Advancing Understanding of Vulvodynia as a Pain Disorder

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“Today, idiopathic. Tomorrow, understood.”

JOEL R. COOPER

Goals

- Review Magnitude of Problem
- Summarize Women's Experiences Seeking Help
- Historical/Clinical Overview
- Summarize Research Progress
- Summarize NIH and Congressional Involvement
- Overview of NVA Research Programs
- Discuss *Foundational* Research Gaps Necessary to Address to Advance Understanding of Vulvodynia as a *Pain Disorder*

Magnitude of the Problem

PREVALENCE, HEALTH CARE UTILIZATION AND COST

Magnitude of the Problem

- Four NIH-funded population-based studies, three of which included a clinical confirmation component, show that 3-8% of adult women suffer from chronic vulvar pain.**
- Recent study of adolescents (ages 12-19) suggest it may be quite prevalent among younger women also. (Landry. J Sex Med. 2009)
-
- Most recent study finds that 1 in 4 women will be affected at some point in their lifespan. (Reed 2011)
- Remission < 25% (Reed 2008, Reed 2011)

***Harlow. JAMWA. 2003; Arnold. AJOG. 2007; Reed J Low Genit Tract Dis. 2004; Reed. Obstet Gynecol. 2006; Reed. Obstet Gyncol. 2008; Reed. AJOG. 2011*

Magnitude of Problem

- First NIH-funded, population-based epidemiological study conducted at Harvard from 2000-2005
  - 4915 women surveyed, 18-64 years
  - 3358 surveys returned (response rate 68.3%)
  - 15.6% reported a history of "chronic burning, knifelike or sharp pain, or pain on contact that lasted for 3 months or longer" at some point in their lives
    - 12.4% reported pain on contact
    - 3.3% reported burning or knifelike pain
  - 7% were currently experiencing pain

Magnitude of Problem

- Caucasian and African American women reported similar lifetime prevalence
- Hispanic women were 80% more likely to experience symptoms than were white and African American women.
- 39.6% never sought treatment
- Of those who did seek treatment:
  - 57% reported visiting 3 or more providers in seeking a diagnosis
  - 39.1% remained undiagnosed
- Sample brought in for clinical confirmation and to determine the survey's predictive value to delineate Provoked Vestibulodynia (from other common causes of vestibular pain):
  - 78% clinically confirmed based on pelvic exam and Friedrich's criteria

Harlow. JAMWA. 2003

Magnitude of Problem – Cost

- First Economic Impact Vulvodynia Study – Conducted by NVA in Cooperation with Tulane University (Dr. Lizheng Shi) and Analysis Group, Inc. (Dr. Eric Wu)
  - "Real-time" Online Survey

    With the use of a NVA-supplied cost calendar/spreadsheet, women recorded their vulvodynia-related expenses in "real time" and entered the information online 1x/month for 4-6 months
  - Self-reported chronic vulvar pain > 3 months
  - Included additional questions previously demonstrated to correlate with a clinical diagnosis of Provoked Vestibulodynia.*
    - Experience genital pain?
    - Experience genital burning > 3 months?
    - 10 or more episodes of pain on contact with tampon insertion, intercourse or pelvic exam?
    - Does pain on contact limit/prevent intercourse?

*Harlow. J Womens Health (Larchmt). 2009.

Magnitude of Problem – Cost

- Data Collected with Intake Questionnaire
  - Vulvodynia subtype(s)
  - Time since diagnosis
  - Time since symptoms began
  - Age
  - Marital status
  - Education
  - Household income
  - Insurance type(s)
  - Ethnicity
  - Comorbid pain disorders (IC, FM, CFS, IBS, Endo, TMD, Headache)
  - Other chronic illnesses

Magnitude of Problem - Cost

- Data Collected on Returning Questionnaire
  - For every medical appointment, women recorded:
    - Type of provider visited
    - Number of visits
    - All out-of-pocket expenses (co-pay, deductible, transportation, etc.) associated with each visit
  - Out-of-pocket expenses related to:
    - Lab work / diagnostic tests
    - Surgical procedures
    - Hospitalization
    - Prescriptions medications
    - Over-the-counter remedies / self-care measures

Magnitude of Problem - Cost

- Data Collected on Returning Questionnaire
  - Work-related expenses:
    - Number of days unable to work
    - Lost income (both paid/unpaid by employer) due to:
      - Sick leave
      - Leave of absence
      - Direct loss of job
      - Unemployment disability
  - Effects on daily life:
    - Number of days unable to perform household chores
    - Number of days forced to abstain from social activities

Magnitude of Problem – Cost

- Findings
  - Using a prevalence range of 3-7% in the US, the analysis yielded an annual national burden ranging from $31-72 billion.
  - Total costs in 6 months was $8862.4:
    - $6043.34 (68.19%) direct healthcare costs
    - $553.81 (6.25%) direct non-healthcare costs
    - $2265.25 (25.56%) indirect costs
  - Common Co-morbidities:
    - Irritable bowel syndrome (27.2%)
    - Migraine headache (25.2%)
    - TMD (17%)
    - Interstitial cystitis (13.6%)
    - Endometriosis (11.6%)

Xie et al (submitted for publication)

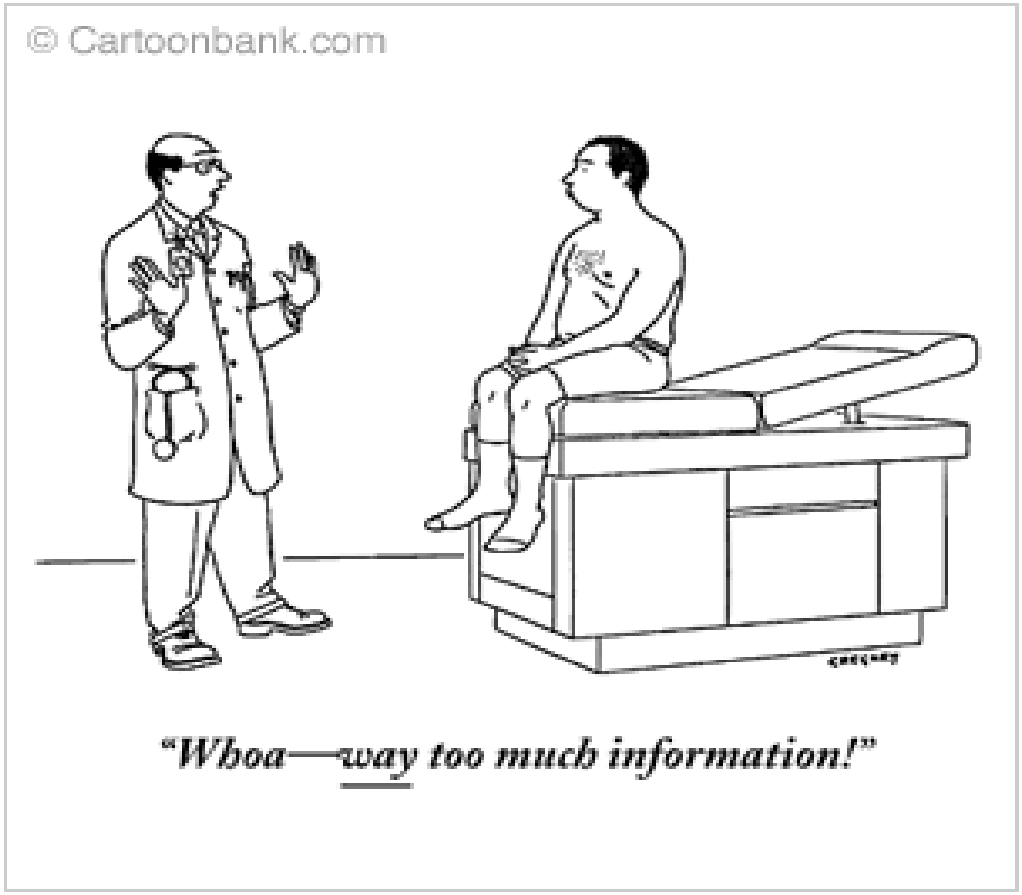
Women's Experiences Seeking Help

What do Women Experience?

What do Women Experience?

Bryant, Adey abr0192

What do Women Experience?



What do Women Experience?

Why is this the common experience for women?

UNDERSTANDING THE HISTORY OF THE DISORDER PROVIDES SOME INSIGHT

Historical Overview

TIMELINE, DEFINITION, CLASSIFICATION AND CLINICAL OVERVIEW

First Described in 1880

"Hyperaesthesia of the Vulva"

First described by Thomas (gynecologist):

"Excessive sensibility of the nerves supplying the mucous membrane of some portion of the vulva, sometimes… confined to the vestibule… other times to one labium minus."

Vulvodynia may have been referred to in earlier medical texts, possibly dating as far back as the 1st Century.

Thomas. Practical Treatise on the Diseases of Women. 1880.
McElhiney. J Sex Med. 2006

Described Again in 1888

"Supersensitiveness of the Vulva"

Skene (gynecologist): "This disease…is characterized by the supersensitiveness of the vulva… No redness or other external manifestation of the disease is visible… When the examining finger comes in contact with the hyperaesthetic part, the patient complains of pain, which is sometimes so great as to cause her to cry out. Sexual intercourse is equally painful and becomes, in aggravated cases, impossible."

Skene. Treatise of the Diseases of Women. 1888.

1920s

"Sensitive deep-red spots"

1928: Kelly describes "exquisitely sensitive deep-red spots in the mucosa of the hymenal ring as a fruitful source of dyspareunia."

No mention of condition appears in medical texts for five decades thereafter.

Kelly. Gynecology. 1928.

1970s & 1980s: ISSVD Addresses Issue

1975: Vulvodynia first addressed by the International Society for the Study of Vulvovaginal Disease (ISSVD) membership at 1975 World Congress as "burning vulva syndrome."

1982: ISSVD membership surveyed on condition

1980s: Defined by ISSVD

1983: ISSVD adopts first formal definition of vulvodynia:

> "Chronic vulvar discomfort, especially that characterized by the patient's complaint of burning and sometimes stinging, irritation or rawness. (McKay. J Reprod. Med. 1984)

Vulvodynia is a symptom rather than a diagnosis and it may have multiple causes.

1985: Definition refined at World Congress but never formally published:

> "Only cases which lack a demonstrable etiology."

1987: Friedrich Describes VVS

"Vulvar Vestibulitis Syndrome"

Friedrich coins the term to describe women who present with:

1: Severe pain on attempted vaginal entry
2: Tenderness to pressure localized within the vestibule
3: Physical findings confined to vestibular erythema of various degrees

Friedrich. J Reprod Med. 1987.

2004: Definition Modified and Published

Because its 1983 definition of vulvodynia did not rule out vulvar pain due to known causes, the ISSVD revised it at the 2003 World Congress and published the new definition in 2004:

> "Vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurologic disorder."

New classification and terminology proposed.

Moyal-Barracco M. J Reprod Med. 2004
Haefner. J Low Genit Tract Dis. 2007

ISSVD Classification

Vulvar pain related to a specific disorder (NOT Vulvodynia)

- Infectious (e.g., candidiasis, herpes, etc.)
- Inflammatory (e.g., lichen sclerosus, contact dermitiis)
- Neoplastic (e.g., Paget disease, squamous cell carcinoma, etc.)
- Neurologic (e.g., herpes neuralgia, spinal nerve compression, etc.)

Vulvodynia

- Generalized
  - Provoked (sexual, nonsexual or both)
  - Unprovoked
    - ***Generalized Vulvodynia*
  - Mixed (provoked and unprovoked)
- Localized (vestibulodynia, clitorodynia, hemivulvodynia, etc.)
  - Provoked (sexual, nonsexual or both)
    - ***Provoked Vestibulodynia / Vulvar Vestibulitis Syndrome*
  - Unprovoked
  - Mixed (provoked and unprovoked)

Haefner. J Low Genit Tract Dis. 2007.

Other Terms - Confusion is Common

Generalized Unprovoked Vulvodynia	Provoked Vestibulodynia
Hyperaesthesia of the vulva	Vulvar Vestibulitis Syndrome
Dysesthetic Vulvodynia	Vestibular Adenitis
Vulvar Dysesthesia	Minor Vestibular Gland Syndrome
Essential Vulvodynia	Localized Provoked Vulvodynia

Gross Subjective Findings

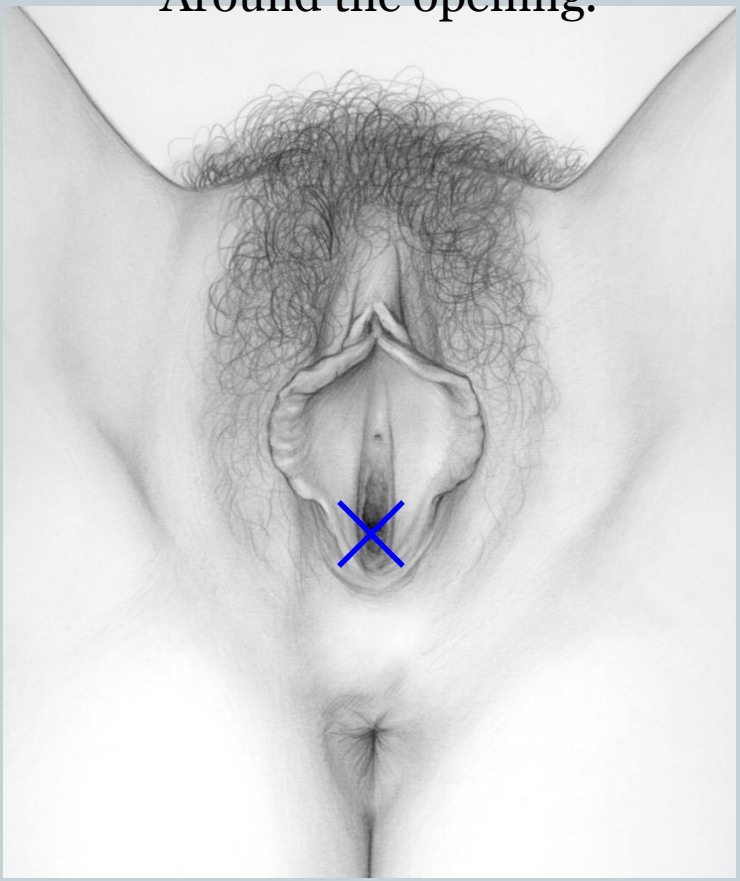
"Where does it hurt?"

Generalized Vulvodynia

"All over."

Provoked Vestibulodynia

"Around the opening."



Current Diagnostic Techniques
Cotton-Swab Test

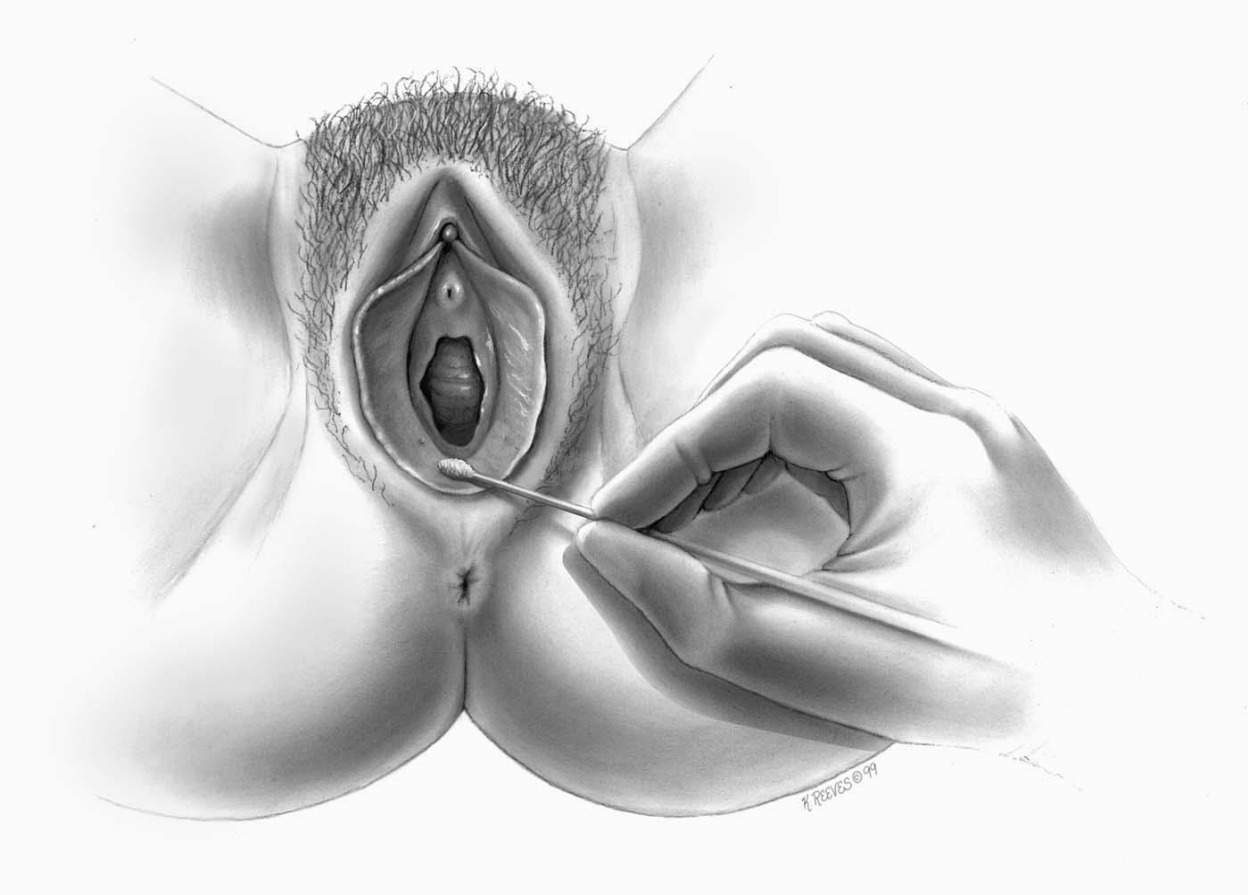
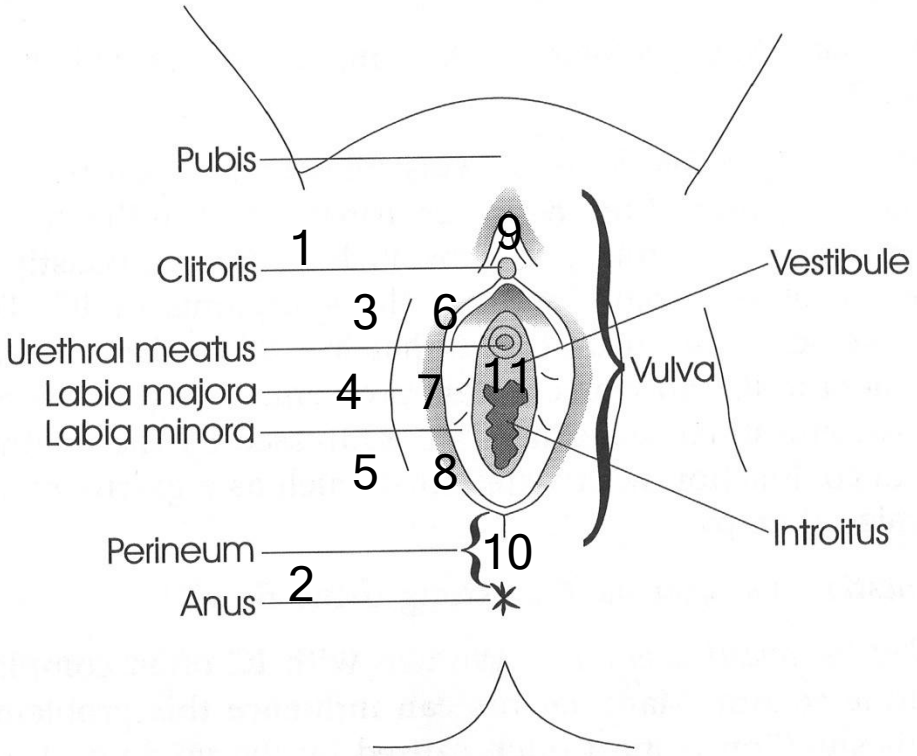


Diagram from Haefner, H.K., Critique of new gynecologic surgical procedures, Clin Obstet Gynecol 2000 Setp;43(3): 689-700.

Current Diagnostic Techniques
Cotton-Swab Test

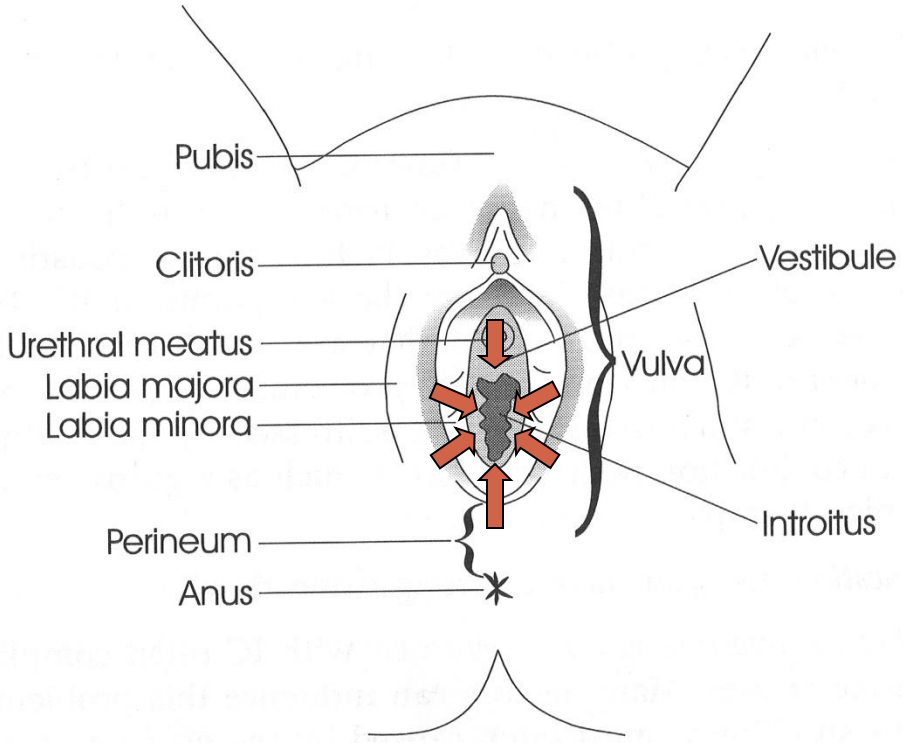


- Diagnosis of Exclusion
- Rule out all other causes for vulvar pain
- Test for allodynia, hypo- or hyperalgesia using cotton-swab test by applying gentle pressure to:

1-2	Inner thigh
3-5	Labia majora
6-8	Interlabial sulcus
9	Clitoris / clitoral hood
10	Perineum
11	Sites within vestibule

- Women rate pain severity at each site

Current Diagnostic Techniques
Cotton-Swab Test



Women are asked to rate the severity of pain as pressure is applied with a cotton-swab to sites surrounding the introitus (1 o'clock thru 12 o'clock).

PVD is diagnosed by Friedrich's Criteria:

1: Severe pain on attempted vaginal entry

2: Tenderness to pressure localized within the vestibule

3: Physical findings confined to vestibular erythema of various degrees (disputed)

Current Diagnostic Techniques
Visual Examination

Patient #1
Severe Erythema

Patient #2
Moderate Erythema

Patient #3
Minimal Erythema

Which woman do you think was not able to have intercourse or insert a tampon?

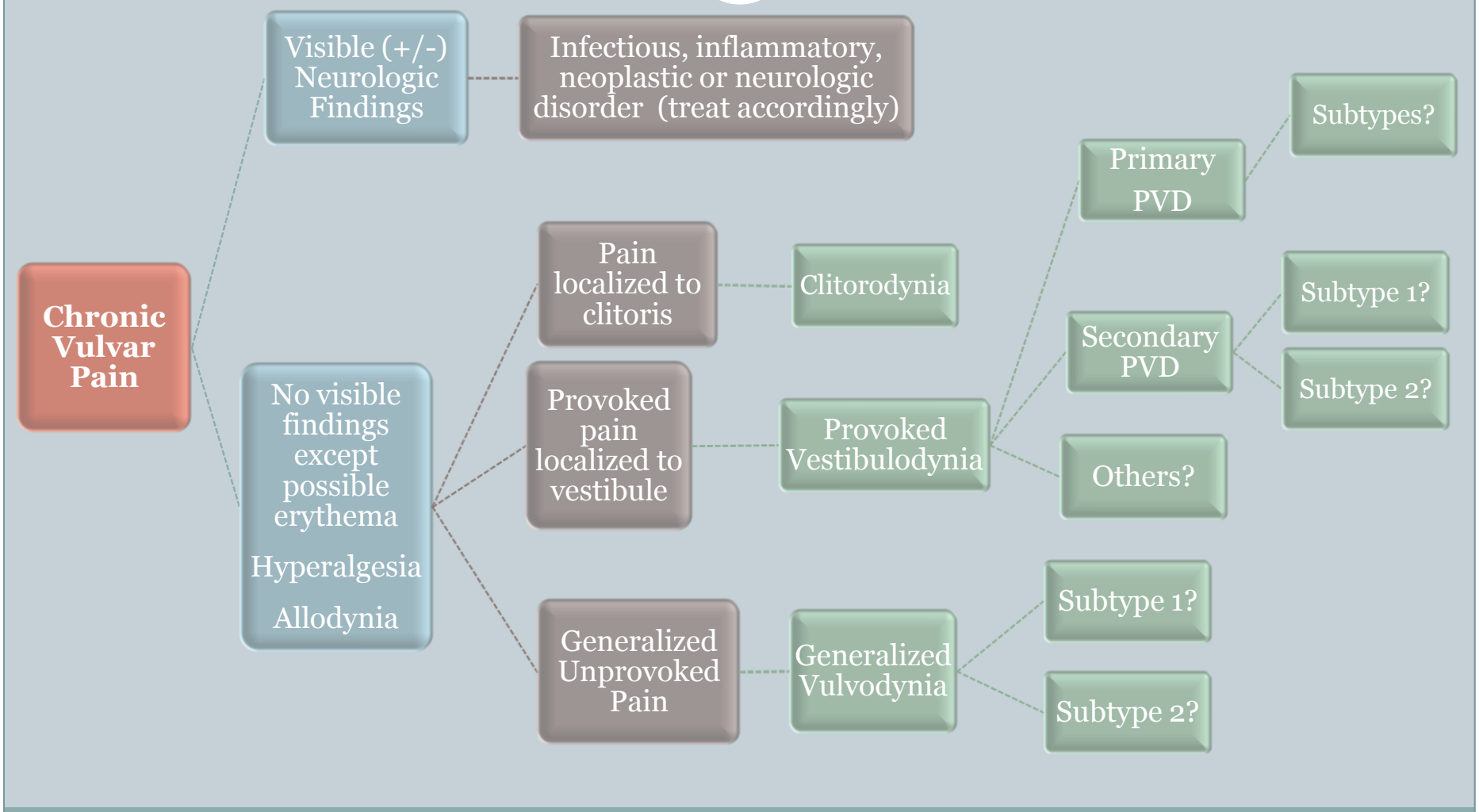
Reprinted with permission from Ledger, W.J. and Witkin, S.S., Vulvovaginal Infections, Manson Publishing, London, 2007, page 103.

Reliability of Visual Inspection of Erythema Disputed

- 2009 study compared unaided visual assessment, colposcopy, visualization (Syris v600) with parallel-polarized light (epithelial surface evaluation) and enhanced visualization with cross-polarized light (epithelial subsurface evaluation) in assessing genital erythema in the vulva, introitus, vagina and cervix of PVD patients.
- Findings:
  - Only the cross-polarized light subsurface visualization technique was significantly more sensitive that other methods at all sites within both the control and symptomatic groups.
  - "Most notable finding" was that although the vulva of patients with PVD appeared clinically normal with all visualization techniques, subsurface visualization revealed a significant increase in erythema relative to controls at the introitus, vagina and cervix.

Farage. Am J Obstet Gynecol. 2009.

Stratification /Subtypes



Current Diagnostic Techniques
Others? Which are clinically relevant?

- Muscle Exam
  - No consensus described or required in Guidelines documents. Which muscles – pelvic floor or back/hips/lower body? No standardization.
- Colposcopy
  - Some use, some don't.
- Blood Draw
  - Some are using to determine if pain may be hormonally mediated
- Instruments for Cotton-Swab Test
  - Some use, some don't. Different instruments – some are calibrated. No standardization. Validated?
- Nerve conduction studies
  - Some order, some don't.
- Neurological Exam
  - Some order, some don't.
- Quantitative Sensory Testing
  - Some utilize, some don't.
- MRI
  - Should this be a gold standard to rule out? Recent report of vulvar pain associated with Tarlov cysts
- Neurography / MRN
  - Some starting to utilize these specialty tests due to complexity of nerve path
- Orthopedic Evaluation
  - Recent reports of hip disorders (e.g., Labrum tears), low back and other orthopedic disorders associated with vulvar pain. No standard.
- Validated Questionnaires
  - Some use, some don't. No consensus.

Most Common Treatments
Efficacy?

- Oral "Pain-blocking" Medications
  - Tricyclic Antidepressants, Anticonvulsants, SSNRIs
- Topical Preparations
  - Estradiol, Anesthetics, Compounded Topicals
- Pelvic Floor Muscle Therapy
- Interventional Pain Management Techniques
  - Nerve Blocks
    - Pudendal, Sequential (caudal, pudendal, subcutaneous), Other
  - Neurostimulation
- Surgery (for PVD)
  - Removal of all/portion of vestibule with vaginal advancement
- Psychotherapy/Sex Therapy
  - To cope with resulting sexual dysfunction, depression, etc.

Other Treatments Reported in Literature
Efficacy Unknown/Disputed Use?

- Diet Modification
  - Low oxalate, yeast-free
- Topical Steroids
- Subcutaneous Steroid/Anesthetic Injections
- Botox Injections
- Leukotriene Receptor Antagonist
- Topical Nitroglycerin
- Topical Capsaicin
- KTP-nd:YAG laser therapy
- Photodynamic Therapy

Excellent Review: Landry. Clinical J Pain. 2008
See Treatment References

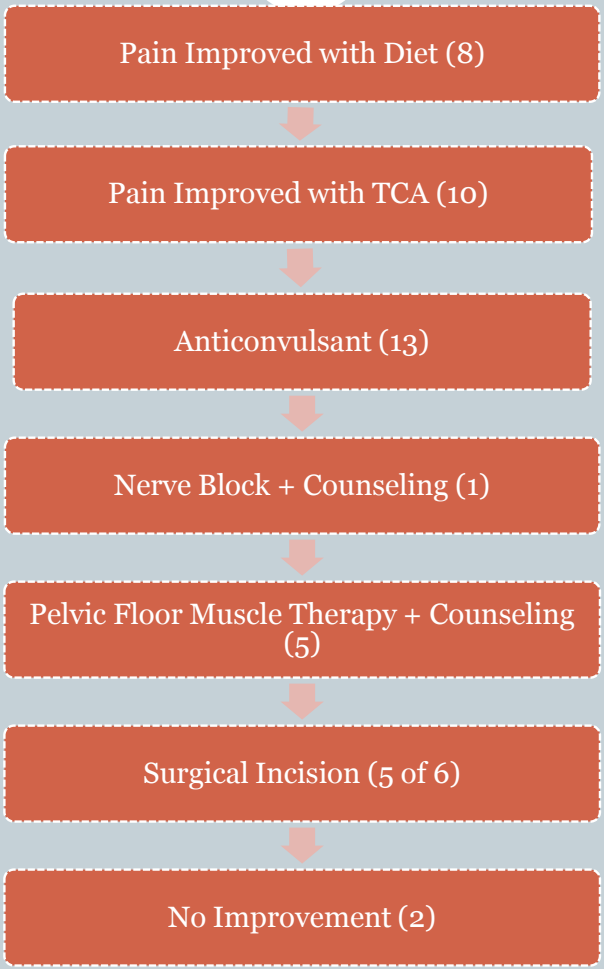
Insufficient Research to Report Efficacy

"Vulvodynia interventions – systemic review and evidence grading."

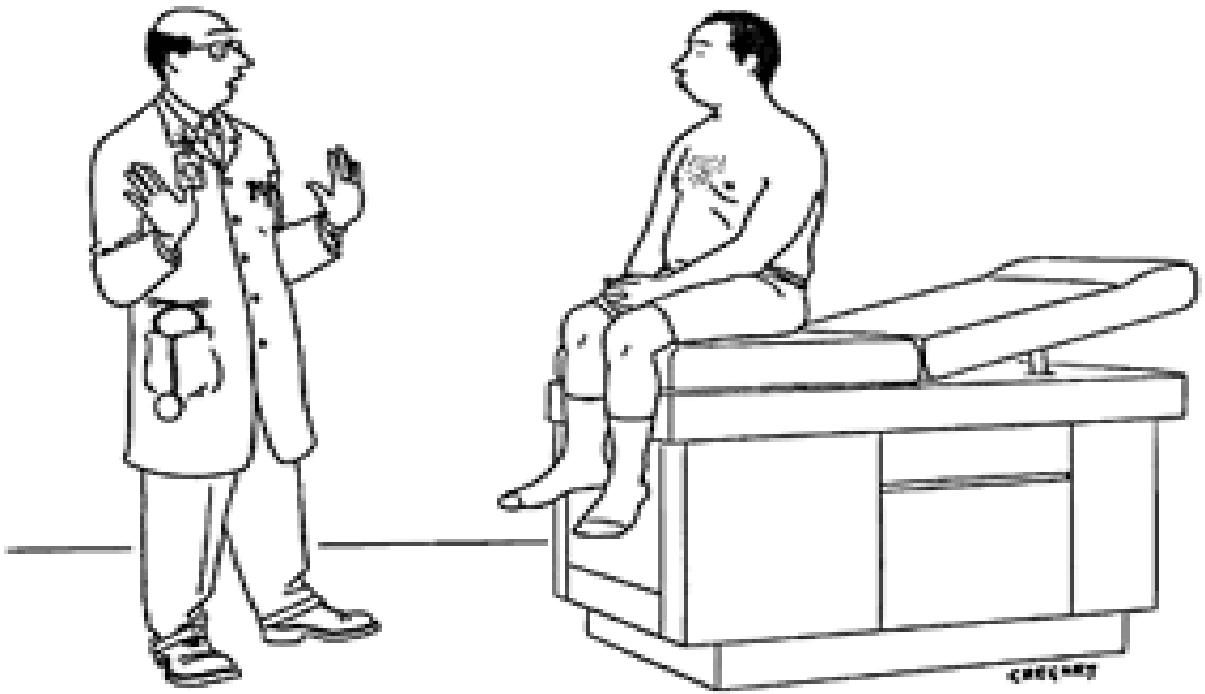
- Purpose:
  - "Although there are many interventional therapies, and their use is increasing, there is also uncertainty or controversy about their efficacy."
- Methods:
  - Systematic review assessed each modality with a grading system similar to the Grades of Recommendations, Assessment, Development, and Evaluation system. The grading system assesses study quality, effect size, benefits, risks, burdens and costs.
- Findings:
  - For improvement of pain and/or function in women with PVD, there was fair evidence that vestibulectomy was of benefit, but the size of the effect cannot be determined with confidence.
  - There was fair evidence of lack of efficacy for several nonsurgical interventions.
  - There were several interventions for which there were insufficient evidence to reliably evaluate.
  - There was insufficient evidence to judge harms or to judge long-term benefits.
  - For clinically meaningful improvement of pain in women with GV, there was insufficient evidence for benefit or any intervention.
- Summary:
  - Providers and patients looking for evidence-based interventions may need to rely on indirect evidences from studies of neuropathic pain and functional pain syndromes.

Andrews. Obstet Gynecol Surv. 2011.

Step-Wise PVD Treatment Study Results Suggest Heterogeneity



Ventolini. J Obstet Gynaecol. 2009.



"Whoa—way too much information!"

"Let the healing begin!"

Research Progress

PREDICTORS

PATHOPHYSIOLOGICAL MECHANISMS

COMORBIDITY

Research Progress

- National Vulvodynia Association
  - Medical Research Fund
    - Have awarded $1 million to 40 pilot grants – data used to obtain larger-scale funding from NIH, etc.
    - Currently funding 12 studies
    - Biannual grant cycle
    - Summaries of funded studies: www.nva.org/research_fund.html
  - Career Development Award
    - Supports small research project or development/enhancement of a vulvar pain clinic
    - Annual grant cycle
    - Summaries of funded awards: www.nva.org/career_development_award.html
- National Institutes of Health
  - Currently devotes $2-3 million/year
  - NICHD/ORWH major contributors, although other Institutes have started to fund vulvodynia research (NINDS, NIDDK)
  - Currently funding 10 studies
  - Summaries of funded studies: www.nva.org/nih_funding.html

Risk Factors/Predictors Reported in Literature

- Vulvovaginal infection (most data is retrospective self-report - infection tested for properly?)
- Oral contraceptive use
- Allergies
- Early age of first intercourse
- Early age of menarche
- Nulliparity
- History of childhood nocturnal enuresis
- Adverse life experiences (parental divorce, pregnancy termination, difficult childbirth, abuse)

- Difficulty or severe pain with first tampon use
- Self-report entry dyspareunia
- "Stinging" pain
- Genital burning > 3 months
- Genital "pain"
- > 10 episodes of pain on contact with tampon insertion, sex or pelvic exam
- Pain on contact that limited/prevented intercourse

Excellent Review: Bohm-Starke. Acta Obstet Gynecol Scand. 2010.
See: Risk Factors/Predictors References

Possible Pathophysiologic Mechanisms

Generalized Unprovoked Vulvodynia

- Really has not been studied
- Hypothesized to be a neuropathic pain syndrome??
- Findings published to date:
  - One study reports increased pressure sensitivity in both the vulva and peripheral body regions, suggesting "central sensitization." (Geisecke. Obstet Gynecol. 2004)
  - Altered neuroadaptation in subgroup of patients with longer duration of pain (Zhang. Clin J Pain. 2011)

Pathophysiologic Mechanisms
Provoked Vestibulodynia

- Pathophysiology inconclusive. Research supports the theory that diverse mechanisms/triggers initiate and maintain symptoms.
- Findings:
  - Vestibular nerve fiber proliferation (2-7)
  - Inflammatory/Cytokine Alterations:
    - Positive Findings
      - Elevated levels of inflammatory cytokines, IL-1beta and TNF-alpha, in vestibular tissue (8)
      - Increased levels of IL-1-beta, IL-6 and IL-8 in vestibular fibroblasts, both at baseline and following in vitro stimulation with Candida albicans (9)
      - Mild exocytosis of lymphocytes in vestibular glands/ducts (10)
      - Increased number of vestibular cells expressing serotonin and CXCR2, leading the author to conclude that the number of cells expressing the inflammatory mediator serotonin and CXCR2, the shared interleukin-8 receptor, are upregulated with inflammation (11)
      - Erythema of the epithelial subsurface in the introitus, vagina and cervix using cross-polarized light technique (Syris v600 enhanced visualization system). These areas appeared normal with colposcopy and unaided visual inspection. (12)
      - Increase in inflammatory infiltrate, number of mast cells and degranulated mast cells in vestibular tissue (5, 7)

Pathophysiologic Mechanisms
Provoked Vestibulodynia

- Positive Findings (con't.)
  - Decreased in vitro production of interferon-alpha after whole blood cultures were stimulated with lipopolysaccharide (LPS) (13)
  - Decreased ratio of IL-1ra/IL-1-beta after whole blood cultures were stimulated with heat shock protein and LPS, i.e., increased induction of pro-inflammatory cytokine and decreased production of anti-inflammatory mediator (14)
  - Presence of NALP3, a component of inflammasomes (regulate IL-1beta production), in vestibular tissue (15)

- Negative Findings
  - No difference in vestibular expression of IL-1alpha, IL-1beta, TNF-alpha (cytokine expression lowest in the area of greatest hyperalgesia) (16)
  - No difference in the number of vestibular cells expressing chromogranin and synaptophysin, regardless of the degree of inflammation (11)
  - No difference in vestibular expression of cyclooxygenase 2 and inducible nitric oxide synthase, compared to controls (17)

Pathophysiological Mechanisms
Provoked Vestibulodynia

- Increased blood flow and erythema in the posterior vestibule (18)
- Increased vanilloid receptor (VR1) expression in vestibular tissue (19)
- Hormone Receptor Alterations:
  - Positive Findings
    - Increased estrogen receptor alpha in the vestibular epithelium and stroma (20)
    - Increased progesterone receptor in primary subtype (20a)
    - Increased estrogen receptor alpha in primary subtype of < 5 years (20b)
  - Negative Findings
    - Reduced estrogen receptor alpha expression predominantly in the basal layer of the vestibular epidermis (some stromal staining was evident) and appearance of “skip lesions” in the basal vestibular layer devoid of estrogen receptor expression (21)
- Vestibular subepithelial heparanase activity (related to an increase in vestibular mast cells and intraepithelial hyperinnervation) (7)
- IgE-mediated allergy to seminal fluid (22, 23)
- Pelvic floor muscle pathology (24)

Pathophysiological Mechanisms
Provoked Vestibulodynia

- Subsets of women with PVD have polymorphisms in certain genes that code for the following, leading to the resultant abnormalities:
  - IL-1ra – reduced capacity to terminate inflammation (25)
  - IL-1beta – increased capacity to initiate inflammatory response (26)
  - Mannose-binding lectin (MBL) – reduced capacity to combat colonization/infection such asCandida albicans and reduced production of TNF-alpha (27)
  - Cold Induced Autoinflammatory Syndrome 1 (CIAS1) – reduced IL-1beta production following a local trigger, i.e., Candida albicans (15)
  - Melanocortin-1 receptor (MC1R) and IL-1ra – combined presence is associated with an 8-fold increased risk for developing PVD (28)
  - Manganese superoxide dismutase (MnSOD) – oxidative nerve damage – in subset who were unable to tolerate vaginal penetration or had a vaginal trauma (28a)

Pathophysiological Mechanisms
Provoked Vestibulodynia

- Studies of central sensitization in women with PVD have demonstrated:
  - Increased pressure sensitivity in both the vulva and peripheral body regions (1)
  - Increased pain intensity and unpleasantness in response to tender-point examination at nine non-genital sites (29)
  - Higher levels of brain activity in primary and secondary somatosensory cortices and insular cortex during application of pressure to the posterior vestibule (30)
  - Enhancement of post-capsaicin pain response extending far beyond the anatomic location of the primary complaint (31)
  - Lower pain pressure thresholds to noxious cold stimulation, suggesting a systemic hypersensitivity (32)
  - Higher gray matter density in pain modulatory and stress-related areas, i.e. the parahippocampal gyrus/hippocampus and basal ganglia (globus pallidus, caudate nucleus, and substantia nigra) (33)

Pathophysiological Mechanisms References 1-44

PVD Subgroups
Primary vs Secondary

- Studies to date have demonstrated:
  - Women with primary PVD tend to be younger at symptom onset, single, and less likely to have had children. (34-37)
  - Two studies found that women with primary PVD are more likely to report histories of childhood enuresis and dysmenorrhea. (38, 39)
  - Primary PVD report more severe vulvar pain, lower heat pain tolerance over the forearm, lower heat and pain detection thresholds in the vulvar vestibule and heightened umbilical sensitivity. (37, 39-41)
  - Two psychosocial survey studies demonstrated that women with primary PVD report heightened anxiety and a lower level of social functioning. (40, 42)
  - Women with primary PVD may be less likely to benefit from surgical intervention, although one study found no differences in surgical success when duration of pain was controlled. (36, 43, 44)
  - Two studies demonstrate increased nerve density in primary subgroup (20a, 20b)
  - Increased lymphocytes in secondary subgroup (20b)
  - Increased progesterone receptor and estrogen receptor alpha expression in women with primary form of disorder. (20b)

Pathophysiological Mechanisms References 34-44

Common Comorbidities

- Interstitial Cystitis
  - Disorder of the urogenital sinus-derived epithelium? Vulvar pain referred from bladder? All one disorder?
- Orofacial Pain
  - Widespread musculoskeletal pain disorder influenced by genetic makeup & CNS dysfunction?
- Irritable Bowel Syndrome
  - Does IBS predispose women to develop vulvodynia? Does vulvodynia treatment lead to bowel symptoms? Pelvic floor pain disorder? CNS pain disorder?
- Fibromyalgia & Chronic Fatigue Syndrome
  - Does untreated vulvar irritation lead to central sensory processing changes in genetically predisposed women, resulting in altered central pain processing and a widespread increase in sensitivity.? Are women with PVD more sensitive to pain in general, i.e., develop chronic vulvar pain after a local trigger?
- Sexual Dysfunction – a RESULT of chronic vulvar pain!!
  - Genital Pain in Women: Beyond Interference with Intercourse: "Genital pain may be best conceptualized as a multidimensional persistent pain condition that constitutes the endpoint of multiple etiologic trajectories and whose understanding goes beyond its interference with intercourse… Further progress in the genital pain field demands an expansion of our research methodologies." (Bergeron. Pain. 2011)

See Comorbid Disorders References

Temporal Relationship

- NVA Preliminary Survey Data
  - N=1511
  - Self-reported:
    - Generalized Vulvodynia (42%)
    - Provoked Vestibulodynia (58%)
  - Average age of 43 years
  - Length of time since diagnosis – 6 years
  - 63% reported at least one disorder
  - Average number of comorbidities – 2 disorders

	IC	FM	CFS	IBS	Endo	TMJ	Head	BMS
% of Women	19%	14%	6.5%	30%	12%	22%	17%	5%

Temporal Relationship

Of those who reported a comorbid diagnosis, that condition preceded, followed or started at the same time as vulvodynia in the following percentages of women:

	Before	After	Same Time
IC	39%	30%	30%
FM	46	44	11
CFS	52	31	17
IBS	70	23	7
Endo	71	19	10
TMJ	70	25	6
Headache	72	22	6
BMS	37	31	33

Recent Developments

NIH AND CONGRESSIONAL INVOLVEMENT

NIH and Congressional Involvement

- NIH Vulvodynia Conferences:
  - 2003: Toward Understanding a Pain Syndrome
  - 2011: Vulvodynia – A Chronic Pain Condition – Setting a Research Agenda
    - Most common theme was that advancements in this field will come by framing vulvodynia in the context of a chronic pain syndrome
    - White paper to result by end of 2011 – open for public comment
    - Hopeful that a RFA will result to address foundational gaps
- Recent DHHS Pain-Related Activities:
  - 2011 Institute of Medicine study on nation's status of pain prevention, care, treatment and research
    - Major Findings
      - 116 adult Americans suffering from chronic pain
      - Costs the US $635 billion annually
      - Medical education is poor
      - Federal agency research investment is poor
      - Evidence-based diagnostic and treatment guidelines lacking
      - Misdiagnosis & inadequate/inappropriate medical treatment common
    - NVA and other advocacy organizations are pushing for the US Senate HELP Committee to convene a hearing by the end of 2011

NIH and Congressional Involvement

- Establishment of the NIH Interagency Pain Research Coordinating Committee
  - Work to begin in October 2011
  - Mandate:
    - Coordinate Federal agency activities related to pain
    - Develop a summary of advances in pain care research supported or conducted by Federal agencies
    - Identify critical gaps in basic and clinical research on the symptoms and causes of pain
    - Make recommendations to ensure that:
      - Activities of the NIH and other Federal agencies are free of unnecessary duplication of effort
      - Information on pain care is widely disseminated and available to those in need
      - Potential partnerships between public and private entities to expand collaborative cross-cutting research are identified and utilized

NIH and Congressional Involvement
2012 Senate Appropriations Report Language

Pain – The Committee has for many years encouraged a stronger emphasis on pain research at NIH, and so it notes with great interest the recent Institute of Medicine report… The report…estimates that chronic pain afflicts at least 116 million adults in the United States and costs the Nation between $560 and $635 billion a year, of which $99 billion is borne by the Federal Government and States. The report documents the growing recognition that chronic pain can be a disease in itself, causing changes throughout the nervous system that often worsen over time. Nevertheless, the biological and psychological aspects of pain, as well as its diagnosis, treatment and prevention, remain poorly understood. NIH took a first step toward addressing these questions in a systematic way by creating the NIH Pain Consortium in 2003. Eight years later, it is clear that NIH must do more. Although every Institute and Center deals in some way with pain, none of them "owns" this critical area of research. If that is to be responsibility of the Pain Consortium rather than an individual IC, then the consortium needs more resources, more staffing and a more elevated status within NIH. The IOM report concludes that "there needs to be a transformation in how pain research is conducted and that the Pain Consortium should take an even more proactive role in effecting that transformation." In addition, the report recommends that the consortium should hold "more frequent, regular, structured and productive meetings" and improve the process for reviewing grant proposals related to pain, and that NIH should consider the possibility of identifying a lead IC on pain. The Committee requests a response to the IOM recommendations in the fiscal year 2013 congressional budget justification.

NIH and Congressional Involvement
2012 Senate Appropriations Report Language

Overlapping Chronic Pain Conditions —The Committee recognizes that NIH has taken seriously its repeated calls for an improved and expanded research effort to better understand overlapping chronic pain conditions including chronic fatigue syndrome, endometriosis, fibromyalgia, headache, interstitial cystitis, irritable bowel syndrome, temporomandibular joint and muscle disorders, and vulvodynia. As noted by the IOM report on pain released in June, these poorly understood and neglected conditions impact 50 million American women and cost the Nation $80 billion annually, an amount that could be substantially reduced with improved research, education and care. The Committee is aware that initial progress is being made toward the development and implementation of a trans-NIH research initiative to support studies aimed at identifying etiological pathways of these overlapping conditions, with the goal of identifying potential therapeutic targets, and expects further substantial progress to be made this fiscal year. This will require continued and expanded efforts by all the relevant ICs. The Committee urges NINDS to take the lead on this effort.

NIH and Congressional Involvement
2012 Senate Appropriations Report Language

Vulvodynia – The Committee is encouraged by positive signs that the NICHD is devoting greater attention to this long-neglected condition, especially with regard to stimulating interest in both the intra- and extramural research community and ensuring adequate representation of vulvodynia experts on peer-review panels. The Committee expects to be updated on progress in these areas. The Committee also notes that vulvodynia coexists with other persistent pain conditions, including interstitial cystitis, fibromyalgia, temporomandibular joint and muscle disorders, irritable bowel syndrome, endometriosis, headache and chronic fatigue syndrome. The Committee strongly urges the creation of a trans-NIH research initiative that will support studies aimed at identifying common etiological pathways among these disorders, with the goal of developing potential therapeutic targets.

NVA-Funded Collaborative Research Projects

NATIONAL VULVODYNIA TREATMENT OUTCOMES REGISTRY

VULVODYNIA BASIC SCIENCE RESEARCH NETWORK

$30 Million Question

How much $$ do you need to take vulvodynia research to the next level?

What program(s) would you put in place to do so?

Address Foundational Research Gaps

Quickly Translates Bench to Bedside

“Today, idiopathic. Tomorrow, understood.”

JOEL R. COOPER

Advancing Understanding of Vulvodynia as a Pain Disorder
UNC CNSD Lecture – September 29, 2011
Christin Veasley

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Magnitude of the Problem

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