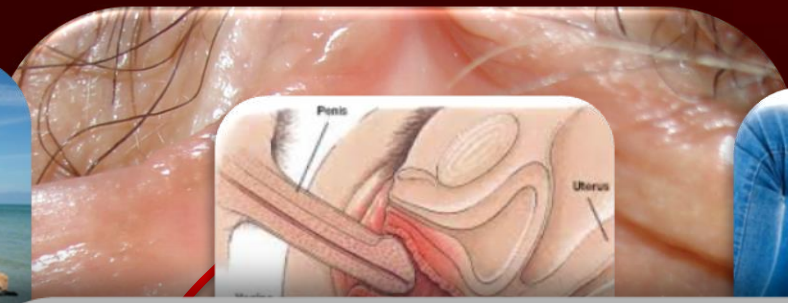
Vulvodinia: lo stato attuale delle conoscenze

R. Felice – F. Murina

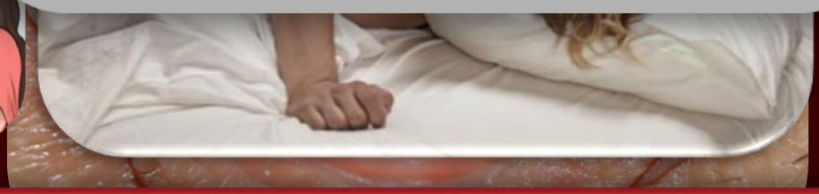
Servizio di Patologia del Tratto Genitale Inferiore

Osp. V. Buzzi –Università degli Studi di Milano

Vulvodinia

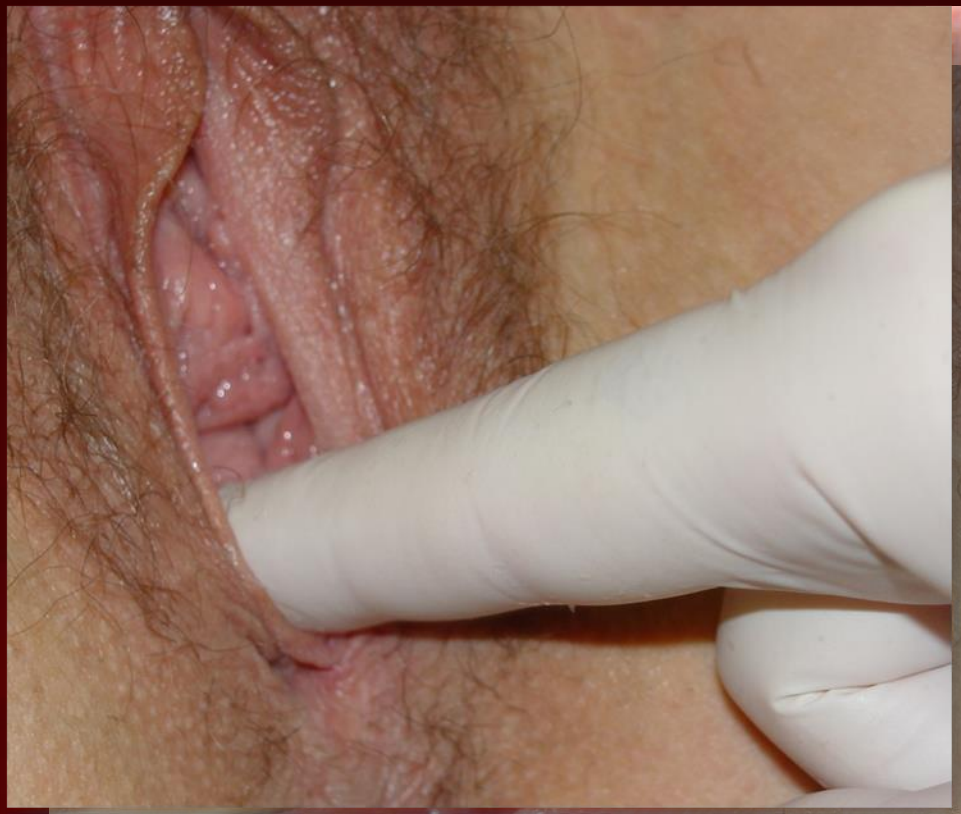


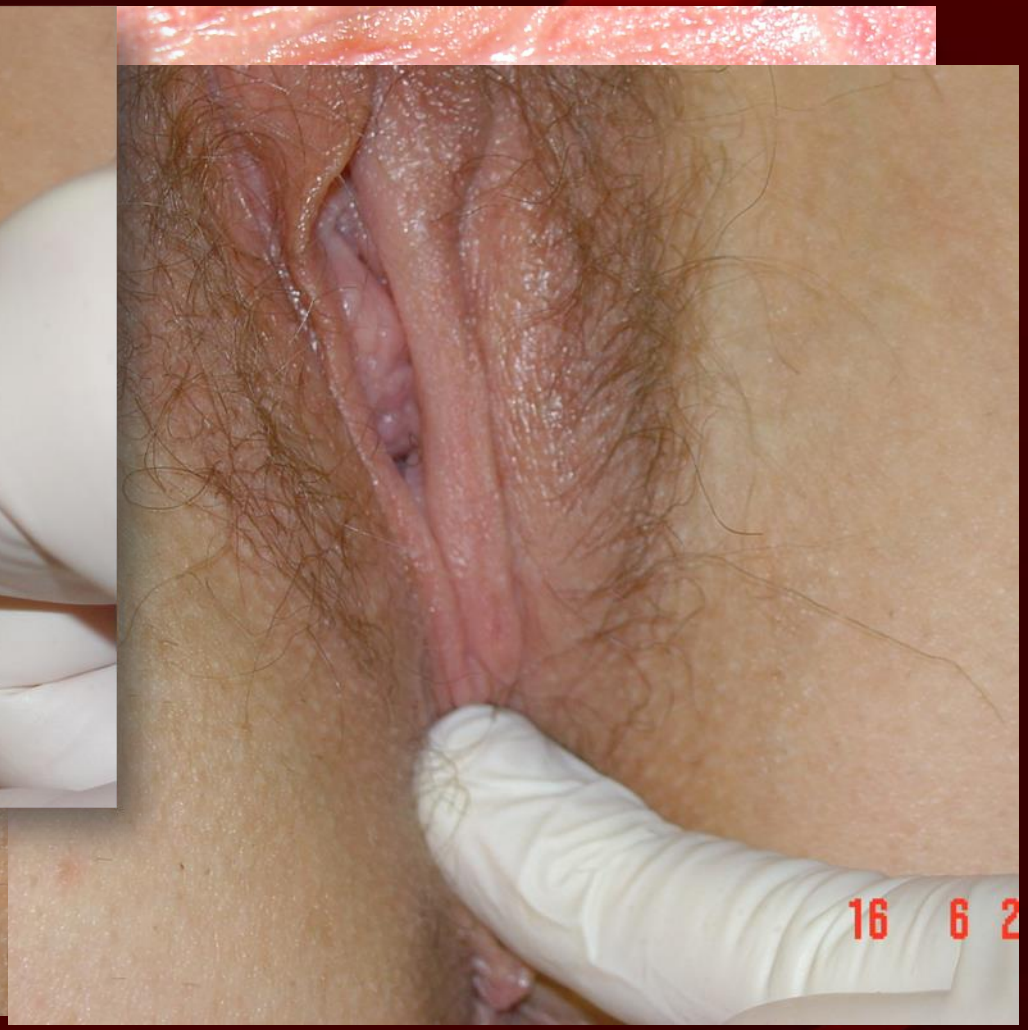
Bruciore
Dolore
Dispareunia



Vestibolodinia Provocata

Vestibolodinia: muscolatura pelvica





Graziottin –Murina .Vulvar Pain: from childhood to old age.-Springer ed. 2017

Vulvodinie

Sommatoria di eventi che in modo sequenziale innesca un’alterata percezione del dolore con un peso differente nelle varie fasi di vita della donna

Vulvodynia: What We Know and Where We Should Be Going

Logan M. Havemann, BA,[1] David R. Cool, PhD,[1,2] Pascal Gagneux, PhD,[3] Michael P. Markey, PhD,[4]

J Low Genit Tract Dis 2017

Iniziali insulti infettivi-irritativi traumatici-allergici

risk.[24] Me ...opment of VVD have been widely hypothesized. The current dogma is that during or after an initial vaginal insult with infection, a "susceptible" individual has an inflammatory response that is potentially composed of an abnormally heightened release of proinflammatory cytokine ...idual is then either ...n or the infectious process alters and sensitizes the neural tissue in the vulvovaginal area, resulting in localized or generalized allodynia and hyperalgesia.[1]

Innescano un processo infiammatorio incontrollato in soggetti predisposti

Neurosensibilizzazione con iperalgesia ed allodinia

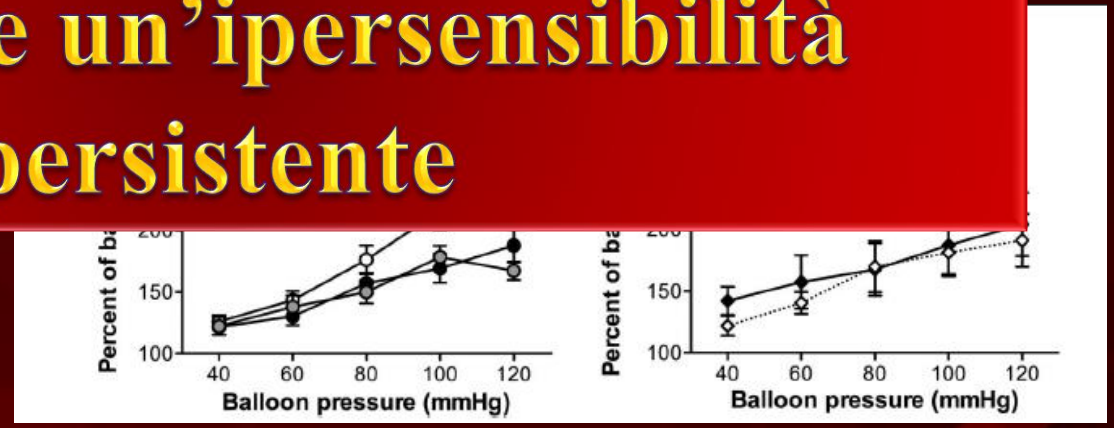
Vestibolodinia e Neurosensibilità

Abstract

Experiencing early life stress or inj
hypothalamic–pituitary–adrenal (H
administered intravaginal zymosan
the visceromotor response to vag
transient receptor potential ankyrin
corticosterone (CORT), mast cell
indicators of peripheral HPA axis
resulting from NVI. Adult NVI mice h
was significantly elevated in the va
significantly decreased in dorsal ro
Serum CORT, vaginal mast cell d
colorectal and hind paw mechanica
zymosan administration largely atte
of the vagina, as well as of adjacent visceral and distant somatic structures, driven in part by increased HPA axis activation.

-Somministrazione vaginale di un agente irritante (zymosan) a 8 e 10 gg di vita
-Valutazione in fase adulta dell'ipersensibilità vaginale e della densità di fibre nervose

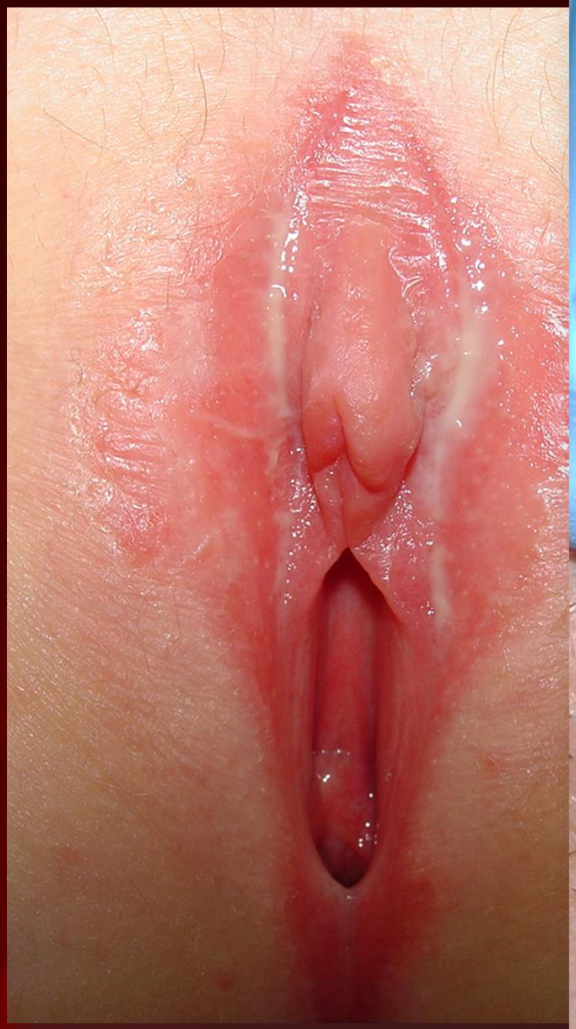
Insulto precoce è in grado di provocare un'ipersensibilità persistente

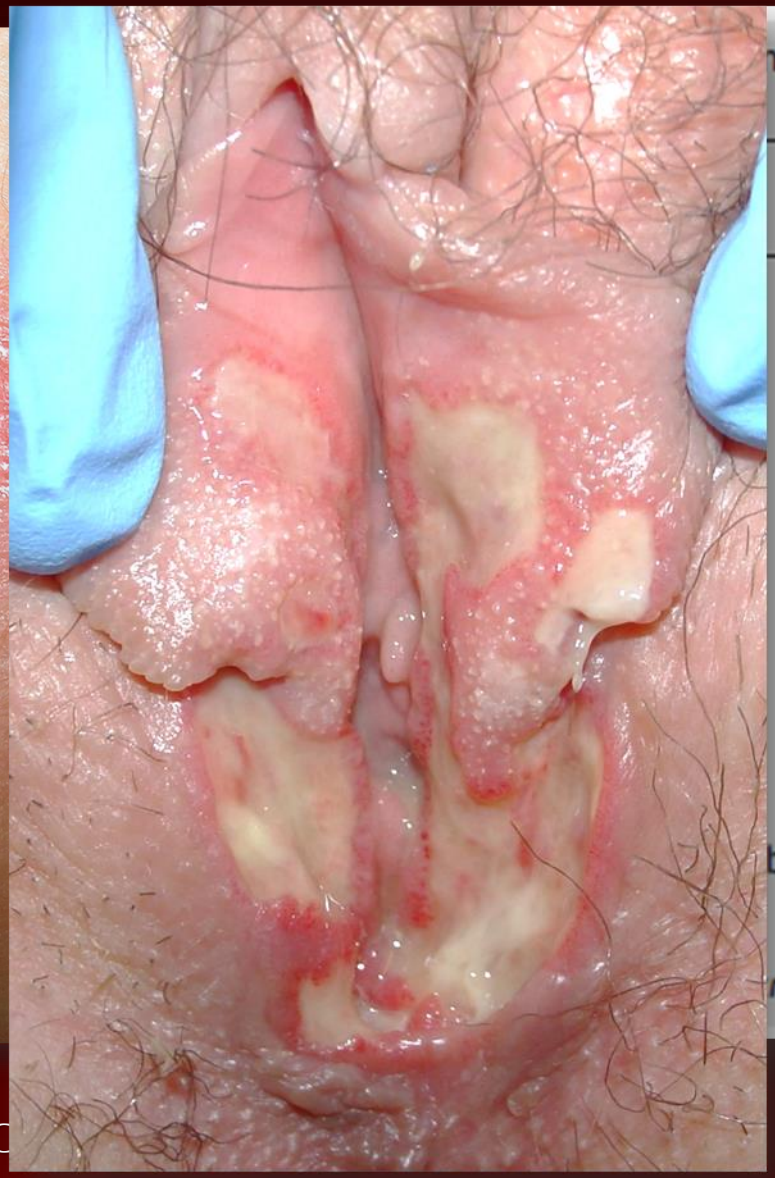


Research Paper
PAIN
Neonatal vaginal irritation results in long-term visceral and somatic hypersensitivity and increased hypothalamic–pituitary–adrenal axis output in female mice
Angela N. Pierce, Zhen Zhang, Isabella M. Fuentes, Ruipeng Wang, Janelle M. Ryals, Julie A. Christianson*

2015·Volume 156·Number 10

Infanzia ed Adolescenza





ngs of patients with positive

	Prepubertal (n = 38)	Pubertal (n = 19)
	n = 24	n = 7
	10	—
	3	—
	2	1
	—	4
	9	1
	—	1
	n = 14	n = 12
	11	—
	1	11
b	2	—
	—	1

reptococcus.

Common prepubertal vulvar conditions

Samantha E. Vilano[a] and Cynthia L. Robbins[b]

C

ELSEVIER journal homepage: www.jfma-online.com

ORIGINAL ARTICLE

Comparison of clinical and microbiological features of vulvovaginitis in prepubertal and pubertal girls

Ayse E. Yilmaz[a,*], Nurullah Celik[b], Gul Soylu[c], Ahsen Donmez[a], Cigdem Yuksel[a]

Characteristics of the pain observed in the focal vulvodynia syndrome (VVS)

Gilbert Donders [a,b,c,*], Gert Bellen [a]

Medical Hypotheses 2012

Table 1
Demographic data and medical history of patients with focal provoked vulvodynia (VVS).

Demography of study population (n = 0)	Mean ± sd N (%)
Age (years)	27.39 ± 7.76
Parous	
Episiotomy	
Menarche	
<12 year	
12–13 year	
>13 year	
Age at first sex	18.5 ± 466
History of genital infection	
Vulvovaginal candidosis	23 (77%)
Herpes genitalis	3 (10%)
Bacterial vaginosis	
Chlamydia trachomatis	
Which therapy did you try before the present vis	
Oral tablet (amitryptiline)	
Special genital soap	
Cryotherapy / electrocoagulation / laser	
Introital hymenplasty*	
Antimicrobial (bacteria/candida)	11
Local injection with cortic steroid	7
Local estriol cream	14
Local corticosteroids	15
Other external cream/oinment	14
Vaginal products	9
Total	28 (93%)

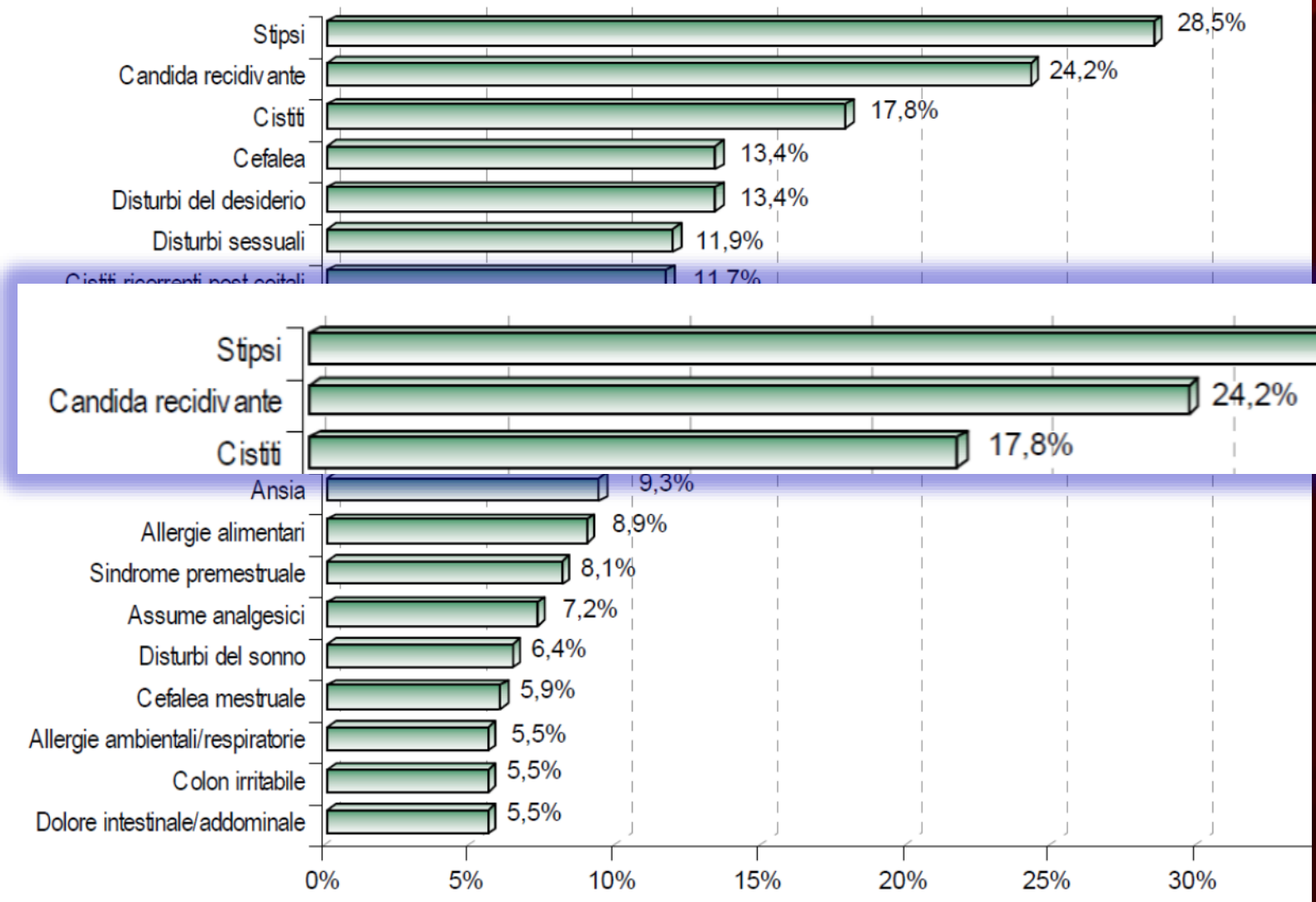
History of genital infection
Vulvovaginal candidosis 23 (77%)
Herpes genitalis 3 (10%)
Bacterial vaginosis 2 (8%)
Chlamydia trachomatis 1 (3.3%)

Rilevanza del legame Infezioni e Vestibolodinia

Il progetto VU-NET

indagine epidemiologica multicentrica sul dolore vulvare in Italia

471 pazienti



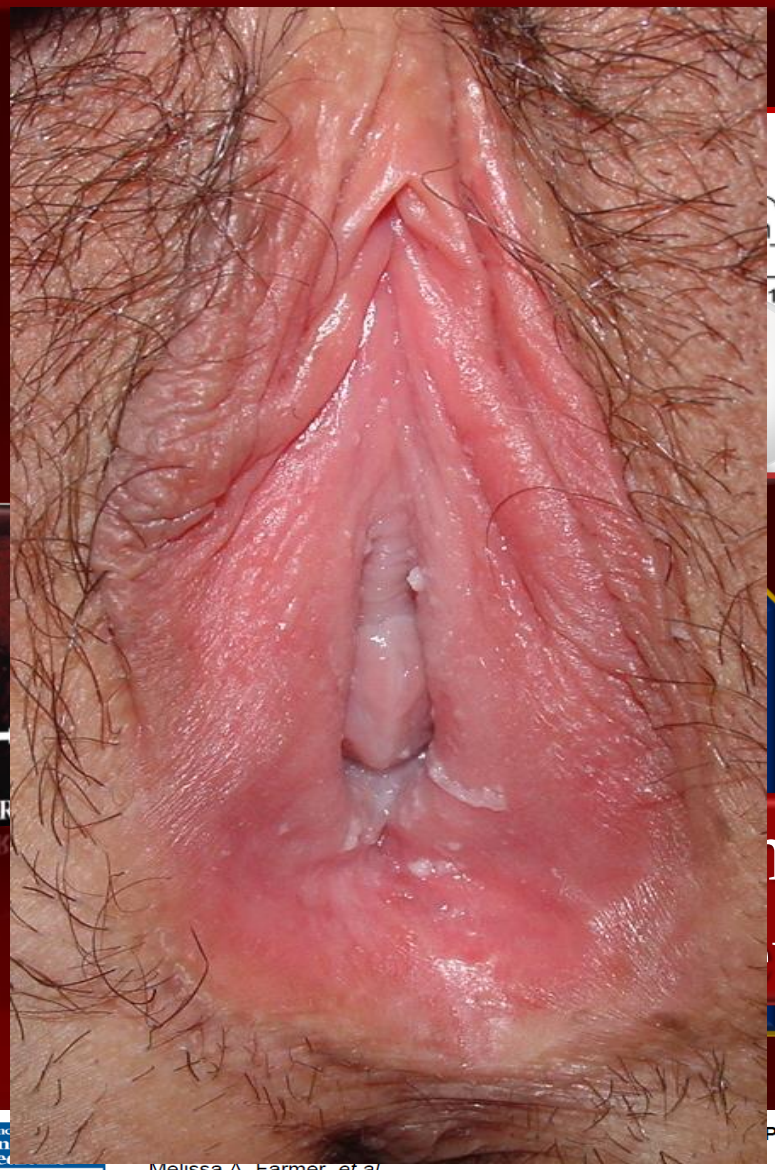
Nel grafico si riportano le patologie con frequenza relativa percentuale superiore al 5%.

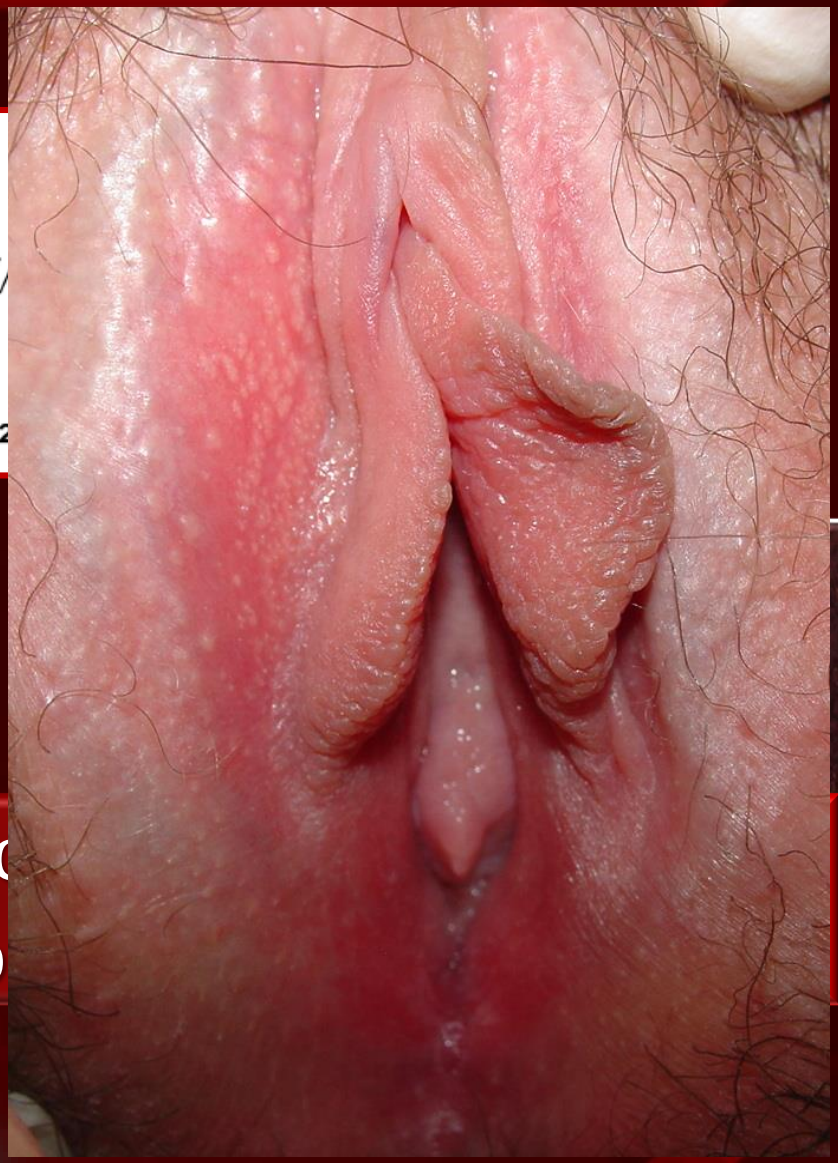
Vu.net

dolorevulvare.net

Il network per la ricerca e la formazione

Candidosi Ricorrente-Vaginiti ripetute e IVU





Melissa A. Farmer, *et al.*
Sci Transl Med **3**, 101ra91 (2011);

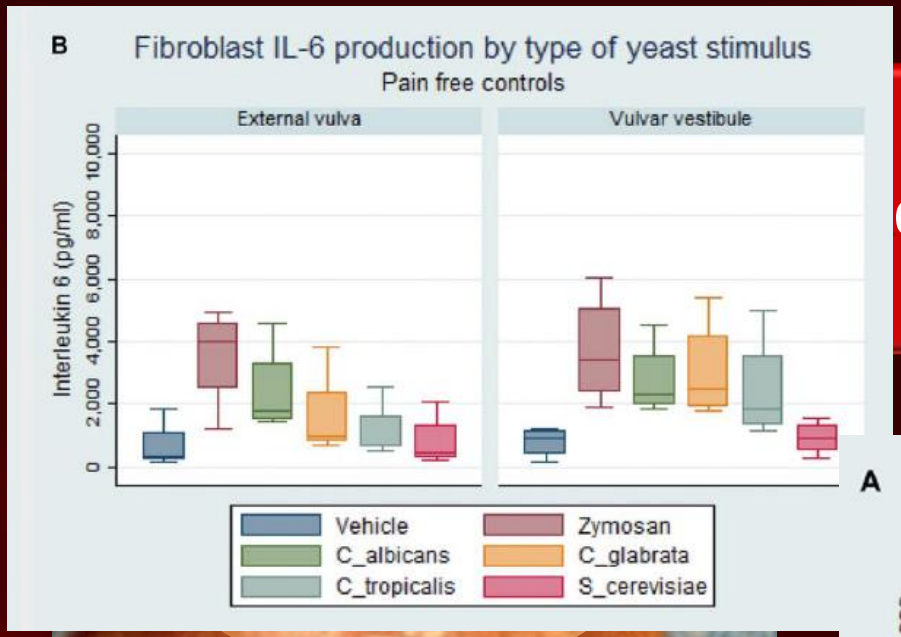
Research Paper
PAIN
OPEN

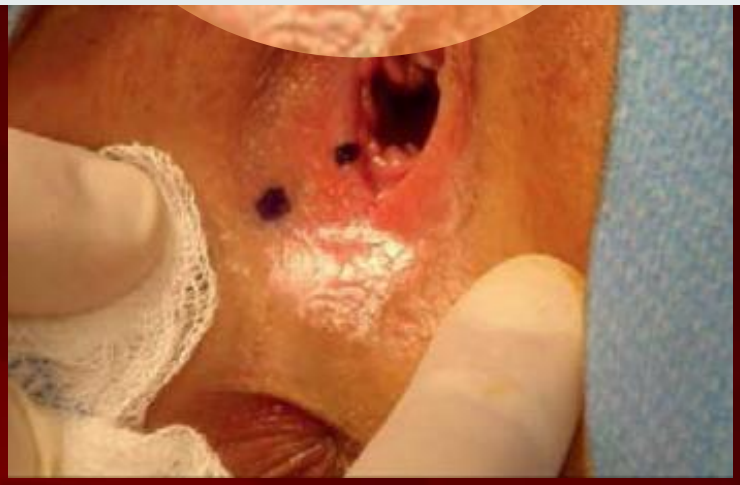
Site-specific mesenchymal control of inflammatory pain to yeast challenge in vulvodynia-afflicted and pain-free women

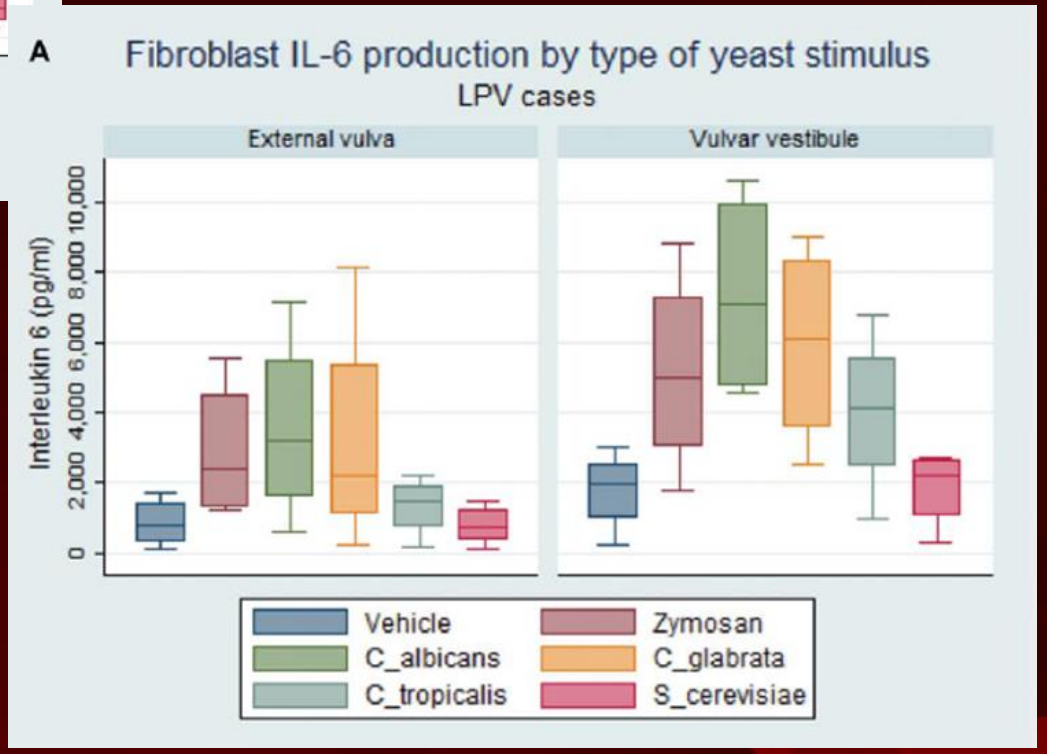
David C. Foster[a,*], Megan L. Falsetta[b], Collynn F. Woeller[b], Stephen J. Pollock[b], Kunchang Song[c],

March 2015·Volume 156·Number 3

Stimolazione di fibroblasti erivanti da prelievi vestibolari in pz con VBD e Controlli







Familiality analysis of provoked vestibulodynia treated by vestibulectomy supports genetic predisposition

Terry K. Morgan, MD, PhD; Kristina L. Allen-Brady, PhD; Martha A. Monson, MD; Catherine M. Leclair, MD; Howard T. Sharp, MD; Lisa A. Cannon-Albright, PhD

Am J Obstet Gynecol 2016

TABLE 1

Relative risk estimates for vestibulectomy in first-, second-, and third-degree relatives of 183 probands based on CPT codes

Relationship to proband	Number of relatives	Observed no. vestibulectomies	Expected no. vestibulectomies	Relative risk [95% CI]; *P* value
First-degree	498	5	0.25[a]	20 [6.6–47]; <.0001
Second-degree	955	<5	-	4.5 [0.5–16]; .07
Third-degree	2194	<5	-	3.4 [1.2–8.8]; .03

CONCLUSION: Our data suggest that vestibulodynia treated by ves-
tibulec ntify
candid ng of
distantly related probands.

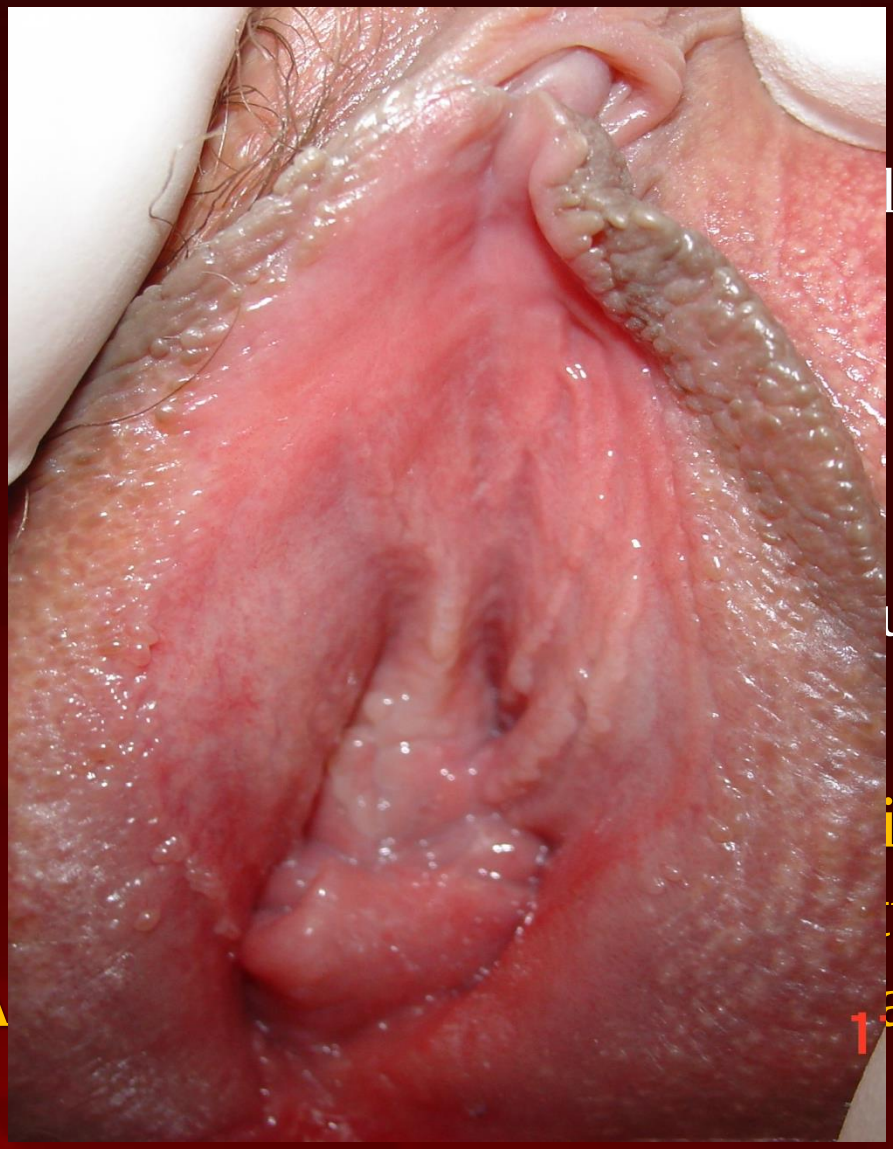
Predisposizione Genetica

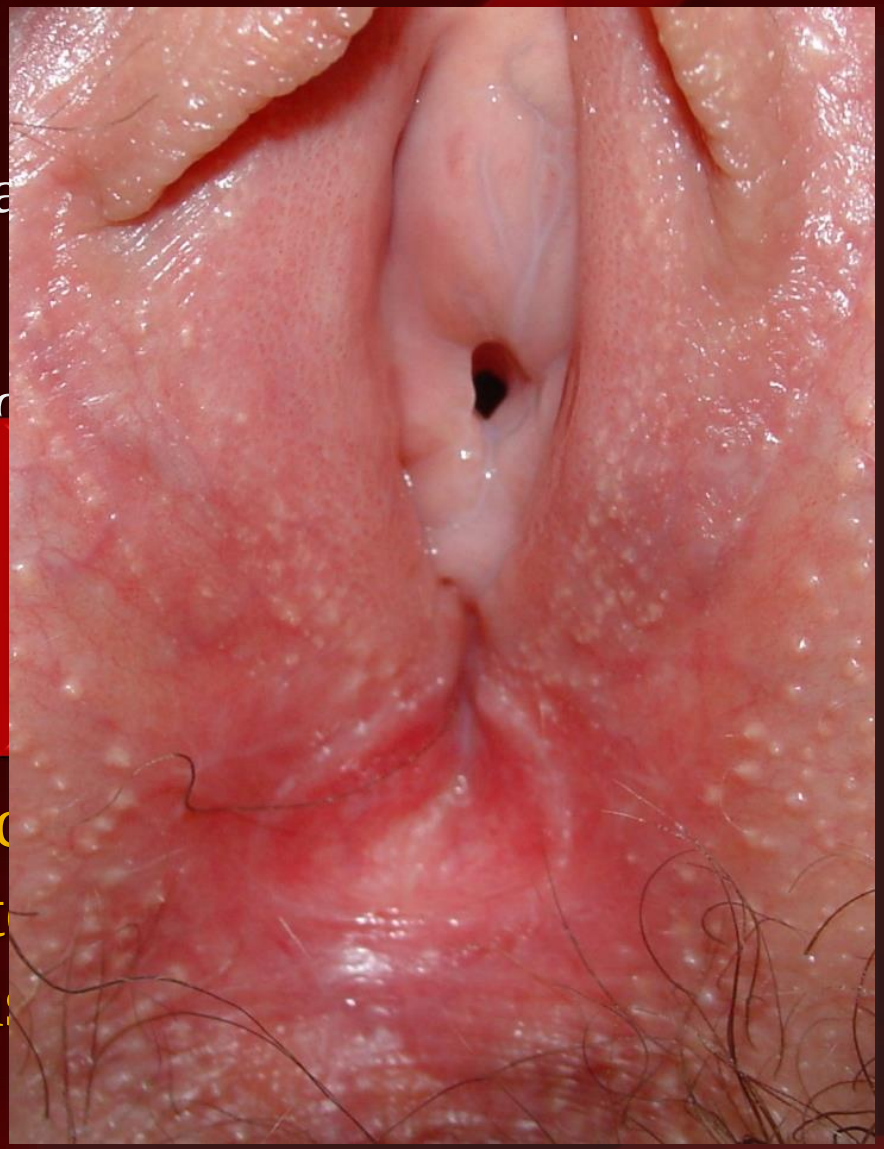
Lev-Sagie A . Recent advances in understanding provoked vestibulodynia *F1000Research* 2016

The vulval vestibular mucosa—morphological effects of oral contraceptives and menstrual cycle

U. Johannesson, B. Blomgren,* M. Hilliges,† E. Rylander and N. Bohm-Starke

British Journal of Dermatology 2007





Polymorphisms of the Androgen Receptor Gene and Hormonal Contraceptive Induced Provoked Vestibulodynia

Andrew T. Goldstein, MD,*† Zoe R. Belkin, MS,*† Jill M. Krapf, MD, MSc,† Weitao Song, PhD,‡ Mohit Khera, MD, MBA, MPH,‡ Sarah L. Jutrzonka, PhD,‡ Noel N. Kim, PhD,§ Lara J. Burrows, MD, MSc,* and Irwin Goldstein, MD¶

J Sex Med. 2014

ABSTRACT

Aim. Women who developed vestibulodynia (vulvar vestibulitis) while taking combined hormonal contraceptives (CHCs) and a control group of women were tested (AR) that is located on the X chromosome.

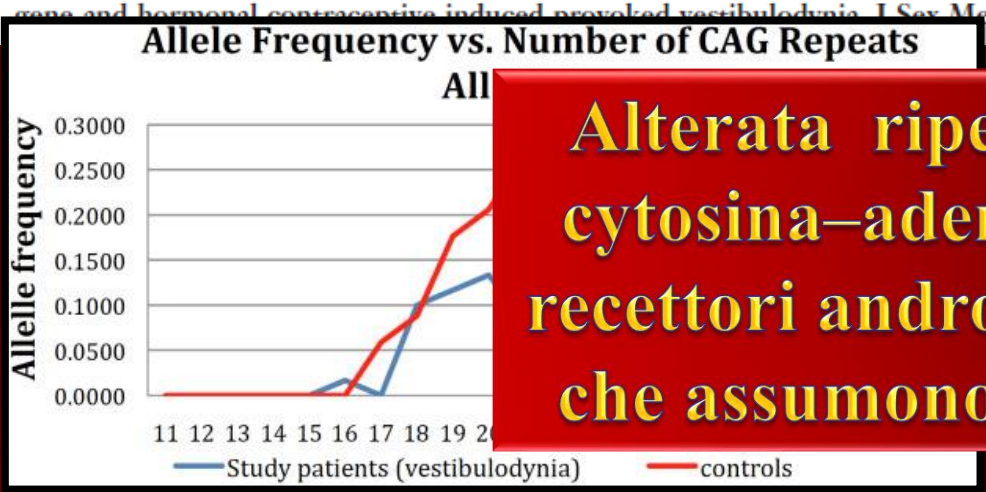
Study Design. DNA from 30 women who develop tested for the number of cytosine–adenine–guanin testosterone was tested in both groups.

Results. The mean number of CAG repeats in th (22.05 ± 2.98 vs. 20.61 ± 2.19, respectively; $P = 0.0$ repeats from the longer allele from each subject. An mean calculated free testosterone was 0.189 ± 0. control group, all of whom were taking drospiren

Conclusion. In the study cohort, women who deve longer CAG repeats in the AR than women who took the same type of CHC but did not develop vestibulodynia. We speculate that the risk of developing CHC-induced vestibulodynia may be due to lowered free testosterone combined with an inefficient AR that predisposes women to vestibular pain. **Goldtein AT, Belkin ZR, Krapf JM, Song W, Khera M, Jutrzonka SL, Kim NN, Burrows LJ, and Goldstein I. Polymorphisms of the androgen receptor gene and hormonal contraceptive induced provoked vestibulodynia. J Sex Med **;**:**–**.**

-Due gruppi di donne che assumono E-P :
- -Gruppo con VBD
- -Gruppo di controllo

- Valutazione eventuale polimorfismo per recettori degli androgeni



Alterata ripetizione del trinucleotide cytosina–adenina–guanina (CAG) nei recettori androgenici in donne con VBD che assumono E-P rispetto ai controlli

Table 4. 2015 Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia

- Musculoskeletal (eg, pelvic muscle overactivity,

Tono di base elevato

Table 3 PFM pressure measuren

		(*n*=35), SD)	*p* value between groups
VRP before the first MVC (cmH_2O		)	0.02
PFM strength (mean of 3× MVC) (		6)	0.57
PFM endurance (10 sH_2O)		3.0)	0.21

-Tono più alto
-Minore resistenza
-Scarso controllo

Alterata capacità contrattile

Pelvic floor muscle function in women with provoked vestibulodynia and asymptomatic controls

Ingrid Næss · Kari Bø

Int Urogynecol J-2015

Heightened Pelvic Floor Muscle Tone and Altered Contractility in Women With Provoked Vestibulodynia

Mélanie Morin, PT, PhD,[1] Yitzchak M. Binik, PhD,[2] Daniel Bourbonnais, OT, PhD,[3] Samir Khalifé, MD,[4]

J Sex Med 2017

Table 4. Pelvic floor muscle contractility in women with PVD and in asymptomatic controls

Conditions	Parameters	PVD (n = 56), mean ± SD	Control (n = 56), mean ± SD	*P* value
Maximal strength	maximal force (N)	2.35 ± 1.25	2.98 ± 1.55	.021
Speed of contraction	Contractions (n)	7.18 ± 1.65	9.64 ± 2.62	<.001
	slope of ascending curve (N/s)	3.58 ± 2.43	5.35 ± 3.84	.005
	slope of descending curve (N/s)	−2.82 ± 2.14	−3.22 ± 2.66	.346
Endurance	normalized area under force curve (% · s)	1,816.27 ± 761.68	2,168.34 ± 830.93	.028

Vulvodynia—Younger Age and Combined Therapies Associate With Significant Reduction in Self-Reported Pain

Anu P. Aalto, MD,[1,2] Silja Vuoristo, BM,[2] Heidi Tuomaala, BM,[2] Riikka J. Niemi, MD,[3] Synnöve M. Staff, MD, PhD,[2,3] and Johanna U. Mäenpää, MD, PhD[2,3]

J Low Genit Tract Dis 2017

Objectives:
pain disorder
the efficacy of
(NRS) for pain
Materials a
VD patient coh
and review of the medical records.
Results: We report here a statistically

Valutazione retrospettiva dell'efficacia terapeutica
(numerical rating scale -NRS- for pain

TABLE 3. Different Treatment Modalities Used for VD Patients

Laser treatment	3 (4.3)
Sacral neuromodulation	2 (2.9)

TABLE 4. Overall Effect of Various VD Treatments on NRS score and the Most Frequent Treatment Combinations

Treatment	No. patients	NRS score before treatments, median (IQR)	NRS score after treatments	*p*
Combination of treatments[a]	70	8 (8–9)	4 (2–7)	<.001

[a]Mos
37 patie

-Multimodalità strategia più efficace
-Vulvodinia in età più avanzata più resistente al trattamento

Dyspar
Nullipa
Postme
Local pain, *n* (%)
Generalized pain, *n* (%)

nseling of

14 (20.0)
13 (18.6)
10 (14.3)

Generalized unprovoked vulvodynia; A retrospective study on the efficacy of treatment with amitriptyline, gabapentin or pregabalin

Heleen J. van Beekhuizen[a,*], Jessica Oost[b], Willem I. van der Meijden[c]

Europ J Obst & Gynecol and Reprod Biol 2018

Side effects amitriptyline	
none	91
drowsiness	36
headache	3
abdominal pain	9
dry mouth	9
psychological disturbances	4
cardiovascular complaints	2
skin abnormalities	3
other	10
patients who	55 (31%)
Side effects gaba	
none	5
drowsiness	3
patients who stopped gabapentin because of side effects	3 (38%)
Side effects pregabalin	
none	17
abdominal discomfort	2
drowsiness	1
dry mouth	1
headache	1
skin abnormalities	1
patients who stopped pregabalin because of side effects	4 (24%)

Efficacy treatment overall	
none	48 (30%)
temporary	17 (10%)
long lasting effect	107 (60%)

dermatosis).

179)

Amitriptilina e Dolore Vulvare

SECOND OF 3 PARTS

VULVAR PAIN SYNDROMES
A bounty of treatments—but not all of them are proven

Treatments for vulvodynia and vestibulodynia range from lifestyle adjustments and application of topical agents to tricyclic antidepressants and nerve blocks—but the data on their efficacy are not as bountiful

Neal M. Lonky, MD, MPH, moderator; Libby Edwards, MD, Jennifer Gunter, MD, and Hope K. Haefner, MD, panelists

and the particular agent used. Amitriptyline is often used as a first-line medication. I start the patient on 10 to 25 mg nightly and increase that amount by 10 to 25 mg weekly, not to exceed 150 mg daily. A sample regimen might be 10 mg at bedtime for 1 week. If symptoms persist, increase the dose to 20 mg at bedtime for another week, and so on. Once a dose is established that provides relief, the patient should continue to take that amount nightly. Advise the patient not to discontinue the drug abruptly. Rather, it should be weaned.

3 gtt la sera (6 mg)

6 gtt la sera (12 mg)

10 gtt la sera (20 mg)

15 gtt la sera (30 mg)

hildhood to old age.-Springer ed. 2017

Alpha Lipoic Acid Plus Omega-3 Fatty Acids for Vestibulodynia Associated With Painful Bladder Syndrome

J Obstet Gynaecol Can 2017;

Filippo Murina, MD;[1] Alessandra Graziottin, MD;[2] Raffaele Felice, MD;[1] Dania Gambini, MD[2]

Abstract

Objective: This study assessed the effectiveness of alpha lipoic acid (ALA) plus omega-3 polyunsaturated fatty acids (n-3 PUFAs) in co ve

Metho am pre co ac bu sc Qu

Resul sta wit as sc sig ad amitriptyline treatment was also associated with improvements in dyspareunia and pelvic floor muscle tone. The overall incidence of adverse events was low, and none led to treatment discontinuation.

Conclusions: The addition of ALA/n-3 PUFAs to amitriptyline treatment in patients with VBD/PBS appears to improve outcomes and may allow for a lower dosage of amitriptyline, which may lead to fewer adverse effects.

Table 1. Patient demographics and disease characteristics

		Group A	Group B
	All patients (n = 84)	Amitriptyline plus ALA + n-3 PUFAs (n = 43)	Amitriptyline (n = 41)
Age (years)[a]	30.1 ± 7.7/29 (18 to 50)	30.0 ± 8.2/29 (18 to 50)	30.2 ± 7.3/29 (18 to 45)
Months from disease onset[a]	28.4 ± 19.4/24 (2 to 84)	28.4 ± 21.1/24 (2 to 84)	28.3 ± 17.7/24 (4 to 72)
<12	10 (11.9%)	6 (14.0%)	4 (9.8%)
12–24	28 (33.3%)	14 (32.5%)	14 (34.1%)
>24	46 (54.8%)	23 (53.5%)	23 (56.1%)
Amitriptyline (mg)[a]	21.7 ± 6.6/20 (12 to 30)	21.8 ± 6.8/20 (12 to 30)	21.6 ± 6.5/20 (12 to 30)

[a]Mean ± SD/median (minimum to maximum).

Alpha Lipoic Acid Plus Omega-3 Fatty Acids for Vestibulodynia Associated With Painful Bladder Syndrome

Filippo Murina, MD;[1] Alessandra Graziottin, MD;[2] Raffaele Felice, MD;[1] Dania Gambini, MD[2]

J Obstet Gynaecol Can 2017;

Figure 1. Relative change (%) in pain from baseline t visit two measured using a VAS pain score and the McGill Pain Questionnaire ($P < 0.001$)

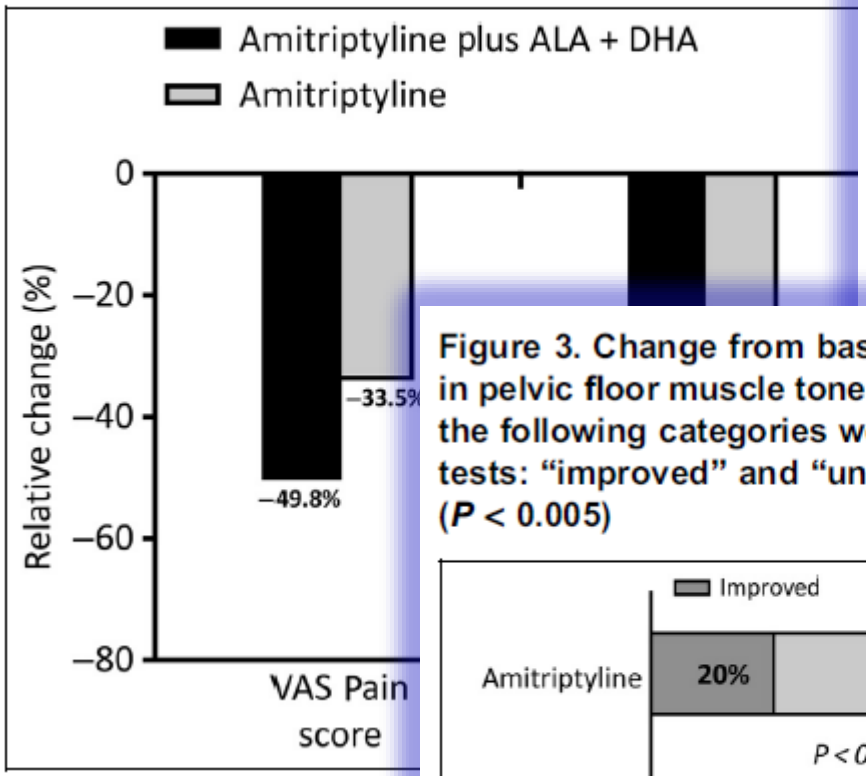


Figure 2. Change in pelvic dyspareunia from baseline to visit two; the following categories were considered for the two tests: "improved" and "unchanged/worsened" ($P < 0.03$)

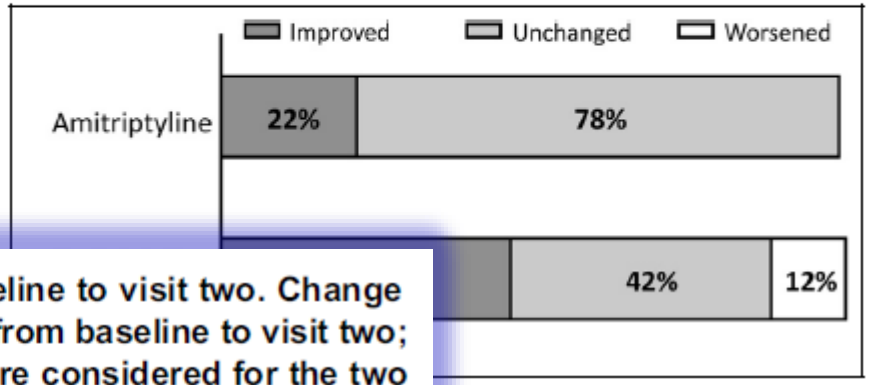
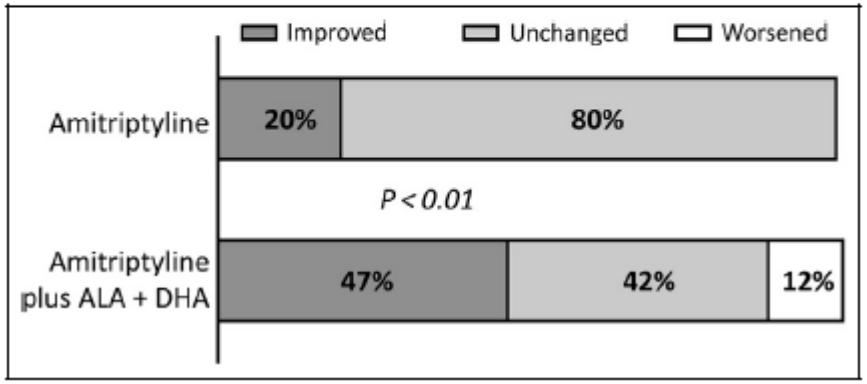


Figure 3. Change from baseline to visit two. Change in pelvic floor muscle tone from baseline to visit two; the following categories were considered for the two tests: "improved" and "unchanged/worsened" ($P < 0.005$)



SEXUAL MEDICINE REVIEWS

Systematic Review of the Effectiveness of Physical Therapy Modalities in Women With Provoked Vestibulodynia

Mélanie Morin, PT, PhD,[1] Marie-Soleil Carroll, MA,[2] and Sophie Bergeron, PhD[3]

Sex Med Rev 2017

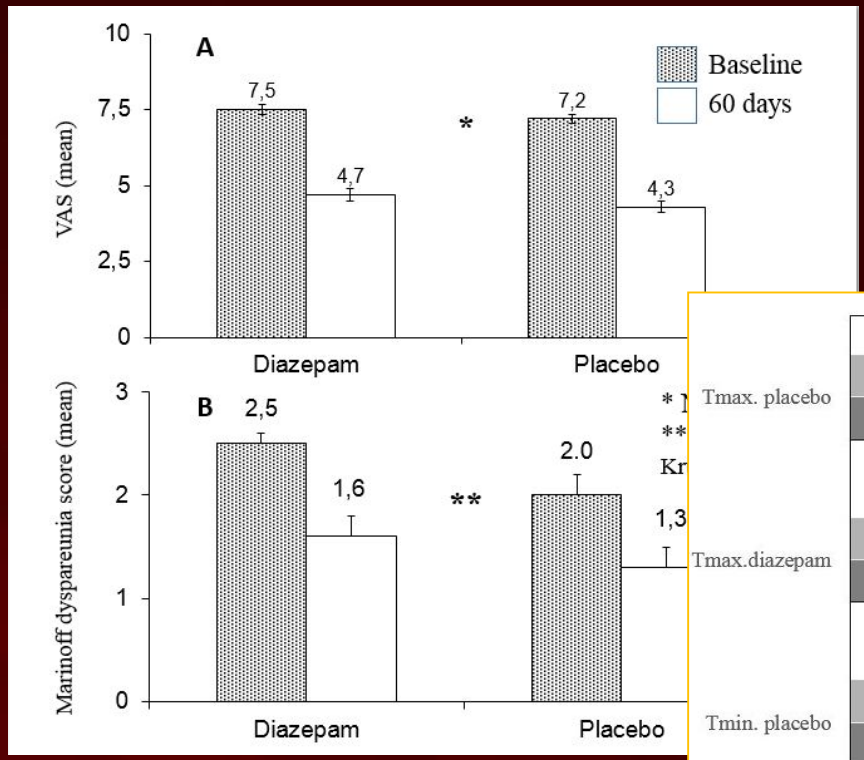
"The vast majority of studies showed that physical therapy modalities such as biofeedback, dilators, electrical stimulation, education, manual physical therapy, were effective for decreasing pain during intercourse and improving sexual function"

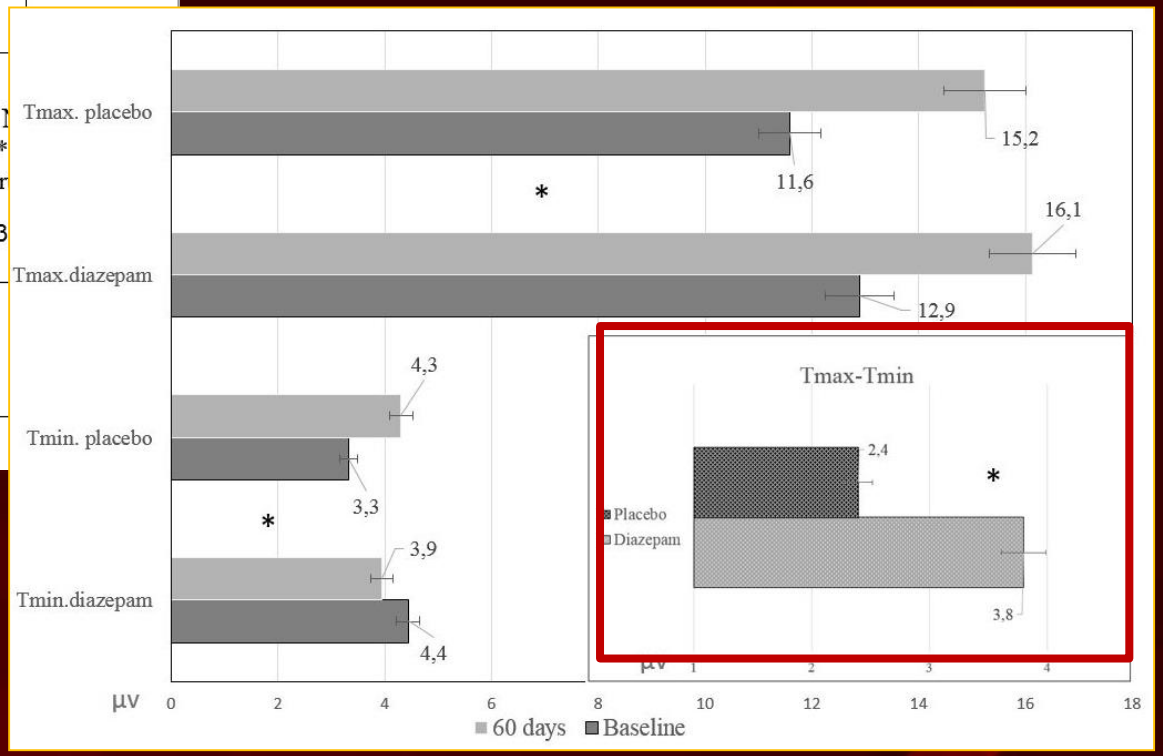
PVD. Physical therapy was shown to be a good adjunct to ves-

Article in Press

Vaginal diazepam plus transcutaneous electrical nerve stimulation to treat vestibulodynia: a randomized controlled trial

Filippo Murina, Raffaele Felice, Stefania Di Francesco, Silvia Oneda
Lower Genital Tract Disease Unit, V. Buzzi Hospital–University of Milan, Milan, Italy



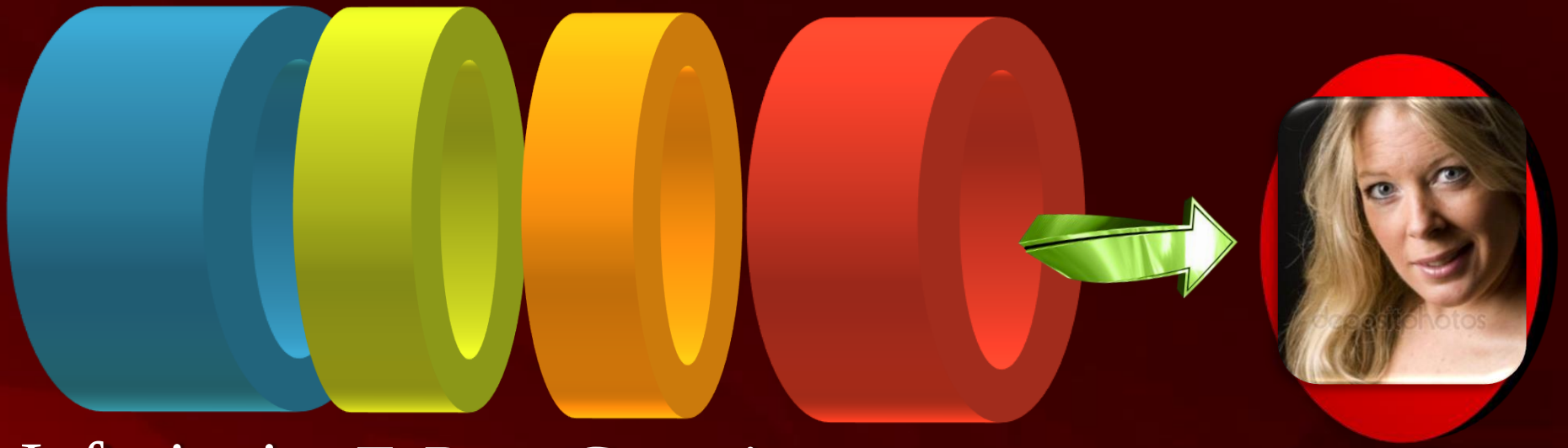


Vulvodinie

Sommatoria di eventi che in modo sequenziale innesca un'alterata percezione del dolore con un peso differente nelle varie fasi di vita della donna

Vulvodinie

Sommatoria di eventi che in modo sequenziale innesca un'alterata percezione del dolore con un peso differente nelle varie fasi di vita della donna



Infezioni E-P Genetica Psico

Grazie per l'attenzione!!!!

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