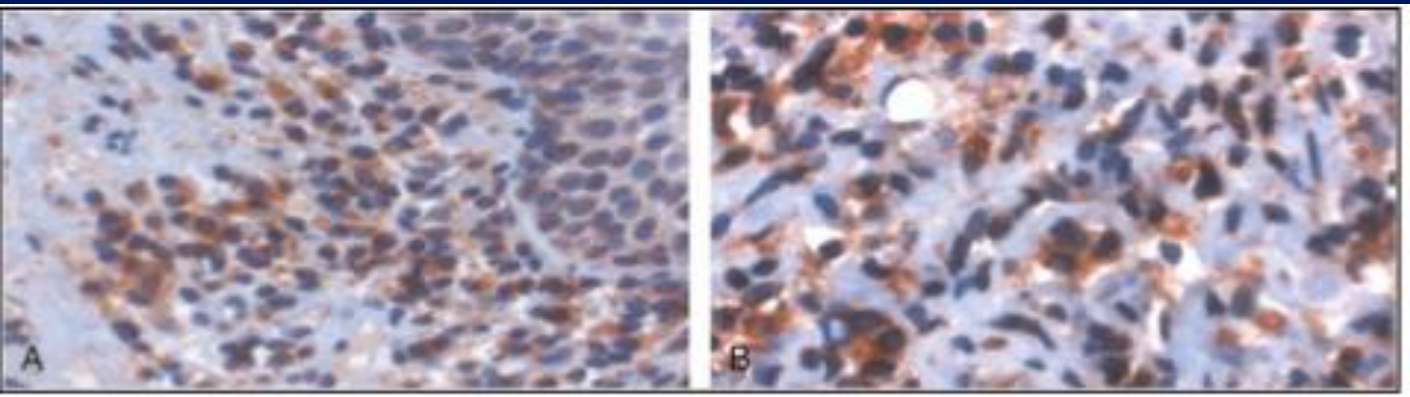


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FIG. 3 . Heparanase expression. x400 (A) and x600 (B). Positive cytoplasmatic staining is seen in the subepithelial layer, close to the epithelial basement membrane.

Neuroproliferative Vestibulodynia

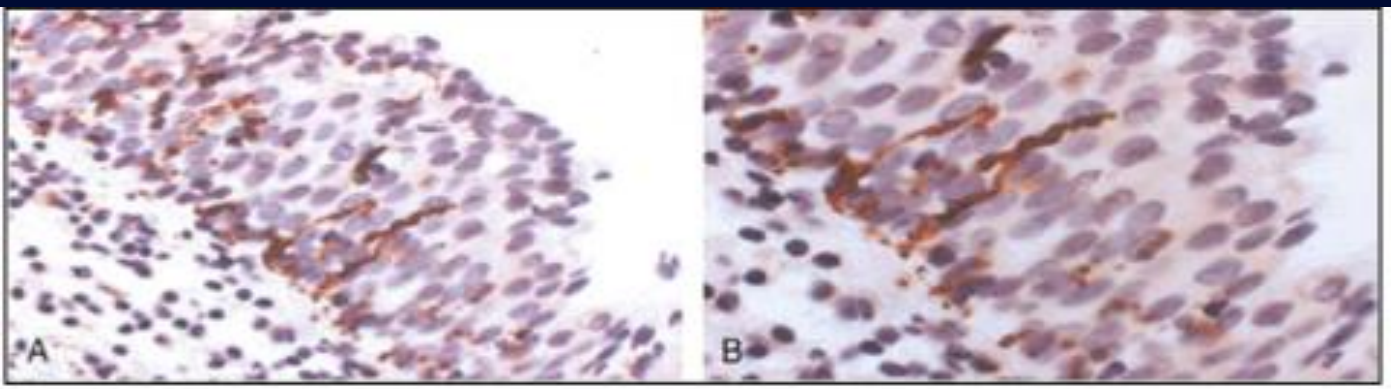

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FIG. 4 . x400 (A) and x600 (B) staining for PGP 9.5. The nerve fibers are seen intruding into the epithelium to more than half its depth.

Characteristic	Score (0–3)						
	Localized Vulvodynia			Control			
	Mean ± SD	Median	Range	Mean ± SD	Median	Range	2-Sided *P**
No. mast cells (Giemsa stain)	2.14 ± 0.378	2.0	2–3	0.14 ± 0.378	0.0	0–1	0.001
Heparanase expression	2.71 ± 0.488	3.0	2–3	0.14 ± 0.378	0.0	0–1	0.001
Subepithelial innervation (PGP 9.5)	2.0 ± 0	2.0	2–2	0.71 ± 0.488	1.0	0–1	0.001
Intraepithelial innervation (PGP 9.5)	2.0 ± 0	2.0	2–2	0.14 ± 0.378	0.0	0–1	0.001

*Wilcoxon rank sum test (Mann-Whitney *U* test).

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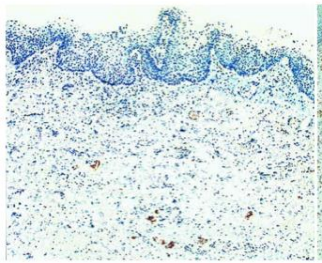
TABLE 1 . Comparison of semiquantitative scores in localized vulvodynia and controls

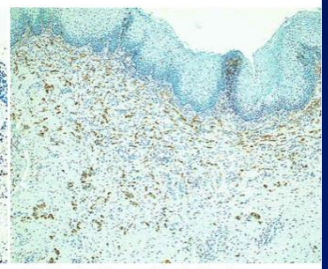
Neuroproliferative Vestibulodynia

S-100 Immunostain



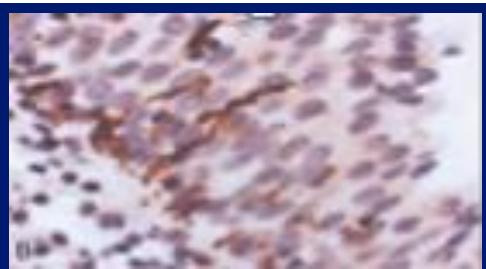
29-year-old control

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

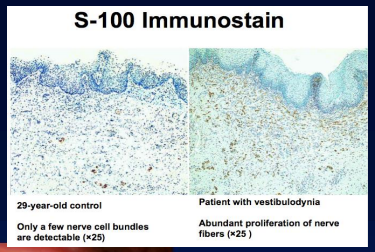


Patient with vestibulodynia

Abundant proliferation of nerve fibers (×25)



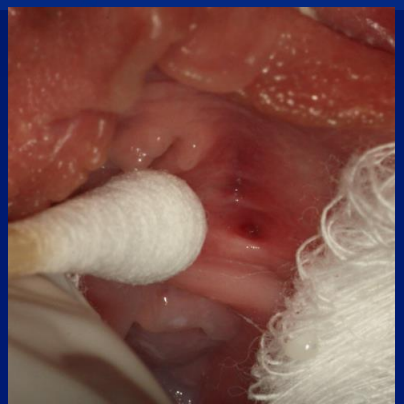
Neuro-Proliferative Vestibulodynia



Introitus with Urethral meatus 1:00 and 11:00 erythematous vestibular glands

1:00 and 3:00 erythematous vestibular glands

9:00 and 11:00 erythematous vestibular glands



CONSERVATIVE TREATMENT OPTIONS FOR NEUROPROLIFERATIVE VESTIBULODYNIA

1. Interferon, montelukast, Neogyn, if within 6 months of onset of symptoms
2. If after 6 months: topical lidocaine, capsaicin 0.025%, desipramine, gabapentin
3. Experimental treatments in development

Surgical Techniques

Vestibular Anesthesia Test for Neuroproliferative Vestibulodynia

Catherine Gagnon, NP, Julea Minton, NP, and Irwin Goldstein, MD
San Diego Sexual Medicine, San Diego, CA, USA

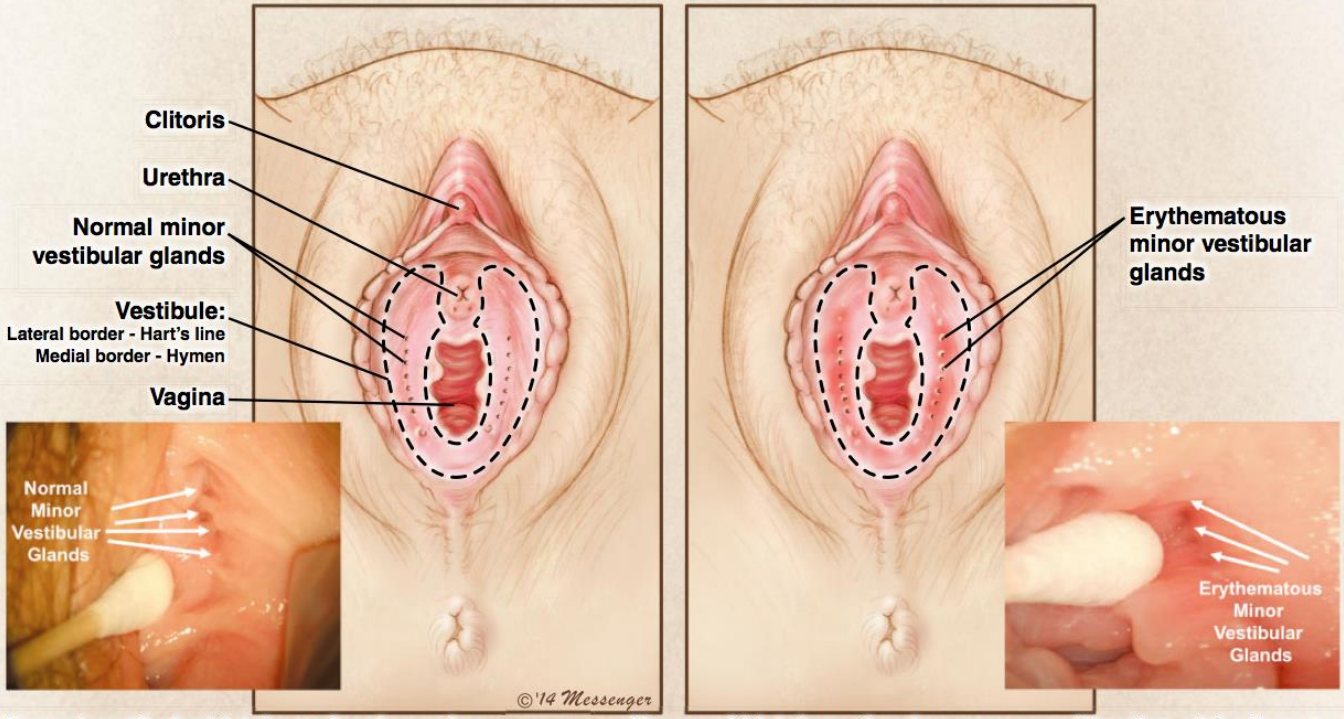
J Sex Med 2014

Position of patient for vulvoscopy

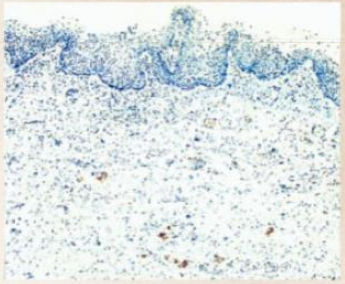
Biologic Issues in Neuroproliferative Vestibulodynia

- 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

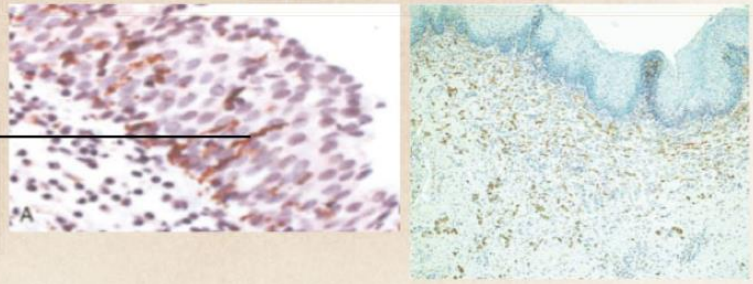
Vulvoscopy



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



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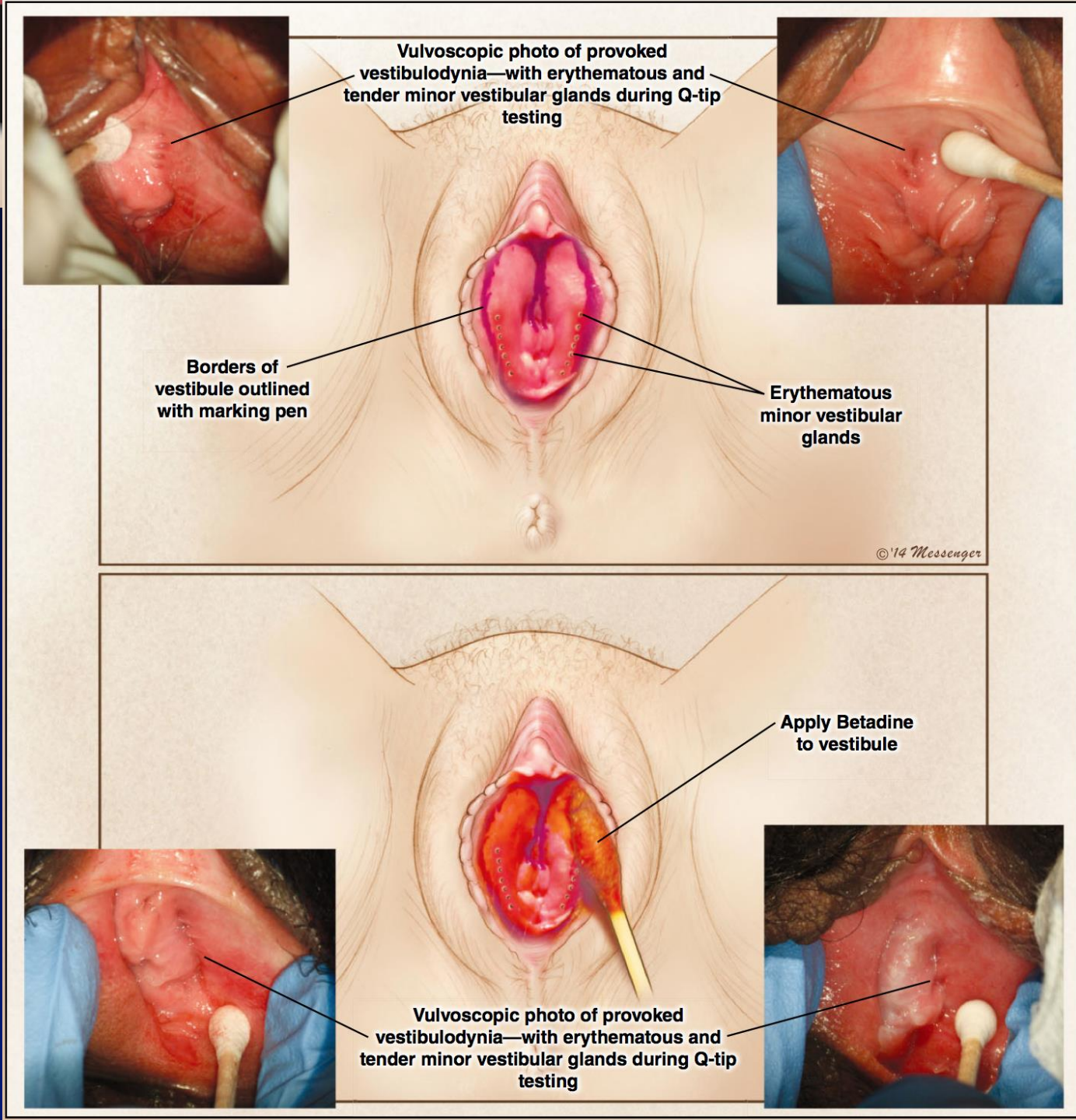

Bupivicaine (20%), lidocaine (8%), and tetracaine (8%) - BLT

Bupivicaine (20%, lidocaine (8%), and tetracaine (8%) - BLT

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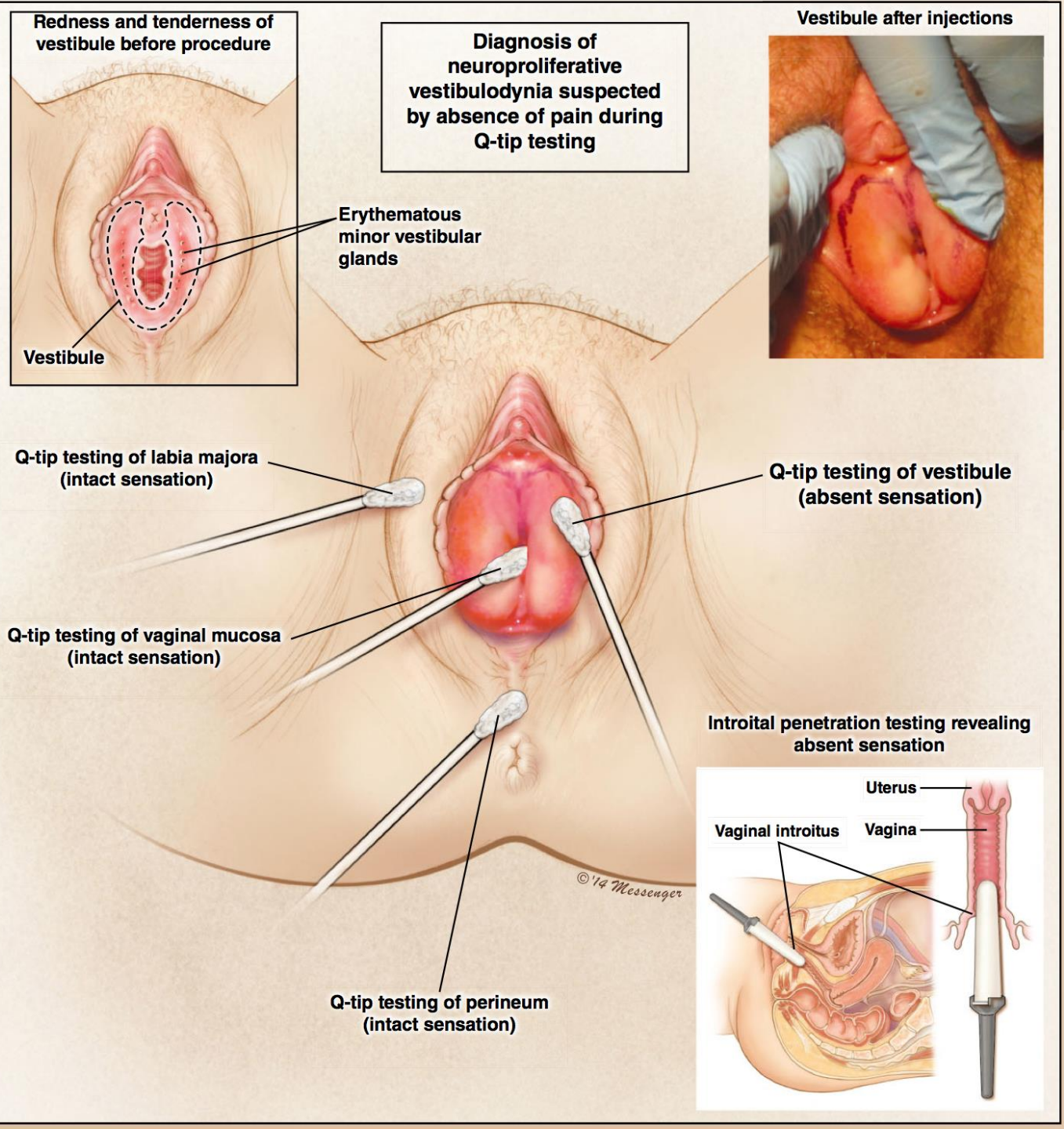
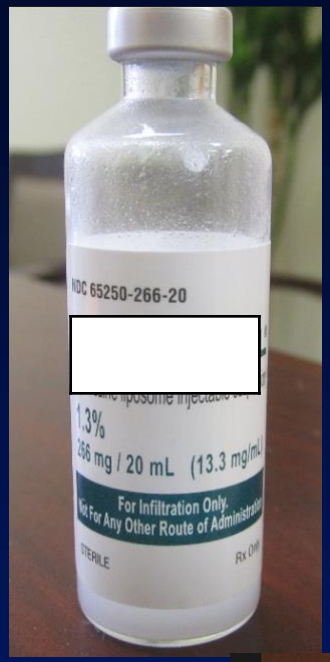
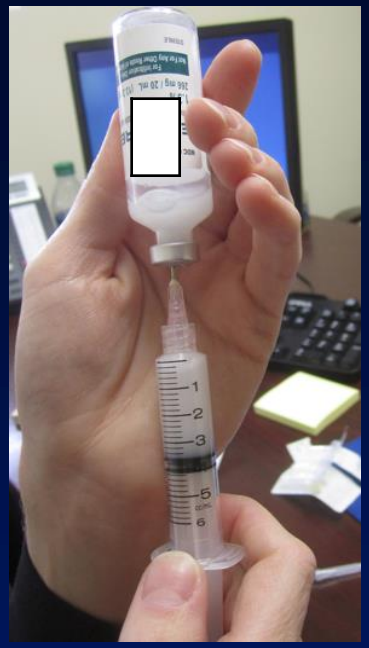
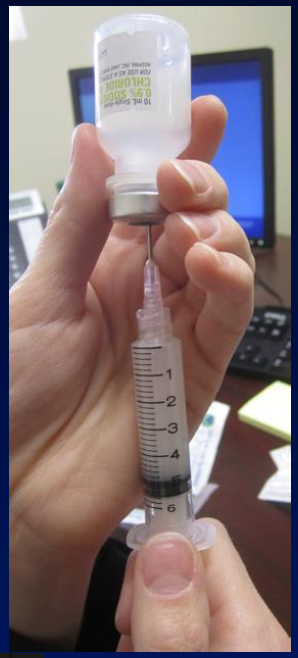


VESTIBULAR ANESTHESIA TEST







Bupivicaine in liposome

VESTIBULAR ANESTHESIA TEST

Neuro-Proliferative Vestibulodynia

COMPLETE VESTIBULECTOMY SURGERY

Sexual Medicine Surgery

Surgical therapy may be selected in women with sexual health concerns - based upon failure of or insufficient response of or adverse side effects associated with *conservative non-surgical therapies*, or patient preference

Surgical treatments for sexual health concerns are highly invasive, associated with potential complications, and are generally reserved for select cases of *conservative treatment-refractory sexual dysfunction*

Despite their significant cost and potential invasiveness, surgery has been associated with high rates of patient satisfaction in several studies

Neuro-Proliferative Vestibulodynia

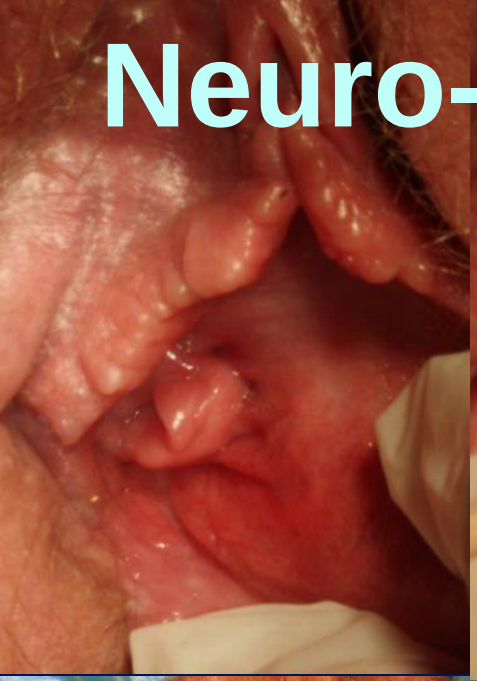
Positive vestibular anesthesia test can help predict surgical outcome

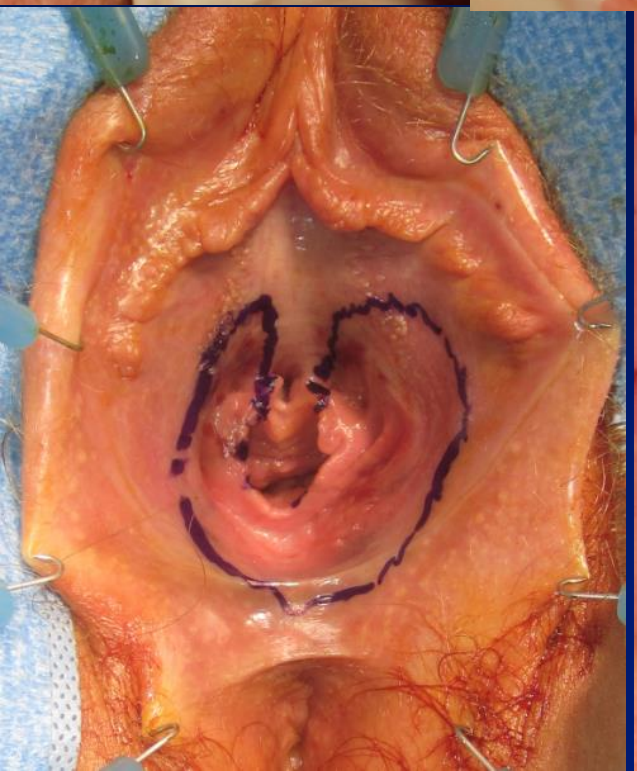
A positive vestibular anesthesia test predicts that the patient can be pain-free if there is:

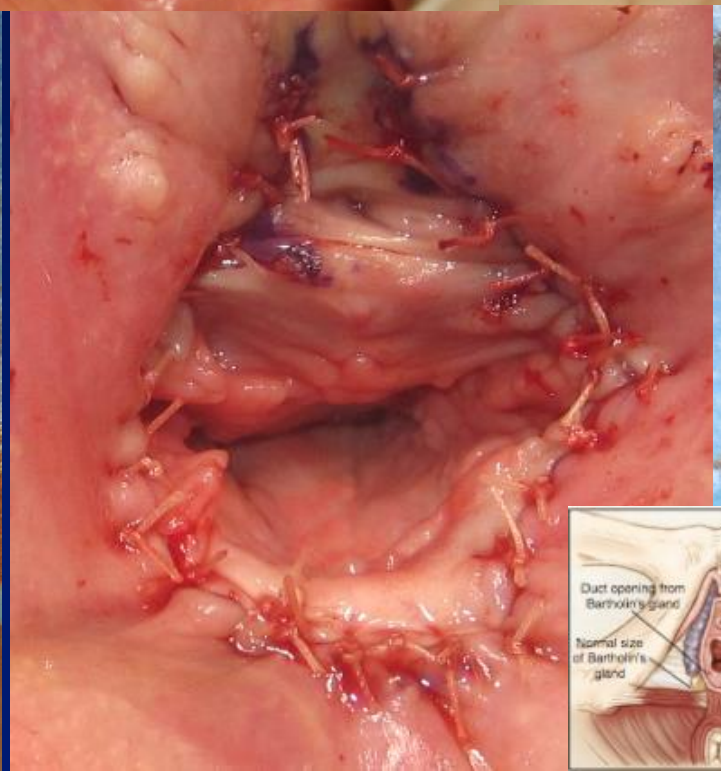
1) elimination of diseased vestibular tissue that is associated a high density and proliferation of C-afferent nociceptors that has led to unrelenting and conservative treatment resistant vestibulodynia

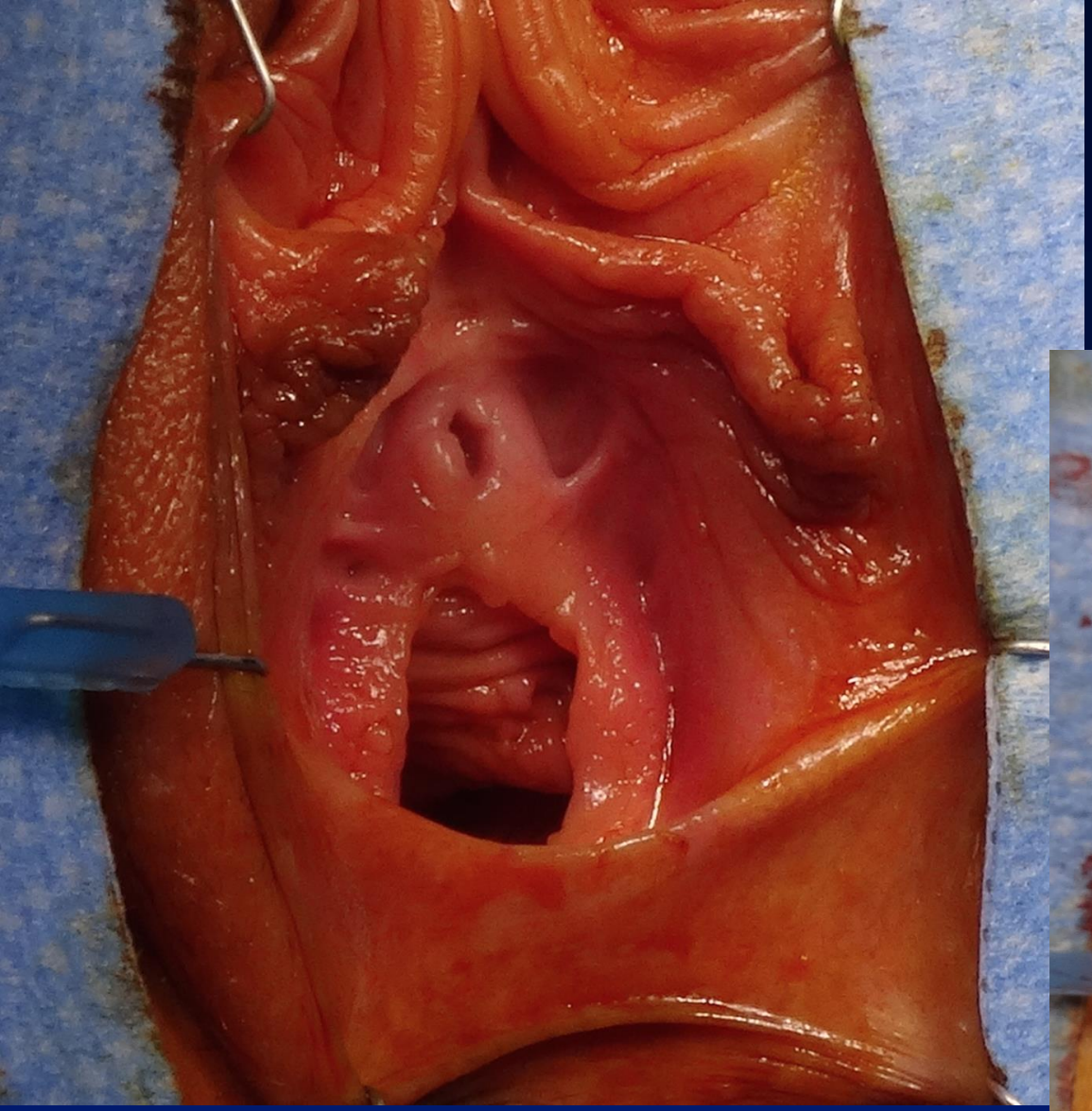
2) the healthy vagina (NO PATHOLOGY) is surgically connected to the healthy vulva (NO PATHOLOGY)

Neuro-Proliferative Vestibulodynia










INCHES
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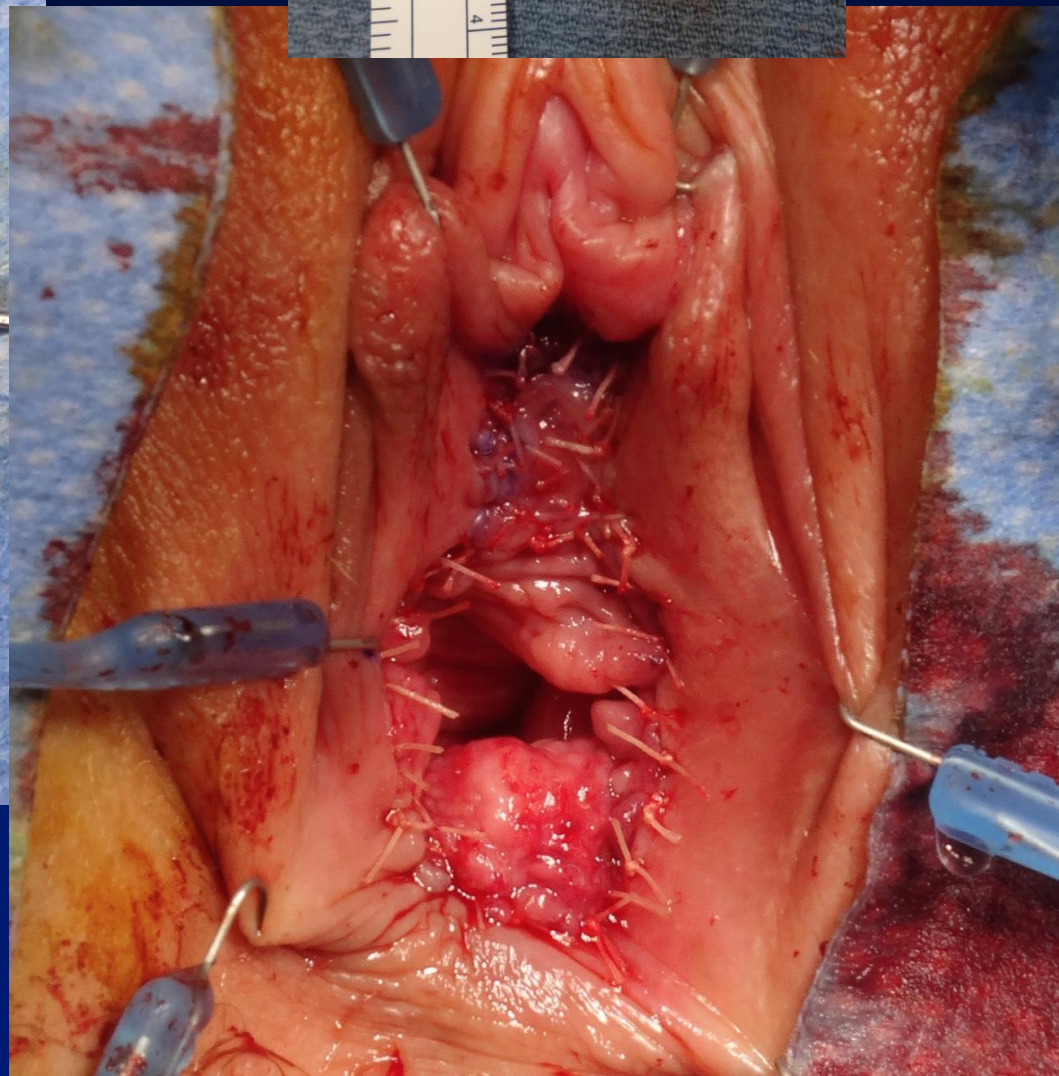
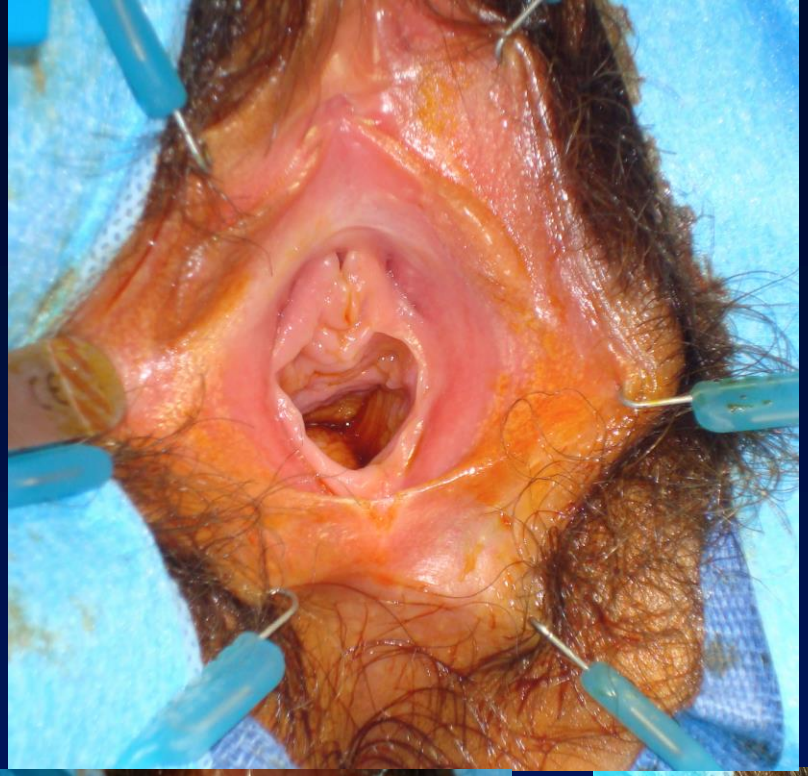
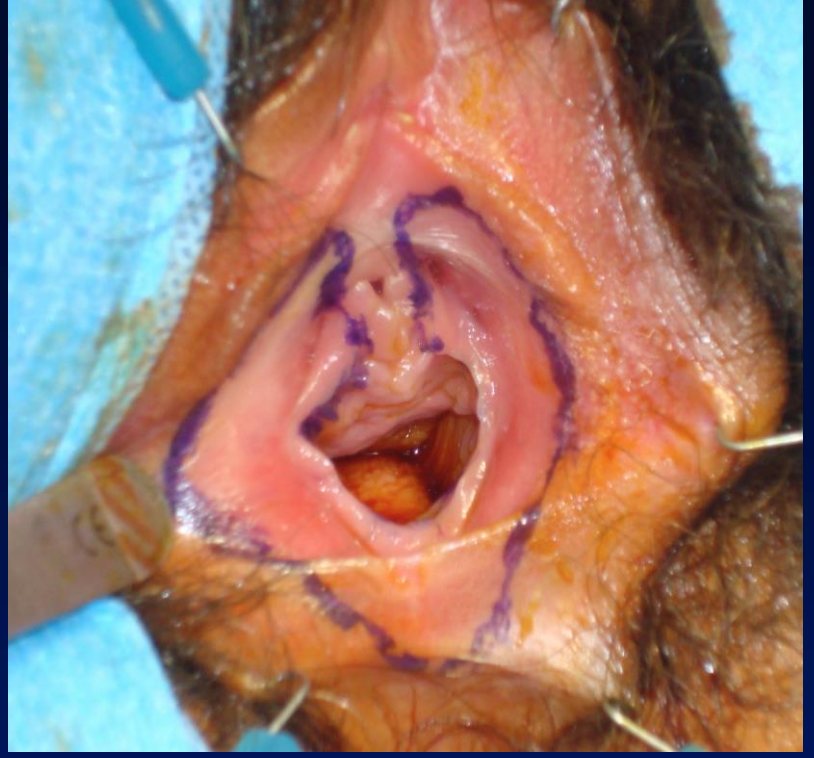
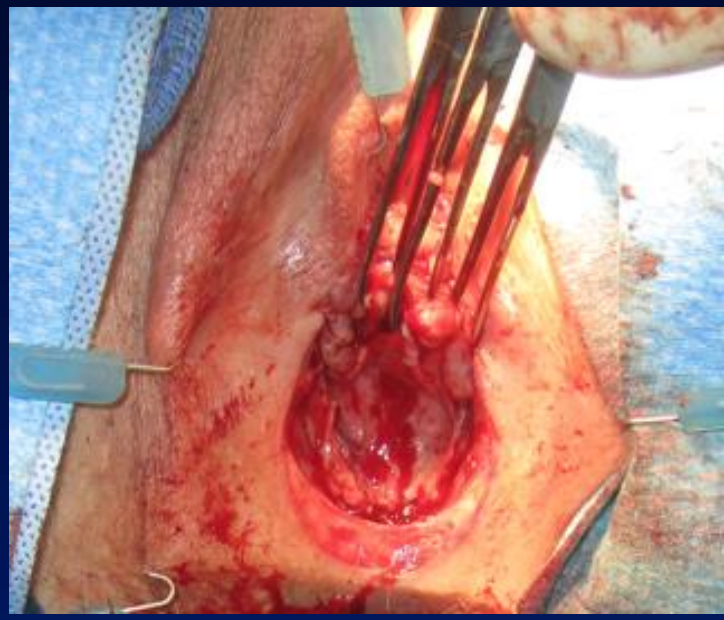
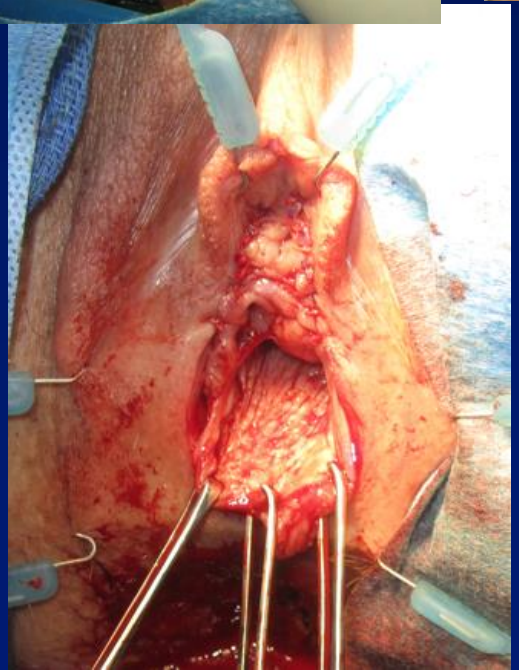


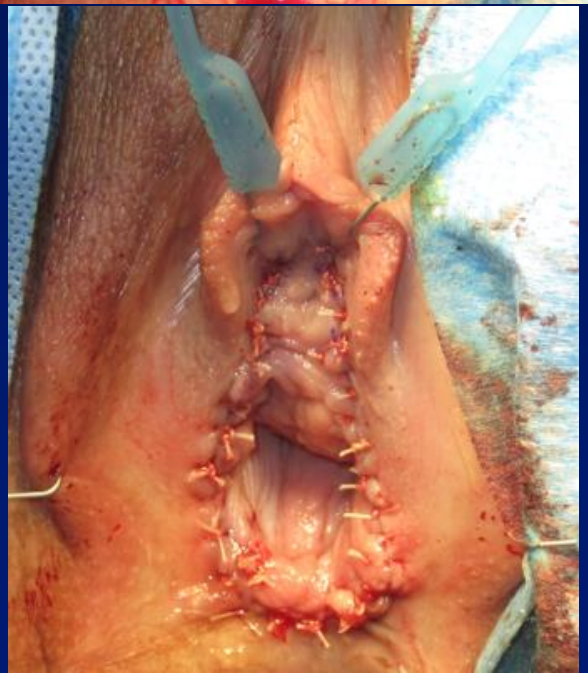


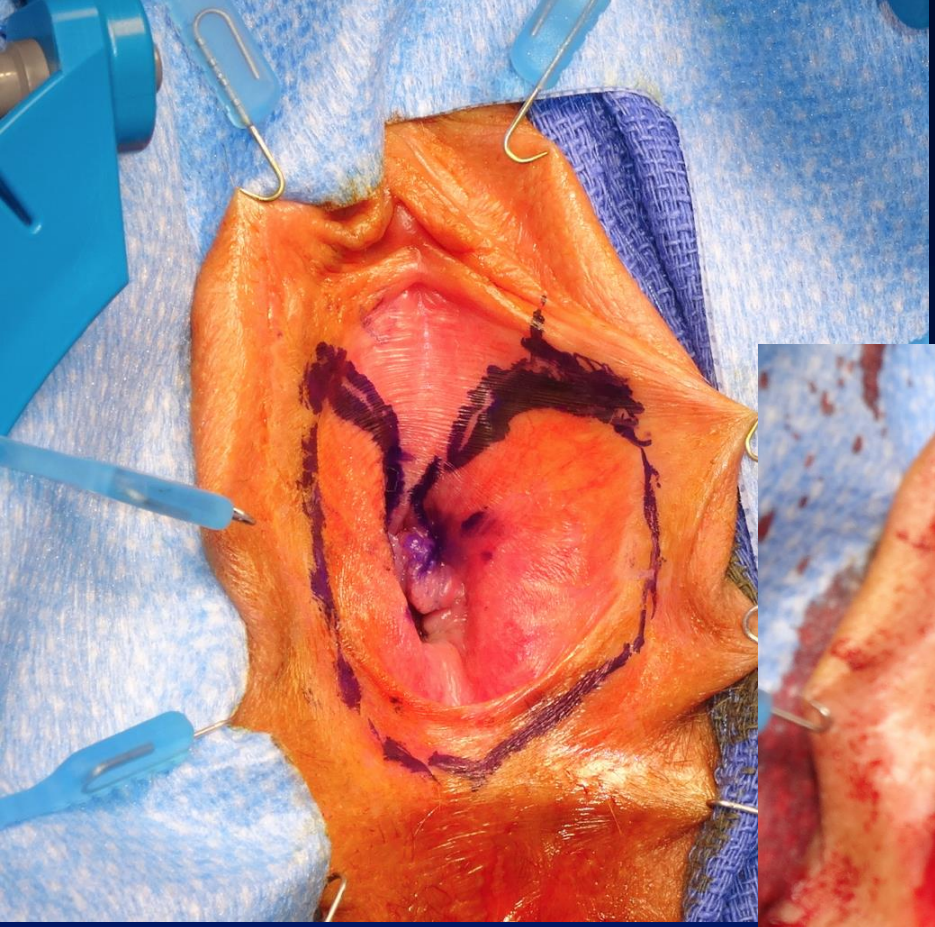


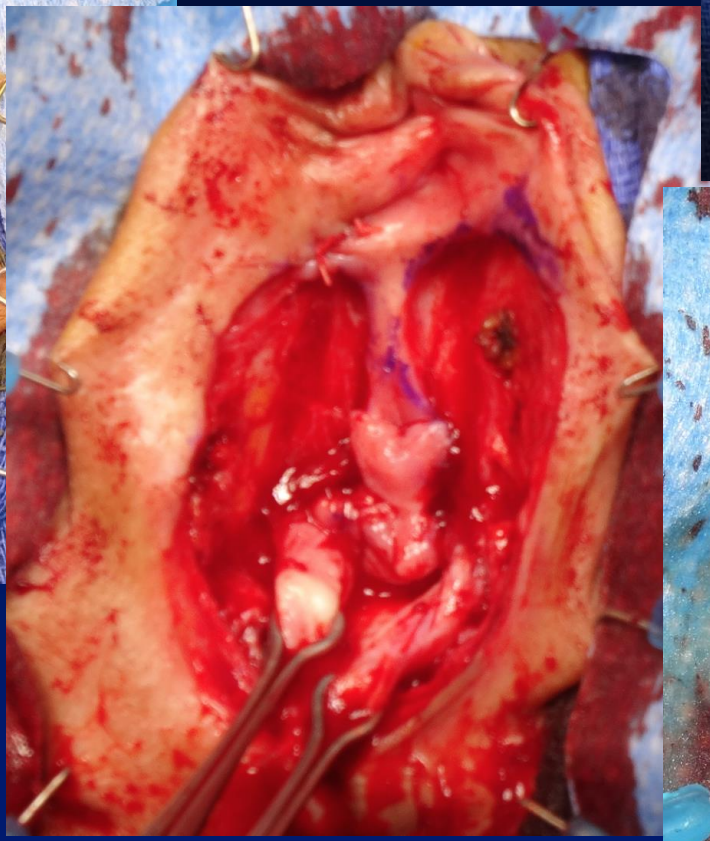
COMPLETE VESTIBULECTOMY REMOVING ALL VESTIBULAR TISSUE – EVEN 1-2 MMS FROM THE URETHRAL MEATUS









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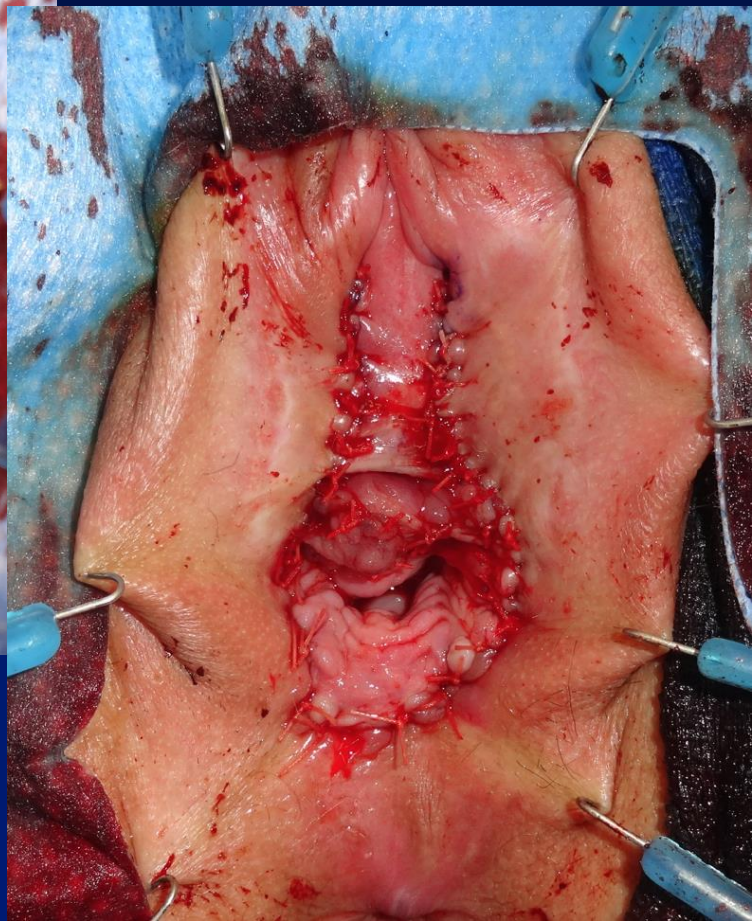

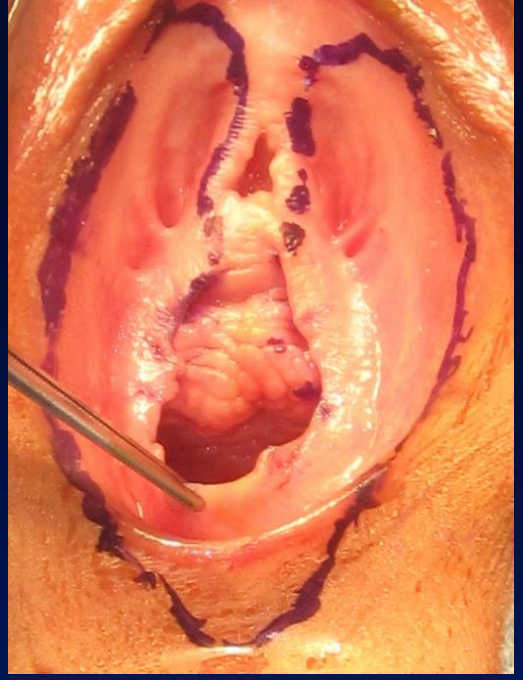

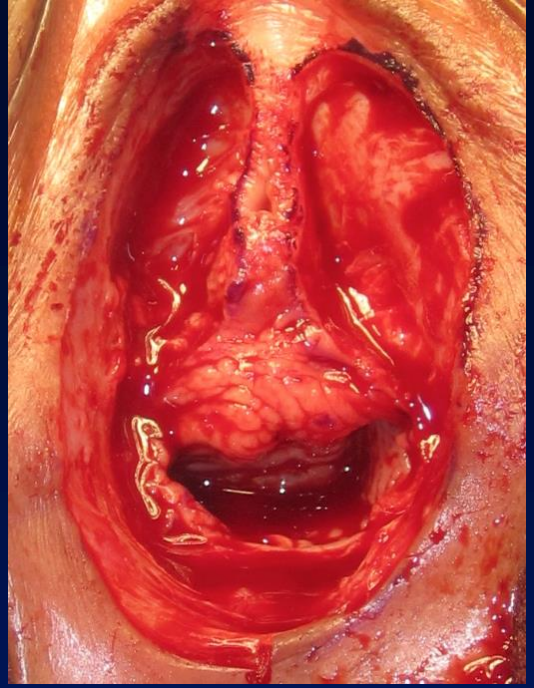

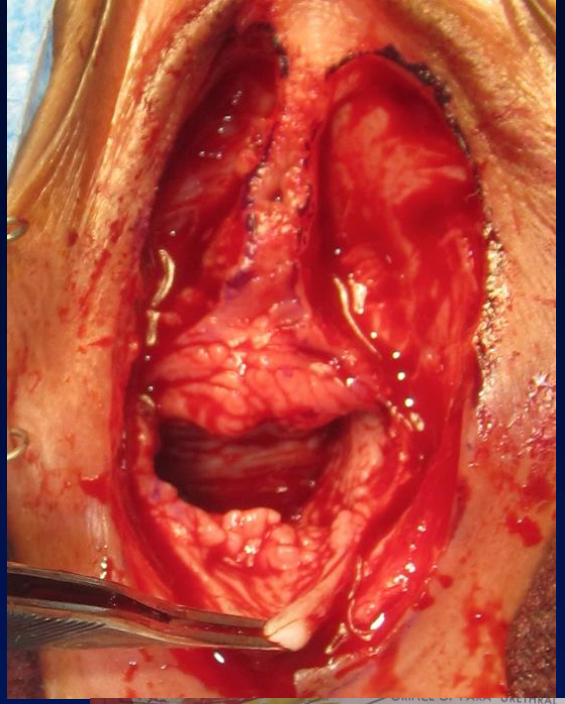

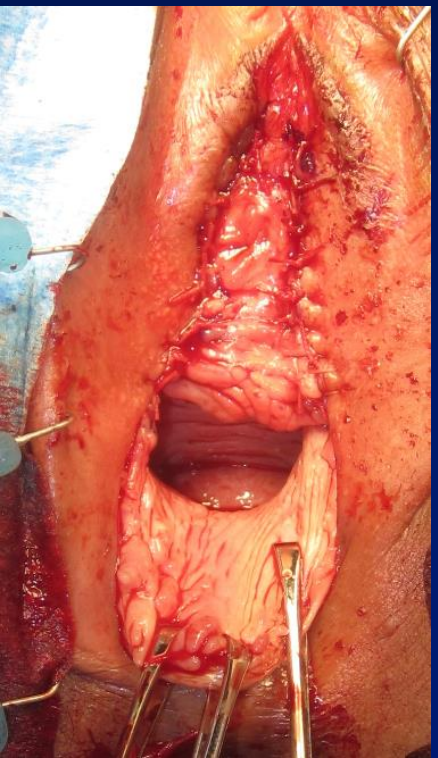

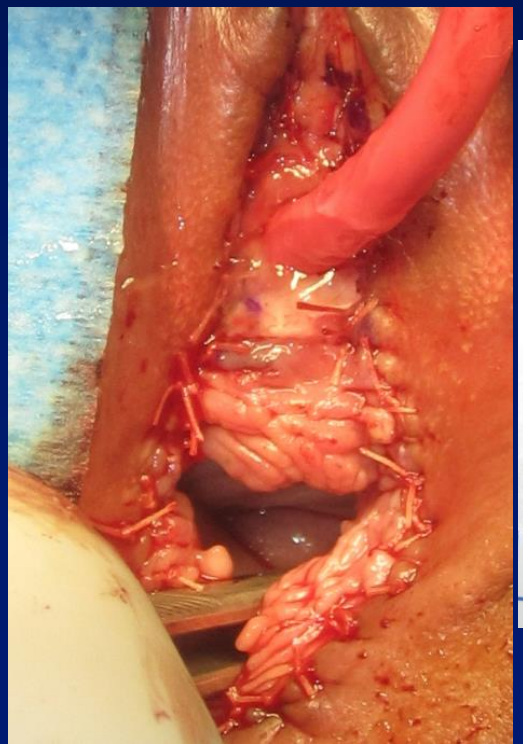


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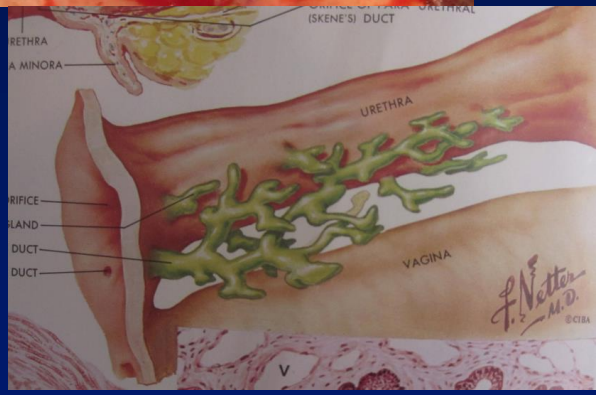
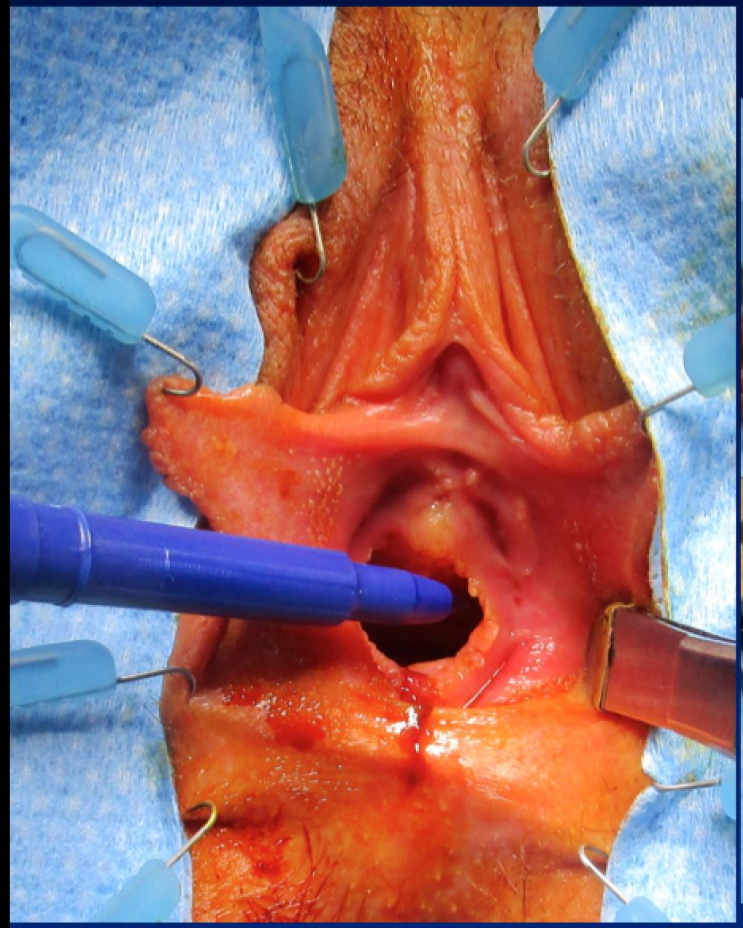
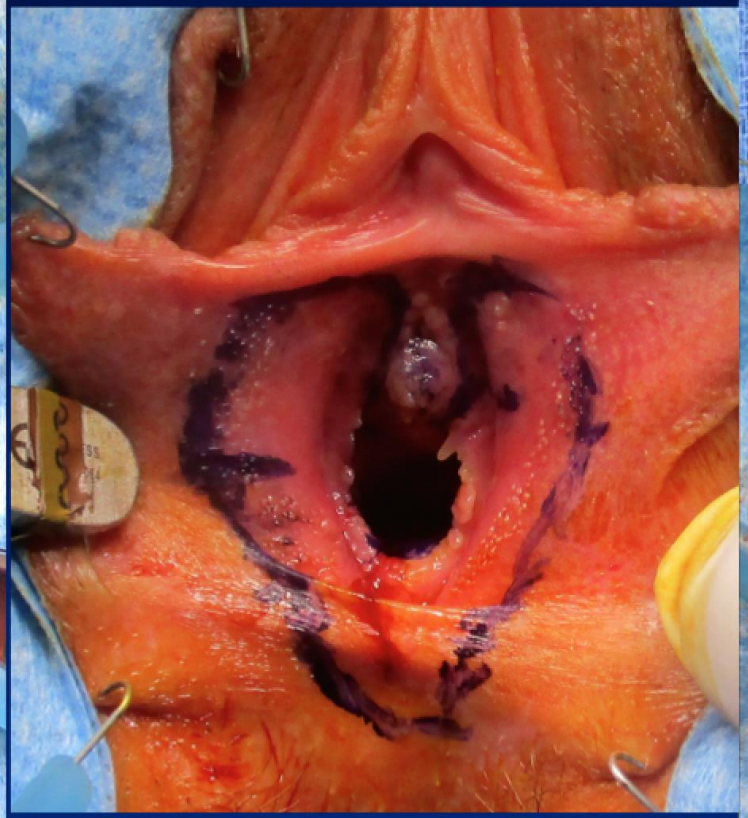

(SKENE'S) DUCT
URETHRA
VAGINA


Likely location of blockage is in the proximal Bartholin's duct
Duct opening from Bartholin's gland
Normal size of Bartholin's gland
Outline of Bartholin's cyst



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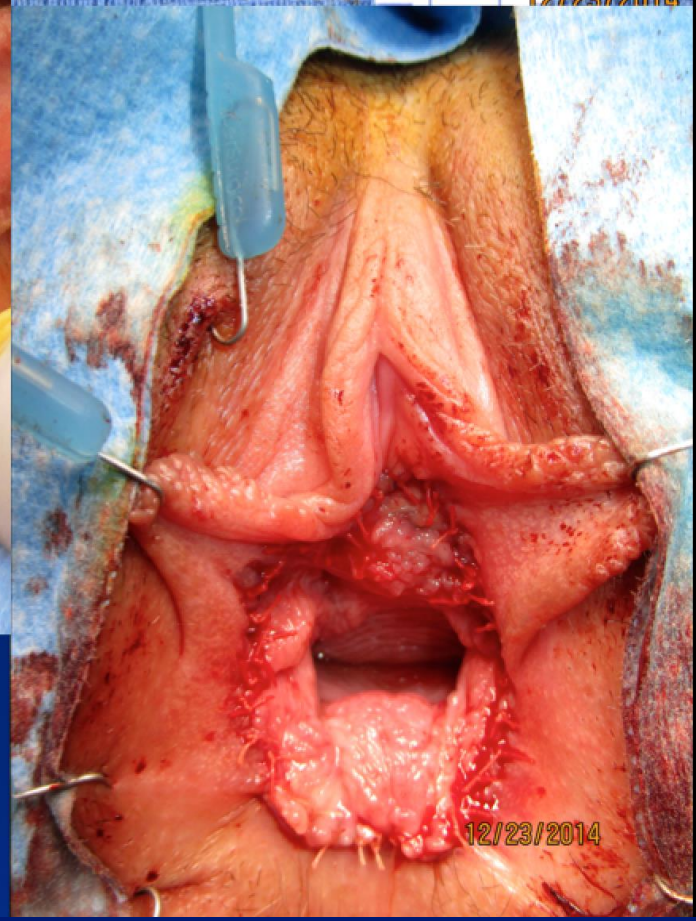
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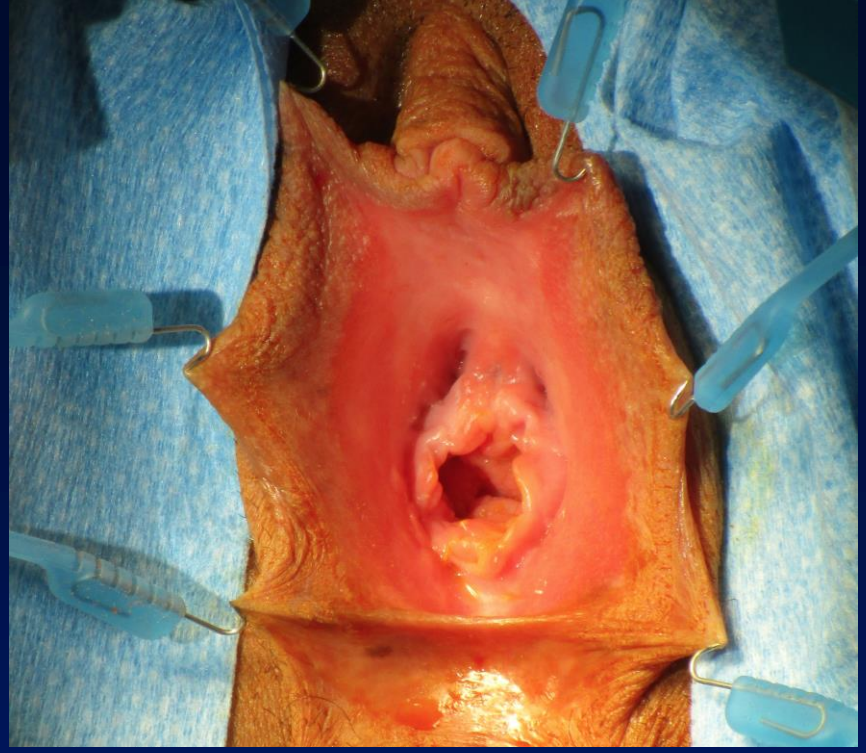

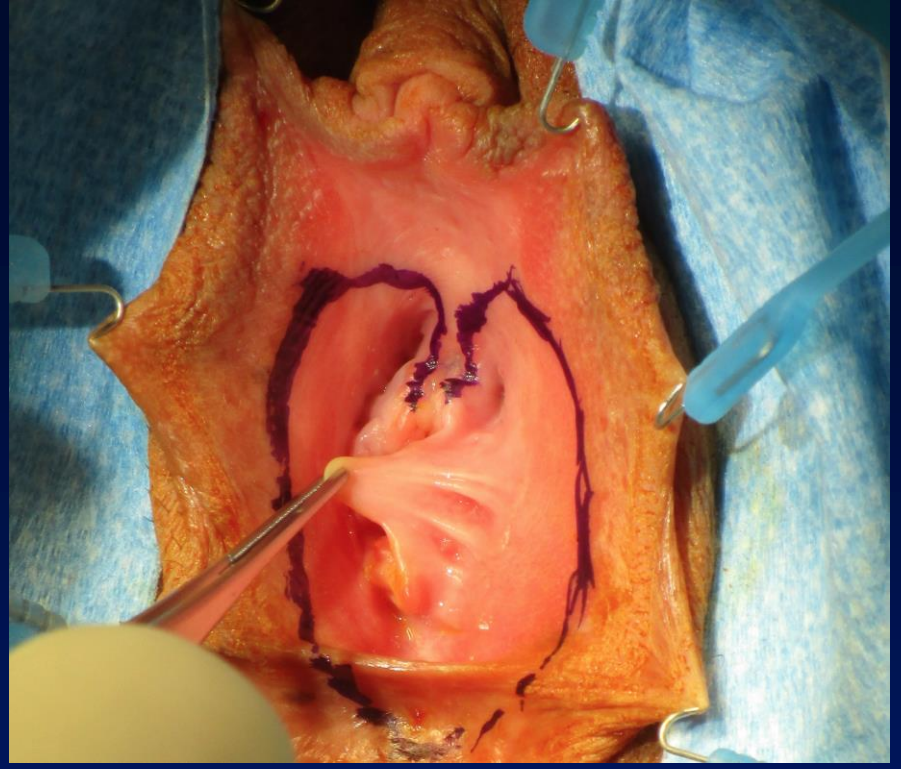


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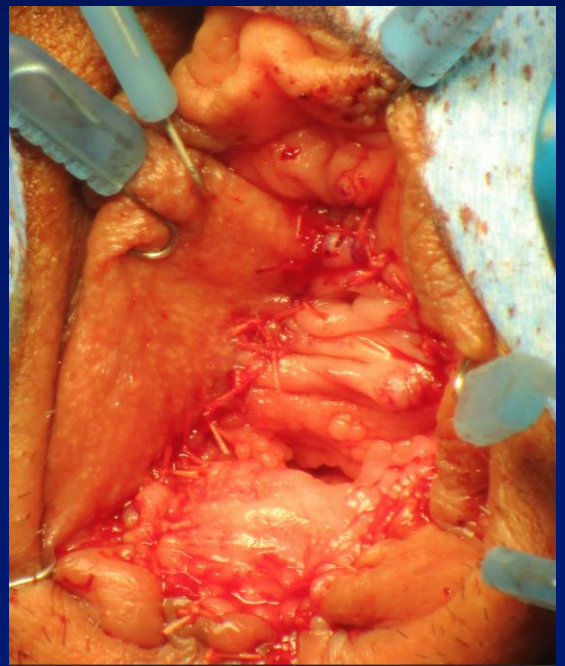

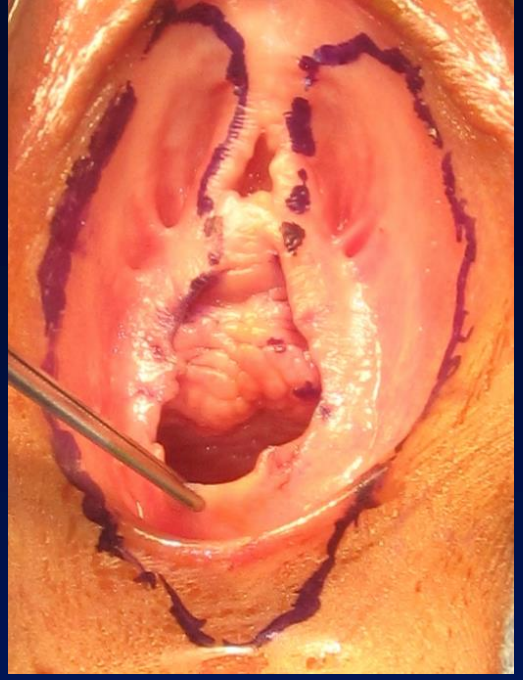

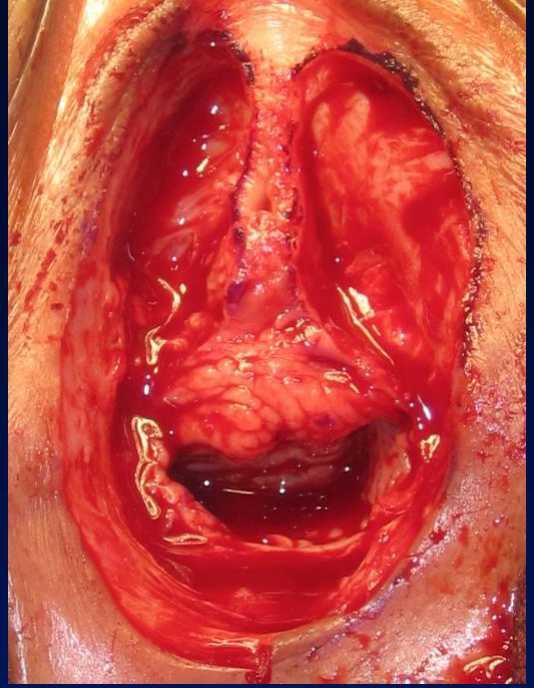

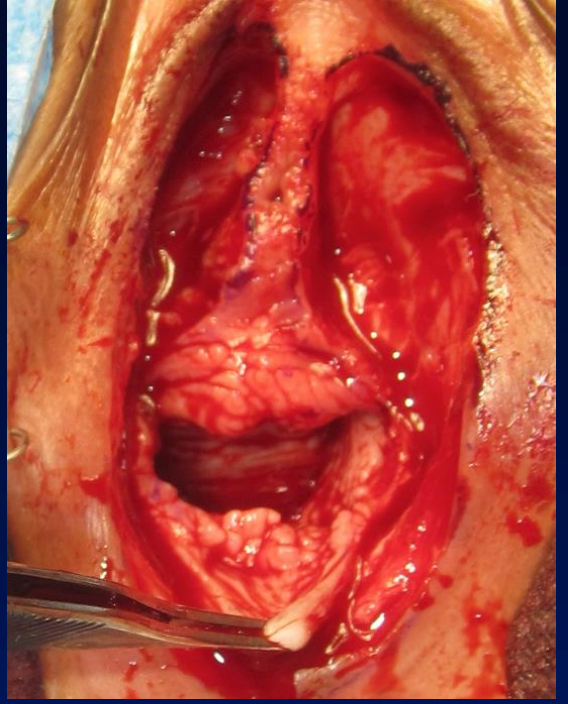

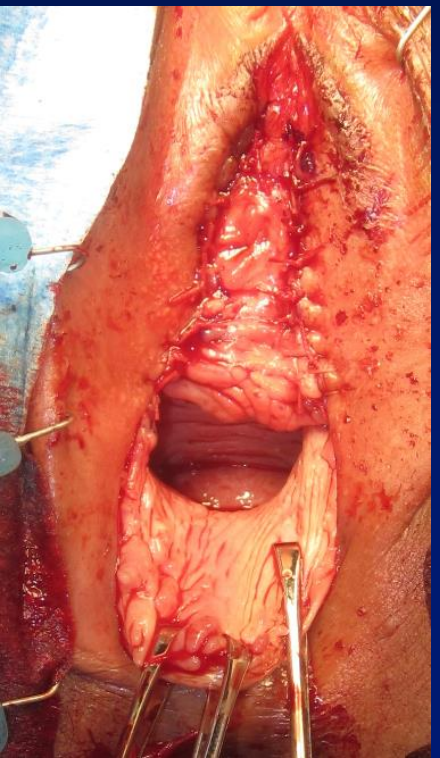

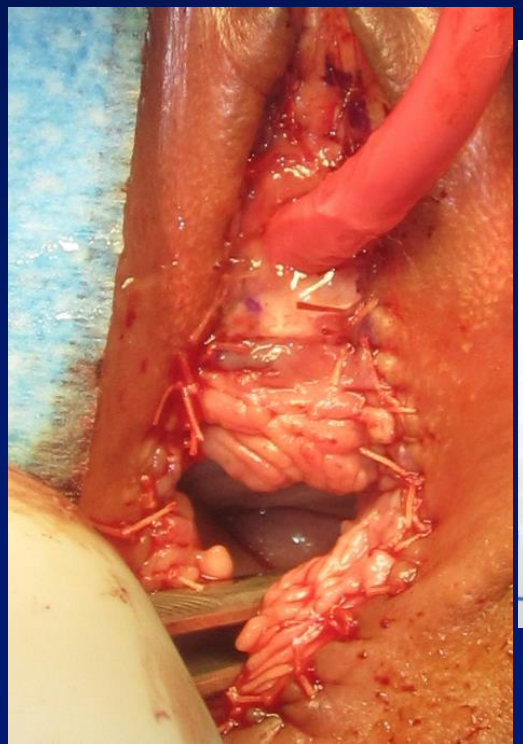


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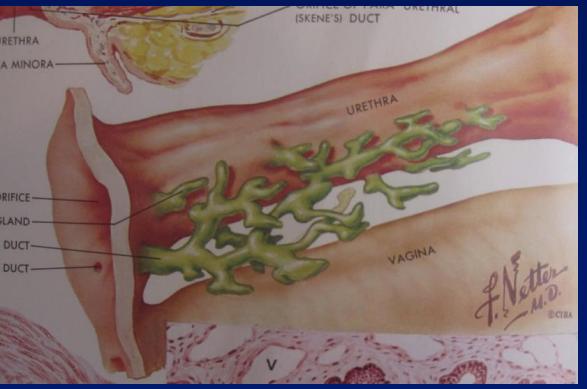
Neuro-Proliferative Vestibulodynia



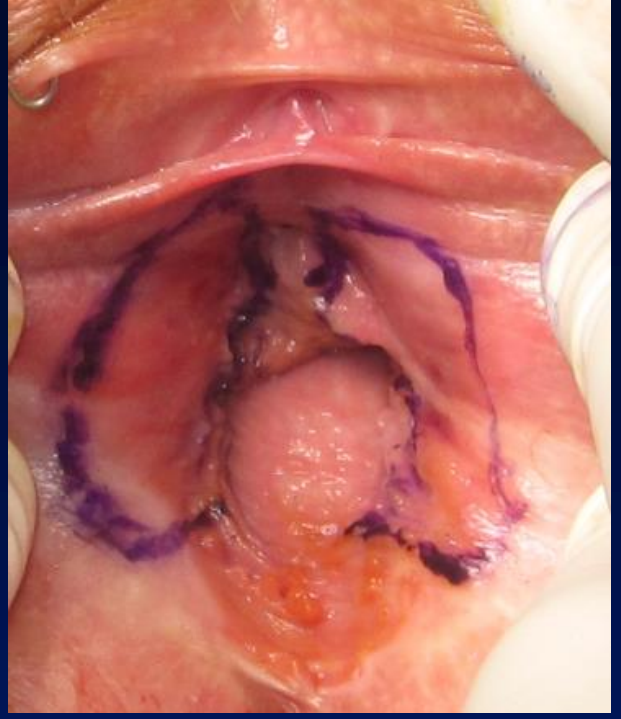
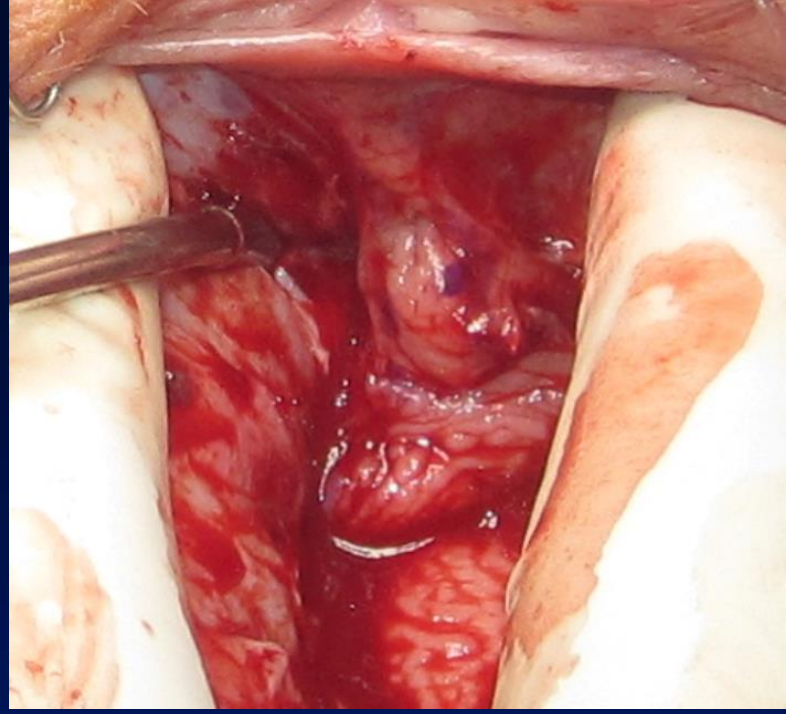
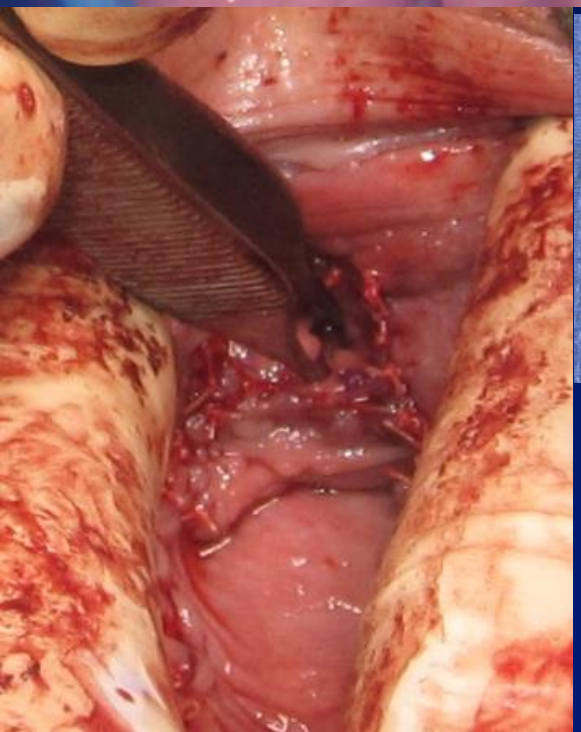

9/29/09
4/27/10
3/14/13

FAILURES OF "COMPLETE" VESTIBULECTOMY SURGERY

1. INCORRECT DIAGNOSIS OF NEURO-PROLIFERATIVE VESTIBULODYNIA

2. RECURRENT/ PERSISTENT NEURO-PROLIFERATIVE DISEASE AT 1-3:00 /9-11:00 O'CLOCK - (Post-op refraining from sexual activity)

1. BARTHOLIN'S CYST - (Post-op refraining from sexual activity)

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