

Female Sexual Pain Disorders

Female Sexual Pain Disorders Evaluation and Management

Second Edition

Edited by

Andrew T. Goldstein

*George Washington University School of Medicine
Washington, DC, USA*

Caroline F. Pukall

*Queen's University
Kingston, Ontario, Canada*

Irwin Goldstein

*Alvarado Hospital
San Diego, CA, USA*

Associate Editors

Jill M. Krapf

*George Washington University School of Medicine
Washington, DC, USA*

Sue W. Goldstein

*San Diego Sexual Medicine
San Diego, CA, US*

Gail Goldstein

*Annapolis Dermatology Center
Annapolis, MD, USA*

WILEY Blackwell

This edition first published 2021
© 2021 John Wiley & Sons Ltd

Edition History

John Wiley & Sons (1e, 2009)

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by law. Advice on how to obtain permission to reuse material from this title is available at <http://www.wiley.com/go/permissions>.

The right of Andrew T. Goldstein, Caroline F. Pukall, and Irwin Goldstein to be identified as the author(s) of the editorial material in this work has been asserted in accordance with law.

Registered Office(s)

John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA
John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Office

9600 Garsington Road, Oxford, OX4 2DQ, UK

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com. Wiley also publishes its books in a variety of electronic formats and by print-on-demand. Some content that appears in standard print versions of this book may not be available in other formats.

Limit of Liability/Disclaimer of Warranty

The contents of this work are intended to further general scientific research, understanding, and discussion only and are not intended and should not be relied upon as recommending or promoting scientific method, diagnosis, or treatment by physicians for any particular patient. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of medicines, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each medicine, equipment, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. While the publisher and authors have used their best efforts in preparing this work, they make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of merchantability or fitness for a particular purpose. No warranty may be created or extended by sales representatives, written sales materials or promotional statements for this work. The fact that an organization, website, or product is referred to in this work as a citation and/or potential source of further information does not mean that the publisher and authors endorse the information or services the organization, website, or product may provide or recommendations it may make. This work is sold with the understanding that the publisher is not engaged in rendering professional services. The advice and strategies contained herein may not be suitable for your situation. You should consult with a specialist where appropriate. Further, readers should be aware that websites listed in this work may have changed or disappeared between when this work was written and when it is read. Neither the publisher nor authors shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages.

Library of Congress Cataloging-in-Publication Data

Names: Goldstein T., Andrew, M.D., editor. | Pukall, Caroline F., editor. | Goldstein, Irwin, editor.

Title: Female sexual pain disorders : evaluation and management / edited by Andrew T. Goldstein, Caroline F. Pukall, Irwin Goldstein.

Description: Second edition. | Hoboken, NJ : Wiley-Blackwell, 2021. | Includes bibliographical references and index.

Identifiers: LCCN 2020024749 (print) | LCCN 2020024750 (ebook) | ISBN 9781119482666 (hardback) | ISBN 9781119482611 (adobe pdf) | ISBN 9781119482659 (epub)

Subjects: MESH: Sexual Dysfunction, Physiological–diagnosis | Sexual Dysfunction, Physiological–therapy | Sexual Dysfunctions, Psychological–therapy | Genital Diseases, Female | Pain | Pain Management

Classification: LCC RC560.S45 (print) | LCC RC560.S45 (ebook) | NLM WP 610 | DDC 618.1/7–dc23

LC record available at <https://lcn.loc.gov/2020024749>

LC ebook record available at <https://lcn.loc.gov/2020024750>

Cover Design: Wiley

Cover Image: © Chris Tefme/Shutterstock

Set in 9.5/12.5pt STIXTwoText by SPi Global, Pondicherry, India

Contents

List of Contributors ix

- 1 Nosology of Pelvic Pain and Vulvodynia 1**
Tami S. Rowen and Andrew T. Goldstein
- 2 The Prevalence and Relevance of Vulvodynia 9**
Ruby H.N. Nguyen
- 3 Pathophysiology of Pain: Peripheral and Central 15**
Melissa A. Farmer
- 4 The Role of Inflammation in Vulvodynia 31**
David C. Foster
- 5 Neuroproliferative Processes in Vulvodynia 43**
Jacob Bornstein and Eilam Palzur
- 6 Pelvic Floor Muscle Dysfunction and Structural Processes in Vulvodynia 53**
Pamela Morrison and Kaitlyn Parrotte
- 7 Hormonal Causes of Dyspareunia 63**
Andrew T. Goldstein
- 8 Genetic Factors in Vulvodynia 69**
Steven S. Witkin and Iara M. Linhares
- 9 Central Factors in Vulvodynia 75**
Ursula Wesselmann and Peter P. Czakanski
- 10 Comorbidities of Vulvodynia 81**
Nancy A. Phillips and Gloria Bachmann
- 11 Psychosocial Factors in Vulvodynia 87**
Sophie Bergeron and Natalie O. Rosen
- 12 Pain Assessment in Vulvodynia: Self-report Measures 97**
Caroline F. Pukall and Stéphanie C. Boyer

- 13 Pain Assessment in Vulvodynia: Objective Measures 103**
Linda McLean and Caroline F. Pukall
- 14 An Overview of the Evaluation of Dyspareunia, Vulvovaginal Pain, and Pelvic Pain 115**
Andrew T. Goldstein
- 15 Vulvoscopic Evaluation of Vulvodynia 125**
Ashley G. Winter and Rachel S. Rubin
- 16 Pelvic Floor Assessment of Vulvodynia 133**
Stephanie Prendergast and Elizabeth Akincilar
- 17 Psychosocial Assessment of Vulvodynia 143**
Sophie Bergeron and Natalie O. Rosen
- 18 Neurological Assessment in Genito-pelvic Pain 151**
Irwin Goldstein and Barry R. Komisaruk
- 19 Diagnostic and Treatment Algorithm for Women with Vulvodynia and Sexual Pain Disorders 157**
Andrew T. Goldstein
- 20 Medical Treatment of Inflammatory-associated Provoked Vestibulodynia 163**
Susan Kellogg-Spadt
- 21 Treatment of Neuroproliferative-associated Provoked Vestibulodynia with Topical Medications 171**
Candace Brown
- 22 Hormonal Factors in Women's Sexual Pain Disorders 177**
Irwin Goldstein
- 23 Physical Therapy Treatment of Pelvic Floor Dysfunction 185**
Amy Stein, Dee Hartmann, and Kaitlyn Parrotte
- 24 Treatment of Vulvodynia with Pelvic Floor Muscle Relaxants/Injections 193**
Andrea M. Avondstondt and Michael S. Ingber
- 25 Psychosocial Treatments for Vulvodynia 201**
Sophie Bergeron and Natalie O. Rosen
- 26 Complementary and Integrative Health Approaches for the Treatment of Vulvodynia 209**
Judith M. Schlaeger and Meryl J. Alappattu
- 27 Vulvar Vestibulectomy 219**
Andrew T. Goldstein
- 28 Vulvovaginitis 227**
Jack D. Sobel and Paul Nyirjesy

- 29 Vulvar Dermatoses as a Cause of Dyspareunia** 239
Gail R. Goldstein and Andrew T. Goldstein
- 30 Genitourinary Syndrome of Menopause: The Role of Estrogens and Androgens** 251
Rachel S. Rubin and James A. Simon
- 31 Female Genital Cutting** 261
Crista E. Johnson-Agbakwu and Jasmine Abdulcadir
- 32 Interstitial Cystitis/Bladder Pain Syndrome** 273
Esther Han, Laura N. Nguyen, Lauren Tennyson, Larry T. Sirls, and Kenneth M. Peters
- 33 The Basic Science of Endometriosis** 289
Paul Yong
- 34 Endometriosis Treatment** 301
Catherine Z. Wu, Jordan Klebanoff, and Gaby Moawad
- 35 Chronic Pelvic Pain** 313
Juliana Taney and Frank Tu
- 36 Postpartum Genito-pelvic Pain** 323
Jill M. Krapf and Erryn Tappy
- 37 Pudendal Neuralgia** 333
Richard P. Marvel
- 38 Cancer and Genito-pelvic Pain** 349
Beverly Long and Areta Bojko
- 39 Irritable Bowel Syndrome and Female Sexual Dysfunction** 359
Sarah Cigna
- 40 Inability to Experience Penetrative Vaginal Intercourse: Evaluation and Management** 367
Elke D. Reissing
- 41 Chronic Clitoral Pain and Clitorodynia** 375
Stephanie M. Radke and Colleen K. Stockdale
- 42 Generalized Unprovoked Vulvodynia** 381
Ariel Arbel and Ahinoam Lev-Sagie
- 43 Persistent Genital Arousal Disorder** 387
Robyn Jackowich, Caroline F. Pukall, and Irwin Goldstein
- 44 Fibromyalgia and Female Sexual Pain Disorders** 395
Mollie Rieff, Sarah Bedell, and Sarah Cigna

- 45 Animal Models of Genito-pelvic Pain** 403
Megan L. Falsetta, Ronald W. Wood, and David C. Foster
- 46 Patient Advocacy for Vulvodynia** 411
Phyllis Mate and Lisa Goldstein
- 47 Practical Aspects of Establishing a Vulvovaginal Pain Center** 417
Sue W. Goldstein
- 48 Editors' Wish List** 423
Andrew T. Goldstein, Caroline F. Pukall, and Irwin Goldstein
- Index** 429

List of Contributors

Jasmine Abdulcadir, MD, PD, FECSM

Chief, Obstetric and Gynecological Emergency Unit
Chief of Outpatient Clinic for Female Genital Mutilation
Department of Woman, Child and Adolescent
Geneva University Hospitals
Geneva, Switzerland

Elizabeth Akincilar, MSPT

Clinical Director
Pelvic Health and Rehabilitation Centers
Lexington, MA, USA

Meryl J. Alappattu, DPT, PhD

Research Assistant Professor
Department of Physical Therapy
University of Florida
Gainesville, FL, USA

Ariel Arbel, MD

Sackler Faculty of Medicine
Tel Aviv University, Tel Aviv;
Department of Obstetrics and Gynecology
Mayanei Hayeshua Medical Center
Bnei Brak, Israel

Andrea M. Avondstondt, MD

Female Pelvic Medicine and Reconstructive Surgery
Atlantic Health System
Morristown, NJ, USA

Gloria Bachmann, MD

Associate Dean for Women's Health
Department of Obstetrics, Gynecology and
Reproductive Sciences
Women's Health Institute
Rutgers Robert Wood Johnson Medical School
New Brunswick, NJ, USA

Sarah Bedell, MD

The Centers for Vulvovaginal Disorders
Washington, DC, USA

Sophie Bergeron, PhD

Professor
Department of Psychology
Université de Montréal
Montréal, Québec, Canada

Areta Bojko, BS

George Washington University School of Medicine
and Health Sciences
Washington, DC, USA

Jacob Bornstein

Professor and Chairman, Department of Obstetrics
and Gynecology, Galilee Medical Center and Azrieli
Faculty of Medicine, Bar-Ilan University, Nahariya,
Israel;
Chairman of the ISSVD Terminology Committee,
Past President of ISSVD, Past chairman of IFPCPC
Nomenclature Committee

Stéphanie C. Boyer, PhD

Psychologist (Supervised Practice)
Department of Psychology, Psychology Clinic
Queen's University
Kingston, Ontario, Canada

Candace Brown, MSC, PharmD

Professor Emeritus
College of Pharmacy
University of Tennessee Health Science Center
Memphis, TN, USA

Sarah Cigna, MSc, MD

Assistant Professor
Department of Obstetrics and Gynecology
George Washington University School of Medicine
and Health Sciences
Washington, DC, USA

Peter P. Czakanski MD, PhD

Assistant Professor
Departments of Anesthesiology and Perioperative
Medicine (Division of Pain Medicine), and Obstetrics
and Gynecology
University of Alabama at Birmingham
Birmingham, AL, USA

Megan L. Falsetta, PhD

Research Assistant Professor
Department of Obstetrics and Gynecology
University of Rochester
Rochester, NY, USA

Melissa A. Farmer, PhD

Department of Physiology
Feinberg School of Medicine
Northwestern University
Chicago, IL, USA

David C. Foster, MD, MPH

Professor Emeritus
Department of Obstetrics and Gynecology
University of Rochester
Rochester, NY, USA

Andrew T. Goldstein, MD, FACOG, IF

Clinical Professor, Department of Obstetrics and
Gynecology
George Washington University School of Medicine
Washington, DC;
Director, The Centers for Vulvovaginal Disorders
Washington, DC and New York, NY, USA

Gail R. Goldstein, MD, FAAD

Annapolis Dermatology Center
Annapolis, MD, USA

Irwin Goldstein, MD, IF

Director of Sexual Medicine, Alvarado Hospital
Director, San Diego Sexual Medicine;
Clinical Professor of Surgery
University of California
San Diego, CA, USA

Lisa Goldstein

Executive Director
National Vulvodynia Association
Silver Spring, MD, USA

Sue W. Goldstein, CCRC, CSE, IF

AASECT Certified Sexuality Educator
Clinical Research Manager, San Diego Sexual
Medicine
San Diego, CA, USA

Esther Han, DO

Orlando Health Medical Group
Orlando, FL, USA

Dee Hartmann, PT, DPT

Dee Hartmann Physical Therapy
Effingham, IL, USA

Michael S. Ingber, MD

Female Pelvic Medicine and Reconstructive Surgery
Atlantic Health System
Morristown, NJ, USA

Robyn Jackowich, MSc, PhD candidate

Department of Psychology
Queen's University
Kingston, Ontario, Canada

Crista E. Johnson-Agbakwu, MD, MSc, IF

Director, Refugee Women's Health Clinic, Valleywise
Health
Research Associate Professor, School of Social
Work
Director, Office of Refugee Health, Southwest
Interdisciplinary Research Center (SIRC)
College of Public Service and Community Solutions
Arizona State University
Phoenix, AZ, USA

Susan Kellogg-Spadt, PhD, CRNP, IF, CSC

Center for Pelvic Medicine
Bryn Mawr, PA, USA

Jordan Klebanoff, MD

George Washington University School of Medicine
and Health Sciences
Washington, DC, USA

Barry R. Komisaruk, PhD

Distinguished Professor of Psychology
Rutgers University Board of Governors Distinguished
Service Professor
Adjunct Professor, Radiology
Rutgers University
Newark, NJ, USA

Jill M. Krapf, MD, MEd

Clinical Associate Professor
Department of Obstetrics and Gynecology
George Washington University School of Medicine;
Associate Director, The Centers for Vulvovaginal
Disorders
Washington, DC, USA

Ahinoam Lev-Sagie, MD

Faculty of Medicine
Department of Obstetrics and Gynecology
Hadassah Medical Center
Hebrew University of Jerusalem
Jerusalem, Israel

Iara M. Linhares, MD

Department of Gynecology and Obstetrics
São Paulo University Medical School
São Paulo, Brazil

Beverly Long, MD

Assistant Professor
Department of Obstetrics and Gynecology
George Washington University School of Medicine
and Health Sciences
Washington, DC, USA

Linda McLean, PhD

Professor and Chair in Women's Health Research
School of Rehabilitation Sciences
University of Ottawa
Ottawa, Ontario, Canada

Richard P. Marvel, MD

Anne Arundel Medical Center
Center for Pelvic Pain at Annapolis
Annapolis, MD, USA

Phyllis Mate

Co-founder and President of the Board of
Directors
National Vulvodynia Association
Silver Spring, MD, USA

Gaby Moawad, MD, FACOG

Associate Professor
Department of Obstetrics and Gynecology;
Director of GYN Robotic Surgery
AAGL/ASRM Fellowship Co-Director
George Washington University School of Medicine
and Health Sciences
Washington, DC, USA

Pamela Morrison, PT, MS, DPT, BCB-PMD, IMTC, IF

Pamela Morrison Physical Therapy, PC
New York, NY, USA

Laura N. Nguyen, MD

Assistant Professor of Urology
Michael G. DeGroote School of Medicine
McMaster University
Hamilton, Ontario, Canada

Ruby H.N. Nguyen, PhD

Associate Professor
Division of Epidemiology and Community Health
School of Public Health
University of Minnesota
Minneapolis, MN, USA

Paul Nyirjesy, MD

Vulvovaginal Health Center
Thomas Jefferson University Hospitals
Philadelphia, PA, USA

Eilam Palzur, PhD

Research Institute of Galilee Medical Center and
Azrieli Faculty of Medicine, Bar-Ilan University
Nahariya, Israel

Kaitlyn Parrotte, PT, DPT, OCS, CFMT

H&D
Physical Therapy
New York, NY, USA

Kenneth M. Peters, MD

Professor and Chair of Urology
Oakland University William Beaumont School of
Medicine
Chief of Urology, Beaumont Hospital
Royal Oak, MI, USA

Nancy A. Phillips, MD

Associate Professor
Department of Obstetrics, Gynecology and
Reproductive Sciences
Women's Health Institute
Rutgers Robert Wood Johnson Medical School
New Brunswick, NJ, USA

Stephanie Prendergast, MPT

Clinical Director
Pelvic Health and Rehabilitation Centers
Los Angeles, CA, USA

Caroline F. Pukall, PhD, CPsych

Director, Sex and Relationship Therapy Service
Professor, Department of Psychology
Queen's University
Kingston, Ontario, Canada

Stephanie M. Radke, MD

Clinical Assistant Professor
Department of Obstetrics and Gynecology
University of Iowa, Carver College of Medicine
Iowa City, IA, USA

Mollie Rieff, DNP

The Centers for Vulvovaginal Disorders
Washington, DC, USA

Elke D. Reissing, PhD, CPsych

Professor
School of Psychology
University of Ottawa
Ottawa, Ontario, Canada

Natalie O. Rosen, PhD

Associate Professor
Departments of Psychology and Neuroscience,
and Obstetrics and Gynaecology
Dalhousie University
Halifax, Nova Scotia, Canada

Tami S. Rowen, MD, MS

Assistant Professor
Director Sexual Health Program
Department of Obstetrics, Gynecology and
Reproductive Sciences
University of California San Francisco
San Francisco, CA, USA

Rachel S. Rubin, MD, IF

Assistant Clinical Professor
Department of Urology, Georgetown University;
Clinical Instructor, Department of Urology, George
Washington University
IntimMedicine Specialists
Washington, DC, USA

Judith M. Schlaeger, PhD, CNM, LAc, FAAN

Associate Professor
Department of Human Development Nursing
Science
University of Illinois at Chicago
Chicago, IL, USA

James A. Simon, MD, CCD, NCMP, IF, FACOG

Clinical Professor
George Washington University
IntimMedicine Specialists
Washington, DC, USA

Larry T. Sirls, MD

Professor of Urology
Oakland University William Beaumont School of
Medicine;
FPMRS Program Director, Beaumont Hospital
Royal Oak, MI, USA

Jack D. Sobel, MD

Division of Infectious Diseases
Wayne State University
Detroit, MI, USA

Amy Stein, PT, MPT, DPT, BCB-PMD, IF

Multicenter Director
Beyond Basics Physical Therapy, LLC
New York, NY, USA

Colleen K. Stockdale, MD, MS

Clinical Professor
 Department of Obstetrics and Gynecology
 William C. Keettel Chair in Obstetrics and
 Gynecology
 University of Iowa, Carver College of Medicine
 Iowa City, IA, USA

Juliana Taney, MD

Department of Obstetrics and Gynecology
 Pritzker School of Medicine
 University of Chicago
 Chicago, IL, USA

Erryn Tappy, MD

Department of Obstetrics and Gynecology
 George Washington University School of Medicine
 Washington, DC, USA

Lauren Tennyson, MD

Female Pelvic Medicine and Reconstructive Surgery
 Fellow, Department of Urology, Beaumont Hospital
 Royal Oak, MI, USA

Frank Tu, MD, MPH

Department of Obstetrics and Gynecology
 NorthShore University Health System
 Evanston, IL, USA
 Pritzker School of Medicine
 University of Chicago
 Chicago, IL, USA

Ursula Wesselmann, MD, PhD

William A. Lell, MD and Paul N. Samuelson, MD
 Endowed Professorship
 Professor of Anesthesiology, Neurology and Psychology
 Departments of Anesthesiology and Perioperative
 Medicine (Division of Pain Medicine), Neurology and
 Psychology
 University of Alabama at Birmingham
 Birmingham, AL, USA

Ashley G. Winter, MD

Physician
 Department of Urology
 NW Permanente
 Portland, OR, USA

Steven S. Witkin, PhD

Department of Obstetrics and Gynecology
 Weill Cornell Medicine
 New York, NY, USA

Ronald W. Wood, PhD

Research Associate Professor
 Department of Obstetrics and Gynecology
 University of Rochester
 Rochester, NY, USA

Catherine Z. Wu, MD

Assistant Professor
 Department of Obstetrics and Gynecology
 George Washington University School of Medicine
 and Health Sciences
 Washington, DC, USA

Paul Yong, MD, PhD, FRCSC

Assistant Professor, UBC Divisions of Gynaecologic
 Specialties and REI;
 Co-Director, UBC Reproductive and Developmental
 Sciences Graduate Program;
 Research Director, BC Women's Centre for Pelvic Pain
 and Endometriosis;
 Investigator, Women's Health Research Institute
 Health Professional Investigator, Michael Smith
 Foundation for Health Research
 University of British Columbia
 Vancouver, British Columbia, Canada

1

Nosology of Pelvic Pain and Vulvodynia

Tami S. Rowen¹ and Andrew T. Goldstein^{2,3}

¹Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, San Francisco, CA, USA

²Department of Obstetrics and Gynecology, George Washington University School of Medicine, Washington, DC, USA

³The Centers for Vulvovaginal Disorders, New York, NY, USA

1.1 Introduction

Sexual pain is very common and can involve a wide range of disorders that involve the vulva, vagina, cervix, uterus, adnexa, pelvic floor muscles, and the nerves that innervate these structures. The terminology of these disorders has changed over time and this relates to the changing understanding of these conditions. In order to fully understand sexual pain and urogenital pain, a thorough examination of the historical and current terminology is very useful. A thorough history of the terminology, nosology, and associated prevalence has recently been published [1]. Additionally, other substantial reviews have been conducted in terms of terminology and mechanisms of chronic pelvic pain that encompass sexual and genital pain. It is important to consider that pelvic pain mechanisms may involve acute and chronic processes, both peripheral and central, and may also have a significant emotional component. This chapter introduces the definitions of chronic pelvic pain, vulvodynia, and bladder pain syndrome (BPS). We then focus on the history of the nosology of sexual pain syndromes.

1.2 Chronic Pelvic Pain Nosology

Chronic pelvic pain is multifactorial but always involves a persistent perception of pain perceived by the person to originate in the pelvis. Often women associate their pain with their gynecological organs but the pain can originate in any pelvic structure, including the bowel, bladder, blood vessels, nerves, and muscles. The fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) characterized genito-pelvic pain disorder as requiring six months of symptoms, which is also in line with other societies [2]. Chronic pelvic pain can affect everyday activities separate from sexual activity but can also encompass sexual pain disorders as well as organ-specific pain disorders. Chronic pelvic pain is discussed in detail in Chapter 35.

1.3 Bladder Pain Syndrome

BPS has been defined as the occurrence of persistent or recurrent pain in the urinary bladder region, and is accompanied by other symptoms, including pain with

filling/emptying or increased urgency and frequency [2]. This syndrome was previously called interstitial cystitis and this terminology is still frequently used. The distinguishing characteristic of BPS is that the current etiology is not infectious, though these patients may have experienced infections in the past, and the symptoms may have begun with an infection. The diagnosis is made based on the location and quality of pain being related directly to the bladder and usually relieved by emptying. BPS frequently occurs with other chronic pelvic pain syndromes such as overactive pelvic floor muscle dysfunction as well as sexual pain syndromes such as vulvodynia. BPS is examined in depth in Chapter 32.

1.4 Nosology of Sexual Pain

In clinical practice and in research settings, the three most frequently used terms to describe sexual pain in women are vulvodynia, dyspareunia, and vaginismus. The term “vulvodynia” (chronic vulvar pain) is derived from the combination of the words “vulva” (the external genitalia in females) and *Odyne*, the Greek Goddess of Pain. Ancient texts include descriptions of vulvodynia, including the writings of Soranus of Ephesus [3]. It was not until the nineteenth century, however, that the term “dyspareunia” (i.e. pain during intercourse) was first used by Robert Barnes in 1878 in his treatise *A Clinical History of the Medical and Surgical Diseases of Women* [4]. Finally, the term “vaginismus,” which refers to an involuntary contraction of the musculature of the vagina that interferes with intercourse, was coined by J. Marion Sims in 1862 [5]. The first scientific description of vulvodynia was published in the late nineteenth century by Thomas [6]. He characterized this condition as an “excessive sensibility of the nerves supplying the mucous membrane of some portion of the vulva, sometimes confined to the vestibule ... and other times to one labium minus.” In addition, the Scottish gynecologist Alexander Skene, for whom the periurethral glands are named, reported “a super sensitiveness of the vulva. When, however, 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” [7]. There has always been controversy on the source of

the pain in dyspareunia and in the mid twentieth century Dickinson documented that in a majority of women suffering from dyspareunia the source of pain could be localized to the hymen, urethra, and fourchette [8]. Further research examined the role of inflammation in vulvodynia. Because the connection between inflammation and pain was becoming clear, various authors coined the terms “focal vulvitis,” “vestibular adenitis,” “focal vestibulitis vulvae,” and later “vulva vestibulitis syndrome” [3].

In the 1980s Friedrich and Woodruff published a detailed description of the vulvar vestibule, addressing anatomical features that are most associated with pain [3]. Friedrich also published an early account of 28 women with symptoms of vulvodynia, which he called vulvar vestibulitis syndrome (VVS). The diagnosis was defined as pain on touch, localized to the vestibule and with associated vestibular findings. Friedrich went on to become a founding member of the International Society for the Study of Vulvovaginal Disease (ISSVD), which has since become a leading society in terms of research, advocacy, and nosology related to vulvodynia. The ISSVD was formed in 1970 and had their first congress in 1971 [3]. In 1975, the ISSVD described generalized vulvodynia (GVD), also known as “essential” or “dysesthetic” vulvodynia, as “burning vulva syndrome” at its World Congress. Eight years later, the ISSVD adopted the first standard definition of GVD as “chronic vulvar discomfort, characterized by the patient’s complaint of burning and sometimes stinging, irritating, or raw sensations”. As more providers showed an interest in vulvodynia, the focus narrowed onto the different subtypes of this condition, describing vestibular pain as distinct from generalized vulvar pain and pain that is not solely related to sexual activity. There were significant changes toward the end of the twentieth century in the understanding and nomenclature of vulvar and sexual pain. In 1992, a thorough review of vulvodynia incorporated the role of dermatoses, infection, inflammation, and neuralgia [9]. In 1999 the ISSVD replaced vestibulitis with “vestibulodynia,” which was the result of the new understanding that inflammation is not the only cause of vestibular pain [10]. Later, in 2003, the ISSVD expanded on the term of vulvodynia, distinguishing the role of stimulation and location, labeling it “provoked” or “unprovoked” as well as

“localized or generalized.” The term provoked vestibulodynia (PVD) refers to provoked pain that is localized to the vulvar vestibule, whereas GVD refers to unprovoked, diffuse vulvar pain affecting the entire vulvar region [10].

The updated 2003 ISSVD terminology formed the foundation of vulvodynia research for the next decade. Research continued to explore possible causative factors for vulvodynia such as hormonal, inflammatory, neuroproliferative, musculoskeletal, and genetic. Further research focused on treatment options. Lastly, additional studies introduced new modifying descriptors such as primary/secondary and intermittent/persistent.

Because of the substantial advances in the understanding of vulvodynia made since the start of the twenty-first century, in 2015 the ISSVD, the International Society for the Study of Women’s Sexual

Health (ISSWSH), the International Pelvic Pain Society (IPPS), and representatives from the American Congress of Obstetricians and Gynecologists (ACOG) and the National Vulvodynia Association (NVA) convened a consensus congress to revise the vulvar pain and vulvodynia nomenclature [11]. The final terminology was accepted by all three societies during July and August, 2015 (Table 1.1). This new terminology should be used for both vulvovaginal pain and vulvodynia research.

The consensus terminology is divided into two sections. The first section describes “vulvar pain caused by a specific disorder.” This section contains vulvar pain conditions for which a cause can be clearly identified (e.g. pain due to herpes genitalis, lichen sclerosus, genital cutting). The second section describes the new definition of vulvodynia: vulvar pain of at least three months’ duration, without clear identifiable

Table 1.1 The 2015 ISSVD, ISSWSH, IPPS vulvar pain and vulvodynia nomenclature.

<p>A) Vulvar pain caused by a specific disorder</p> <ul style="list-style-type: none"> ● Infectious (eg, recurrent candidiasis, herpes) ● Inflammatory (eg, lichen sclerosus, lichen planus, immunobullous disorders) ● Neoplastic (eg, Paget disease, squamous cell carcinoma) ● Neurologic (eg, postherpetic neuralgia, nerve compression or injury, neuroma) ● Trauma (eg, female genital cutting, obstetrical) ● Iatrogenic (eg, postoperative, chemotherapy, radiation) ● Hormonal deficiencies (eg, genitourinary syndrome of menopause) ● Vulvodynia—vulvar pain of at least 3 months’ duration, without clear identifiable cause, which may have potential associated factors. The following are potential descriptors: <p>B) Localized (eg, vestibulodynia, clitorodynia) or generalized or mixed (localized and generalized)</p> <ul style="list-style-type: none"> ● Provoked (eg, insertional, contact) or spontaneous or mixed (provoked and spontaneous) ● Onset (primary or secondary) ● Temporal pattern (intermittent, persistent, constant, <p>Appendix: potential factors associated with vulvodynia</p> <ul style="list-style-type: none"> ● Comorbidities and other pain syndromes (eg, painful bladder syndrome, fibromyalgia, irritable bowel syndrome, temporomandibular disorder) ● Genetics ● Hormonal factors (eg, pharmacologically induced) ● Inflammation ● Musculoskeletal (eg, pelvic muscle overactivity, myofascial, biomechanical) ● Neurologic mechanisms <ul style="list-style-type: none"> – Central (spine, brain) – Peripheral: neuroproliferation ● Psychosocial factors (eg, mood, interpersonal, coping, role, sexual function) ● Structural defects (eg, perineal descent) 	
--	--

cause, which may have potential associated factors. A special section of part two defines the descriptors of vulvodynia. These descriptors help to describe the location of the pain as well as the temporal pattern of the pain. This section reflects the findings that pain characteristics typically used to define persistent pain conditions may be more useful for classifying vulvodynia subtypes than specifiers based on hypothesized etiology. Examples of this therefore might include “primary provoked vestibulodynia” or “secondary spontaneous intermittent clitorodynia” [12].

However, the most significant difference between the 2015 terminology and the 2003 terminology is the addition of “potential associated factors” [11]. This addition represents a paradigm shift in the approach to vulvodynia, resulting from research that has shown that several factors may be associated with the development and maintenance of the condition, rendering vulvodynia likely the result of a multifactorial process. Given that these associated factors may be leading the direction of future basic science studies and treatment trials, it is important to elaborate on each of them:

1.4.1 Genetic Factors

Several studies suggest that some women have a genetic predisposition to developing this condition via at least three mechanisms, which can sometimes overlap: genetic polymorphisms that increase the risk of candidiasis or other infections; genetic changes that allow prolonged or exaggerated inflammatory responses; and increased susceptibility to hormonal changes associated with oral contraceptive pills [13–16]. These genetic factors are addressed in Chapter 8.

1.4.2 Hormonal Factors

The tissues of the vulva and vagina are both responsive and dependent on sex steroids (hormones) for proper health and function. There are many causes of decreased sex steroids, both natural and iatrogenic, that can lead to dyspareunia. The most common cause of decreased sex steroids in women is menopause (discussed in Chapter 30). Other physiological causes include anovulation secondary to all of the following: lactation, anorexia, hypothalamic amenorrhea, excessive physical activity or physiological stress, and

hyperprolactinemia. Iatrogenic causes of decreased circulating sex steroids include oophorectomy, which leads to immediate menopause, and hysterectomy (without oophorectomy) and commonly prescribed medications, such as combined hormonal contraceptives (CHCs) [17]. CHC use leads to a reduction in serum estradiol and free testosterone by decreasing ovarian production of estrogen and total testosterone based on negative feedback and by inducing the liver to produce increased levels of sex hormone binding globulin (SHBG). SHBG binds free circulating testosterone and estradiol, with a preference for testosterone. In addition, some CHCs contain synthetic progestogens that act as testosterone antagonists at the androgen receptor, most notably drospirenone, which is an analog of spironolactone [18]. It has been shown that CHCs cause histopathological changes in the vestibular mucosa, thereby increasing vulnerability to mechanical strain and decreasing mechanical pain thresholds [19]. Given their effects on sex steroids, it is perhaps not surprising that studies have shown that CHCs are associated with an increased risk of vestibulodynia. Iatrogenic causes of hormonally associated vestibulodynia are discussed in depth in Chapter 7.

1.4.3 Inflammation

Although women with vestibulodynia and healthy women both have inflammatory cells in the vestibular mucosa, the relative abundance and organization of these cells may differ between women with and without vestibulodynia. Research has demonstrated that women with vestibulodynia have higher densities of B lymphocytes and mature mucosal IgA-plasma cells. In addition, both B and T lymphocytes are arranged into germinal centers in women with vestibulodynia, but not in controls [20]. In addition, other authors have found an increase in mast cell density in the mucosa of women with vestibulodynia [21]. Furthermore, many studies have shown increased proinflammatory cytokines, neurokinines, and chemokines in biopsies of women with vulvodynia [22, 23]. In addition, a heightened systemic inflammatory response has been demonstrated by researchers using a topical cutaneous challenge with yeast in vulvodynia cases compared to controls [24]. The role of inflammation in vulvodynia is further outlined in Chapter 4.

1.4.4 Musculoskeletal

The discomfort of vulvodynia can also be associated with pelvic floor muscle overactivity or hypertonicity. Prolonged use of these muscles can result in decreased tissue oxygenation, muscle overactivity, shortening of sarcomeres, and the development of myofascial trigger points [25]. Hypertonicity of the muscles that insert at the posterior vestibule – the pubococcygeus, puborectalis, and superficial transverse perinei – can lead to allodynia (as seen in vestibulodynia) in the posterior vestibule. Hypertonicity of deeper muscles (e.g. ileococcygeus, coccygeus, and obturator internus) can lead to vaginal or deep thrusting dyspareunia [26]. In addition, overactivity of the bulbocavernosus and ischiocavernosus is associated with clitorodynia [27]. As the pelvic floor musculature plays such an important role in pelvic pain and vulvodynia, it is discussed in greater detail in Chapters 6, 16, 23, and 24.

1.4.5 Neurological Mechanisms

1.4.5.1 Central

Several controlled studies have demonstrated that women with vulvodynia have evidence of central sensitization. Pukall et al. were the first to examine women with vulvodynia using functional magnetic resonance imaging [28]. The results of this study indicated that women with vestibulodynia exhibited evidence of augmented neural activity in response to painful vestibular stimulation in areas involved in pain modulation, such as the somatosensory, insular, and anterior cingulate regions, areas that are commonly activated in patients with other pain conditions. In addition, non-painful pressure led to significant activation levels in insular, frontal, and somatosensory regions in women with vestibulodynia. These results suggest that women with vulvodynia have an increased perception of non-painful and painful stimulation to the vestibule. A detailed exploration of pain processes can be found in Chapters 3 and 9.

1.4.5.2 Peripheral: Neuroproliferation

Researchers have found that women with PVD may have up to 10 times increased density of C-afferent nociceptor nerve endings in their vestibular mucosa

compared with normal women [29, 30]. In addition, Bornstein et al. found increased numbers of mast cells in vestibular tissue of women with vulvodynia. Persistently activated mast cells release nerve growth factor and heparanase that allow newly sprouted nerve endings to invade the superficial mucosa of the vestibule [31]. The role of neuroproliferation in vulvodynia is examined in Chapter 5.

1.4.6 Psychosocial Factors

Population-based studies have shown that anxiety, depression, childhood victimization, and post-traumatic stress are risk factors for the development of vulvodynia [32]. Women with vulvodynia were four times more likely to have a history of a prior mood or anxiety disorder as compared to women without vulvodynia. Psychological factors associated with greater pain intensity or sexual dysfunction in women with vulvodynia include pain catastrophizing, fear of pain, hypervigilance to pain, lower pain self-efficacy, negative attributions about the pain, avoidance, anxiety, and depression [33]. These issues are thoroughly explored in Chapters 11, 17, and 25.

1.4.7 Embryological/Congenital Factors

The co-occurrence of vulvodynia with interstitial cystitis/BPS may be related to a congenital disorder of urogenital sinus-derived endothelium [34]. Additional evidence to support this hypothesis is that women with primary vestibulodynia exhibit umbilical hypersensitivity more often than women with secondary vestibulodynia and non-affected women, suggesting that some cases of primary vestibulodynia may be associated with a congenital neuronal hyperplasia in tissue derived from the primitive urogenital sinus [35].

1.4.8 Associated Factors: Conclusion

It is likely that one or more of these associated factors may be clinically prominent, and may help in choosing further evaluation methods and treatments. In addition, these associated factors may be the basis for future treatment trials.

1.5 Other Definitions of Vulvar Pain

It is important to note that other professional societies have also tried to address terminology related to dyspareunia. For example, the International Association for the Study of Pain includes a section on “Pain of Vaginismus or Dyspareunia” [1]. These classifications were updated in 2011 to include generalized and provoked vulvar pain syndrome, reflecting the growing understanding that vulvar pain presents in a variety of ways. Vulvodynia is included in the International Classification of Disease (ICD-10), and includes modifiers of “other” and “unspecified.”

The American Psychological Association’s fourth edition of the *Diagnostic and Statistical Manual* (DSM-IV) has two separate “Sexual Pain Disorders” included in their section on sexual dysfunctions, which they labeled “dyspareunia” and “vaginismus” [36, 37]. The most recent edition (DSM-5) combined these two into a single category of Genito-pelvic Pain/Penetration Disorder (GPPPD) [36, 37]. This change occurred for several reasons. First, the defining feature required for diagnosis of vaginismus in previous generations of the DSM was the presence of vaginal muscle spasm. Research, however, has failed to prove the presence of muscle spasm as a valid or reliable diagnostic criterion. Second, diagnosis based solely on

vaginal spasm does not address the elements of fear of penetration, anxiety, and pain, which are integral components of this condition. Lastly, several studies have shown that clinicians have a very difficult time distinguishing between dyspareunia, vestibulodynia, and vaginismus, and thus the similarities outweigh the differences.

1.6 Conclusion

The history of modern medicine’s understanding of vulvodynia reflects the slow progress that is being made in addressing women’s sexual health concerns. We now understand that there are many etiologies of sexual pain, and pain confined to the vulva encompasses multiple systems, including neurological, musculoskeletal, hormonal, dermatological, and inflammatory. The importance of a thorough and accurate nosology allows providers and patients to understand both the causes and manifestations of vulvar pain in addition to directing them toward treatment options. Vulvodynia is highly prevalent during a woman’s lifetime and as we train more providers to recognize its multifaceted nature, the more we are able to offer solutions to this common and distressing condition.

References

- 1 Rowen, T.S. and Goldstein, A.T. (2018). Nosology and epidemiology of dyspareunia and vulvodynia. In: *Textbook of Female Sexual Function and Dysfunction* (eds. I. Goldstein, A. Clayton, A.T. Goldstein, et al.), 247–256. Oxford: Wiley-Blackwell.
- 2 Fall, M., Baranowski, A.P., Elneil, S. et al. (2010). EAU guidelines on chronic pelvic pain. *Eur. Urol.* 57 (1): 35–48.
- 3 Amalraj, P., Kelly, S., and Bachmann, G. (2009). Historical perspective of vulvodynia. In: *Female Sexual Pain Disorders* (eds. A.T. Goldstein, C.F. Pukall and I. Goldstein), 1–3. Oxford: Wiley-Blackwell.
- 4 Barnes, R. (1874). *Clinical History of the Medical and Surgical Diseases in Women*. London: J. and A. Churchill.
- 5 Sims, J.M. (1862). On vaginismus. *Trans. Obstet. Soc. Lond.* 3: 356–367.
- 6 Thomas, T. and Mundale, P. (1891). *A Practical Treatise on the Diseases of Women, Volume 6*. Philadelphia, PA: Lea Brothers and Company.
- 7 Skene, A. (1892). *A Treatise on the Diseases of Women*, 2e. D. Appleton and Company: New York, NY.
- 8 Dickinson, R. (1949). *Human Sex Anatomy*, 2e. Baltimore, MD: Williams and Wilkins.
- 9 McKay, M. (1992). Vulvodynia: diagnostic patterns. *Dermatol. Clin.* 10 (2): 423–433.
- 10 Moyal-Barracco, M. and Lynch, P.J. (2004). 2003 ISSVD terminology and classification of vulvodynia:

- a historical perspective. *J. Reprod. Med.* 49 (10): 772–777.
- 11 Bornstein, J., Goldstein, A.T., Stockdale, C.K. et al. (2016). 2015 ISSVD, ISSWSH, and IPPS consensus terminology and classification of persistent vulvar pain and vulvodynia. *J. Sex. Med.* 13 (4): 607–612.
 - 12 Bornstein J, Preti M, Simon JA, et al. Descriptors of Vulvodynia: A Multisocietal Definition Consensus (International Society for the Study of Vulvovaginal Disease, the International Society for the Study of Women Sexual Health, and the International Pelvic Pain Society). *J Low Genit Tract Dis.* 2019;23(2): 161–163. doi:10.1097/LGT.0000000000000461
 - 13 Babula, O., Danielsson, I., Sjöberg, I. et al. (2004). Altered distribution of mannose-binding lectin alleles at exon I codon 54 in women with vulvar vestibulitis syndrome. *Am. J. Obstet. Gynecol.* 191 (3): 762–766.
 - 14 Foster, D.C., Sazenski, T.M., and Stodgell, C.J. (2004). Impact of genetic variation in interleukin-1 receptor antagonist and melanocortin-1 receptor genes on vulvar vestibulitis syndrome. *J. Reprod. Med.* 49 (7): 503–509.
 - 15 Goldstein, A.T., Belkin, Z.R., Krapf, J.M. et al. (2014). Polymorphisms of the androgen receptor gene and hormonal contraceptive induced provoked vestibulodynia. *J. Sex. Med.* 11 (11): 2764–2771.
 - 16 Lev-Sagie, A., Prus, D., Linhares, I.M. et al. (2009). Polymorphism in a gene coding for the inflammasome component NALP3 and recurrent vulvovaginal candidiasis in women with vulvar vestibulitis syndrome. *Am. J. Obstet. Gynecol.* 200 (3): 303.e1–303.e6.
 - 17 Burrows, L.J. and Goldstein, A.T. (2013). The treatment of vestibulodynia with topical estradiol and testosterone. *Sex. Med.* 1 (1): 30–33.
 - 18 Battaglia, C., Battaglia, B., Mancini, F. et al. (2012). Sexual behavior and oral contraception: a pilot study. *J. Sex. Med.* 9 (2): 550–557.
 - 19 Burrows, L.J., Basha, M., and Goldstein, A.T. (2012). The effects of hormonal contraceptives on female sexuality: a review. *J. Sex. Med.* 9 (9): 2213–2223.
 - 20 Tommola, P., Bützow, R., Unkila-Kallio, L. et al. (2015). Activation of vestibule-associated lymphoid tissue in localized provoked vulvodynia. *Am. J. Obstet. Gynecol.* 212 (4): 476.e1–476.e8.
 - 21 Bornstein, J., Goldschmid, N., and Sabo, E. (2004). Hyperinnervation and mast cell activation may be used as histopathologic diagnostic criteria for vulvar vestibulitis. *Gynecol. Obstet. Invest.* 58 (3): 171–178.
 - 22 Bohm-Starke, N., Hilliges, M., Falconer, C., and Rylander, E. (1999). Neurochemical characterization of the vestibular nerves in women with vulvar vestibulitis syndrome. *Gynecol. Obstet. Invest.* 48 (4): 270–275.
 - 23 Foster, D.C. and Hasday, J.D. (1997). Elevated tissue levels of interleukin-1 beta and tumor necrosis factor-alpha in vulvar vestibulitis. *Obstet. Gynecol.* 89 (2): 291–296.
 - 24 Ramirez De Knott, H.M., McCormick, T.S., Do, S.O. et al. (2005). Cutaneous hypersensitivity to *Candida albicans* in idiopathic vulvodynia. *Contact Dermatitis* 53 (4): 214–218.
 - 25 Morin, M., Bergeron, S., Khalifé, S. et al. (2014). Morphometry of the pelvic floor muscles in women with and without provoked vestibulodynia using 4D ultrasound. *J. Sex. Med.* 11 (3): 776–785.
 - 26 King, M., Rubin, R., and Goldstein, A. (2014). Current uses of surgery for the treatment of genital pain. *Curr. Sex. Health Rep.* 6 (4): 252–258.
 - 27 Shafik, A. (2000). The role of the levator ani muscle in evacuation, sexual performance and pelvic floor disorders. *Int. Urogynecol. J. Pelvic Floor Dysfunct.* 11 (6): 361–376.
 - 28 Pukall, C.F., Strigo, I.A., Binik, Y.M. et al. (2005). Neural correlates of painful genital touch in women with vulvar vestibulitis syndrome. *Pain* 115 (1–2): 118–127.
 - 29 Bohm-Starke, N., Hilliges, M., Falconer, C., and Rylander, E. (1998). Increased intraepithelial innervation in women with vulvar vestibulitis syndrome. *Gynecol. Obstet. Invest.* 46 (4): 256–260.
 - 30 Westrom, L.V. and Willen, R. (1998). Vestibular nerve fiber proliferation in vulvar vestibulitis syndrome. *Obstet. Gynecol.* 91 (4): 572–576.
 - 31 Bornstein, J., Cohen, Y., Zarfati, D. et al. (2008). Involvement of heparanase in the pathogenesis of localized vulvodynia. *Int. J. Gynecol. Pathol.* 27 (1): 136–141.

- 32** Pukall, C.F., Goldstein, A.T., Bergeron, S. et al. (2016). Vulvodynia: definition, prevalence, impact, and pathophysiological factors. *J. Sex. Med.* 13 (3): 291–304.
- 33** Khandker, M., Brady, S.S., Vitonis, A.F. et al. (2011). The influence of depression and anxiety on risk of adult onset vulvodynia. *J Womens Health (Larchmt)* 20 (10): 1445–1451.
- 34** Fariello, J.Y. and Moldwin, R.M. (2015). Similarities between interstitial cystitis/bladder pain syndrome and vulvodynia: implications for patient management. *Transl. Androl. Urol.* 4 (6): 643–652.
- 35** Burrows, L.J., Klingman, D., Pukall, C.F., and Goldstein, A.T. (2008). Umbilical hypersensitivity in women with primary vestibulodynia. *J. Reprod. Med.* 53 (6): 413–416.
- 36** Binik, Y.M. (2010). The DSM diagnostic criteria for vaginismus. *Arch. Sex. Behav.* 39 (2): 278–291.
- 37** Binik, Y.M. (2010). The DSM diagnostic criteria for dyspareunia. *Arch. Sex. Behav.* 39 (2): 292–303.

2

The Prevalence and Relevance of Vulvodynia

Ruby H.N. Nguyen

Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, MN, USA

2.1 Introduction

Assessing the impact of chronic vulvar pain is challenging and is marred by methodological challenges including lack of consistent definitions [1], differing assessment techniques [1], inter-person variability of pain reports, the difficulty for women to disclose their genital pain [2], and differences in cultural norms related to the reporting and description of vulvar pain [3], particularly with sex. However, regardless of such study limitations, most studies have found that vulvodynia, generally defined by chronic vulvar pain of any type, is not rare in the general population [4–7] and affects diverse communities [3, 5, 8]. This chapter focuses on the burden of vulvodynia by discussing both its quantitative burden, as described by prevalence rates, as well as the personal and social burden of living with chronic vulvar pain, which is often compounded by gender-specific roles and norms such as with pregnancy [9].

2.2 Prevalence

Prevalence estimates derived from population samples are important in understanding the burden of vulvodynia, particularly because it has been estimated that approximately 40–49% of women with chronic vulvar pain do not seek medical care for their pain [5, 10, 11], therefore leaving clinic-based estimates

unreliable and likely dramatically underestimating the true prevalence. Large population-based studies of vulvodynia have found that in the general population roughly 7–10% of women have experienced some type of chronic vulvar pain in their lifetimes [4–6, 12], whereas other studies have found somewhat wide-ranging prevalence estimates of up to 16% [11, 13]. Ethnicity has been found to affect population-based estimates of the prevalence of vulvodynia. Examining different groups throughout the United States, Hispanic women have consistently been found to be 40–80% more likely to have vulvodynia than their white counterparts [4, 11]. This same group has been found to have increased risk of developing vulvodynia [14]. Other race groups are as likely, or less likely, to report symptoms of vulvodynia.

There are several research-related factors that may influence the variation in population-based prevalence estimates and thus present major challenges to enumerating the burden of vulvodynia. Definitions for vulvodynia have evolved over the course of its study, and at times still differ according to whom is defining it. Addressing the need for a unified definition, particularly with differences in clinical presentation and pathophysiology, a consensus panel recently proposed terminology and schema for the classification of vulvodynia [1]. It is not known how incorporation of these clarifications in definition into research practice may impact future prevalence estimates of vulvodynia. Aside from the definitions themselves, other

methodological issues, such as the need to exclusively use surveys for the determination of prevalence in population-based studies as compared to studies that used clinical examinations, are also a point of variation. However, this issue may not be as important as previously believed: in a study by Harlow et al. in which women who reported symptoms consistent with vulvodynia received a clinical examination to confirm the assessment, 77% were confirmed to have vulvodynia [15]. In addition, Reed et al. found that pain histories reported on a survey had high agreement with histories taken from a medical professional during a clinic visit, and that nearly all (96%) of women who were clinically examined after reporting a positive history of vulvodynia were confirmed to have it [12].

There are also non-survey tools for assessing the prevalence of vulvar pain, including a vulvar algometer [16] to semi-quantitatively measure pain sensitivity, that have been used to assess prevalence. Although these methods standardize the amount of pressure administered across patients, they do not correct for inherent differences in perception of pain between women. Another such test is the tampon test developed by Foster et al. [17], which is a measure of intra-person change in pain and reflects self-administered provoked and pragmatic daily pain experiences for women [18, 19].

It has been reported that a group of women with vulvodynia are commonly affected by other chronic pain conditions, such as fibromyalgia, irritable bowel syndrome, temporomandibular disorder, or interstitial cystitis [2]. Collectively, these conditions have been termed “comorbid chronic pain conditions” or “chronic overlapping pain conditions” and among women who have such diagnoses, the prevalence rates of vulvodynia are higher than among women who lack any history of chronic pain elsewhere in their bodies. It has been estimated that nearly half of women with vulvodynia have at least one comorbid condition [2]. There is evidence also that these comorbid conditions, as well as the number of comorbid conditions, are associated with a more severe clinical presentation of vulvodynia [20]. In addition, it has been found that women with vulvodynia and another comorbid pain condition are more likely to have a more severe natural history in which they are less likely to achieve remission from

their vulvar pain, and if they do achieve remission are more likely to have their vulvar pain return [21]. The natural history and severity of vulvodynia also have great impact on the lives of the women; as an example, women who have intermittent vulvar pain are more likely to achieve pregnancy than their counterparts who report constant pain [22]. Taken together, prevalence estimates confirm that vulvodynia is not rare, and these studies have assisted in delineating the risk factors that may increase women’s risk of developing vulvodynia in the population.

2.3 Comorbid Conditions

Vulvodynia can be considered a chronic pain condition that can be explained by the biopsychosocial model of pain, one in which the chronicity of pain is influenced by the interrelatedness of biological, psychological, and social factors [23–25]. Some of these factors, such as anxiety or catastrophizing, may have developed antecedent to the vulvodynia and therefore could be associated with its development, while others like depression may occur as a result of the condition itself. In addition, the presence of chronic overlapping pain conditions is associated with impaired mental health, such as heightened feelings of isolation and invalidation by others of their pain status, and therefore likely to be associated with women’s psychosocial well-being [26].

2.4 Relevance to the Individual Woman, Family, and Society

Vulvodynia can be associated with reduced quality of life [27]. The burden of vulvodynia for each individual has been measured in many ways, including by how the pain interferes with daily activities, using what is termed “pain interference.” A general measure of pain interference is the Brief Pain Inventory (BPI) scale that measures how pain may affect activity, mood, work, relationships, sleep, and enjoyment – which, in women with vulvodynia, has been associated with vulvar pain levels [28]. High scores on the BPI are expected with any chronic pain condition; however, vulvodynia

presents unique challenges to daily pain interference reports, particularly with social relationships.

With the chronicity of vulvar pain, and growing feelings of isolation and invalidation, reports of increased distress have been reported not only for the affected women themselves but also their sexual partners, thus perpetuating a cycle of distress [29–31]. In fact, women may have higher coital pain and anxiety at times when they perceive that their partner is responding negatively to their vulvar condition [32, 33]. Although it is not currently clear what mechanism is involved in how partner responses directly impact women's coital pain level, there is evidence suggesting that negative partner responses increase pain catastrophizing in the woman and that the couple's responses to vulvar pain may mitigate increased pain during coitus [31].

Women often report that they find it difficult to speak to others about their vulvar pain. This reluctance can even extend to the closest relationships that would otherwise provide the greatest support to them; in one report, 39% of women were comfortable with family and 26% with women friends only [2]. In addition, there is evidence that higher pain levels are associated with speaking about their vulvar pain to friends, indicating that sometimes women may wait to speak of their pain to these loved ones once they simply can no longer hide it [2].

Gender-related norms may also play a role in acceptance of vulvodynia, particularly pertaining to painful sex. In a qualitative study of pregnant women with vulvodynia, a consistent theme of accepting painful sex for the purpose of pregnancy emerged [9].

2.5 Multidisciplinary Treatment

Given the complex biopsychosocial nature of the development and sequelae of vulvodynia, multidisciplinary approaches that include medical, physiological, and psychological approaches to treating the condition have been sought, with some being efficacious for certain outcomes including improved sexual functioning [34, 35]. However, it is currently recognized that more evidence is needed to make recommendations using multidisciplinary approaches [35].

2.6 Recommendations

Clinicians and other researchers should play an important role in the improved understanding of the common occurrence (prevalence) of vulvodynia with other comorbid conditions, including chronic overlapping pain conditions. Better understanding of the co-occurrence of these conditions will assist in identification of high-risk groups for incident and prevalent vulvodynia, elucidation of the potentially separate natural histories for vulvodynia that may differ according to the presence or absent of comorbid conditions, and may call upon the need for multidisciplinary care in treating affected women.

In addition, social interactions altered by chronic pain – and those social relationships that are uniquely influenced by vulvodynia, such as romantic and sexual relationships – should be strengthened. Therefore, it is imperative that we develop an improved understanding of the mechanisms by which social determinants may perpetuate vulvar pain or worsen its severity. From this knowledge, social interventions to mitigate these factors should be sought. Social relations would include partner-focused approaches but also extend to other members of social networks that could ultimately provide support for the woman.

2.7 Conclusion

Vulvodynia carries a high burden in society, due to both its common prevalence and the effect of its sequelae on women, their partners, family, and communities. This condition often occurs in the presence of other comorbid conditions, including other chronic pain conditions, and when this clustering of conditions occurs, an increased prevalence of vulvodynia is expected and can predict the severity of vulvodynia and its prognosis. Future careful description of the prevalence of vulvodynia should incorporate the increased rates in high-risk groups, such as among women with related comorbid conditions. Multidisciplinary approaches to treatment of vulvodynia itself, along with any other comorbid conditions, has been shown to be more effective than unimodal interventions. Women with vulvar pain are reluctant to discuss their pain, and have feelings of isolation. With regard

to social relationships, interventions that include or target sexual partners of affected women have shown promise in promoting healthier, more supportive relationships. Therefore, the development of further interventions to improve social relationships – that extend

beyond sex or romantic partners – should be developed in order to provide further social support for women with vulvodynia. Collectively, the burden of vulvodynia should be recognized as something extending beyond its prevalence alone.

References

- 1 Bornstein, J., Goldstein, A.T., Stockdale, C.K. et al. (2016). 2015 ISSVD, ISSWSH, and IPPS consensus terminology and classification of persistent vulvar pain and vulvodynia. *J. Sex. Med.* 13 (4): 607–612.
- 2 Nguyen, R.H., MacLehose, R.F., Veasley, C. et al. (2012). Comfort in discussing vulvar pain in social relationships among women with vulvodynia. *J. Reprod. Med.* 57 (3–4): 109–114.
- 3 Brown, C.S., Foster, D.C., Bachour, C.C. et al. (2015). Presenting symptoms among black and white women with provoked vulvodynia. *J. Womens Health (Larchmt)* 24 (10): 831–836.
- 4 Harlow, B.L., Kunitz, C.G., Nguyen, R.H. et al. (2014). Prevalence of symptoms consistent with a diagnosis of vulvodynia: population-based estimates from 2 geographic regions. *Am. J. Obstet. Gynecol.* 210 (1): 40.e1–40.e8.
- 5 Reed, B.D., Harlow, S.D., Sen, A. et al. (2012). Prevalence and demographic characteristics of vulvodynia in a population-based sample. *Am. J. Obstet. Gynecol.* 206 (2): 170.e1–170.e9.
- 6 Arnold, L.D., Bachmann, G.A., Rosen, R., and Rhoads, G.G. (2007). Assessment of vulvodynia symptoms in a sample of US women: a prevalence survey with a nested case control study. *Am. J. Obstet. Gynecol.* 196 (2): 128.e1–128.e6.
- 7 Reed, B.D. (2006). Vulvodynia: diagnosis and management. *Am. Fam. Physician* 73 (7): 1231–1238.
- 8 Nguyen, R.H., Reese, R.L., and Harlow, B.L. (2015). Differences in pain subtypes between Hispanic and non-Hispanic white women with chronic vulvar pain. *J. Womens Health (Larchmt)* 24 (2): 144–150.
- 9 Johnson, N.S., Harwood, E.M., and Nguyen, R.H. (2015). “You have to go through it and have your children”: reproductive experiences among women with vulvodynia. *BMC Pregnancy Childbirth* 15: 114.
- 10 Nguyen, R.H., Turner, R.M., Rydell, S.A. et al. (2013). Perceived stereotyping and seeking care for chronic vulvar pain. *Pain Med.* 14 (10): 1461–1467.
- 11 Harlow, B.L. and Stewart, E.G. (2003). A population-based assessment of chronic unexplained vulvar pain: have we underestimated the prevalence of vulvodynia? *J. Am. Med. Womens Assoc. (1972)* 58 (2): 82–88.
- 12 Reed, B.D., Haefner, H.K., Harlow, S.D. et al. (2006). Reliability and validity of self-reported symptoms for predicting vulvodynia. *Obstet. Gynecol.* 108 (4): 906–913.
- 13 Vieira-Baptista, P., Lima-Silva, J., Cavaco-Gomes, J., and Beires, J. (2014). Prevalence of vulvodynia and risk factors for the condition in Portugal. *Int. J. Gynaecol. Obstet.* 127 (3): 283–287.
- 14 Reed, B.D., Legocki, L.J., Plegue, M.A. et al. (2014). Factors associated with vulvodynia incidence. *Obstet. Gynecol.* 123 (2 Pt 1): 225–231.
- 15 Harlow, B.L., Vazquez, G., MacLehose, R.F. et al. (2009). Self-reported vulvar pain characteristics and their association with clinically confirmed vestibulodynia. *J. Womens Health (Larchmt)* 18 (9): 1333–1340.
- 16 Pukall, C.F., Binik, Y.M., and Khalife, S. (2004). A new instrument for pain assessment in vulvar vestibulitis syndrome. *J. Sex Marital Ther.* 30 (2): 69–78.
- 17 Foster, D.C., Kotok, M.B., Huang, L.S. et al. (2009). The tampon test for vulvodynia treatment outcomes research: reliability, construct validity, and responsiveness. *Obstet. Gynecol.* 113 (4): 825–832.
- 18 Brown, C.S., Bachmann, G.A., Wan, J., and Foster, D.C. (2018). Gabapentin for the treatment of vulvodynia: a randomized controlled trial. *Obstet. Gynecol.* 131 (6): 1000–1007.

- 19 Foster, D.C., Kotok, M.B., Huang, L.S. et al. (2010). Oral desipramine and topical lidocaine for vulvodynia: a randomized controlled trial. *Obstet. Gynecol.* 116 (3): 583–593.
- 20 Nguyen, R.H., Veasley, C., and Smolenski, D. (2013). Latent class analysis of comorbidity patterns among women with generalized and localized vulvodynia: preliminary findings. *J. Pain Res.* 6: 303–309.
- 21 Reed, B.D., Harlow, S.D., Plegue, M.A., and Sen, A. (2016). Remission, relapse, and persistence of vulvodynia: a longitudinal population-based study. *J. Womens Health (Larchmt)* 25 (3): 276–283.
- 22 Nguyen, R.H., Stewart, E.G., and Harlow, B.L. (2012). A population-based study of pregnancy and delivery characteristics among women with vulvodynia. *Pain Ther.* 1 (1): 2.
- 23 Paquet, M., Rosen, N.O., Steben, M. et al. (2018). Daily anxiety and depressive symptoms in couples coping with vulvodynia: associations with women's pain, women's sexual function, and both partners' sexual distress. *J. Pain* 19 (5): 552–561.
- 24 Khandker, M., Brady, S.S., Stewart, E.G., and Harlow, B.L. (2014). Is chronic stress during childhood associated with adult-onset vulvodynia? *J. Womens Health (Larchmt)* 23 (8): 649–656.
- 25 Dargie, E., Gilron, I., and Pukall, C.F. (2017). Provoked vestibulodynia: a comparative examination of mental health, sleep, sexual functioning, and relationship adjustment. *Clin. J. Pain* 33 (10): 870–876.
- 26 Nguyen, R.H., Ecklund, A.M., Maclehose, R.F. et al. (2012). Co-morbid pain conditions and feelings of invalidation and isolation among women with vulvodynia. *Psychol. Health Med.* 17 (5): 589–598.
- 27 Xie, Y., Shi, L., Xiong, X. et al. (2012). Economic burden and quality of life of vulvodynia in the United States. *Curr. Med. Res. Opin.* 28 (4): 601–608.
- 28 Brown, C., Bachmann, G.A., Wan, J., and Foster, D. (2016). Pain rating in women with provoked vestibulodynia: evaluating influence of race. *J. Womens Health (Larchmt)* 25 (1): 57–62.
- 29 Bois, K., Bergeron, S., Rosen, N. et al. (2016). Intimacy, sexual satisfaction, and sexual distress in vulvodynia couples: an observational study. *Health Psychol.* 35 (6): 531–540.
- 30 Rosen, N.O., Bergeron, S., Sadikaj, G., and Delisle, I. (2015). Daily associations among male partner responses, pain during intercourse, and anxiety in women with vulvodynia and their partners. *J. Pain* 16 (12): 1312–1320.
- 31 Rosen, N.O., Bergeron, S., Lambert, B., and Steben, M. (2013). Provoked vestibulodynia: mediators of the associations between partner responses, pain, and sexual satisfaction. *Arch. Sex. Behav.* 42 (1): 129–141.
- 32 Rosen, N.O., Bergeron, S., Leclerc, B. et al. (2010). Woman and partner-perceived partner responses predict pain and sexual satisfaction in provoked vestibulodynia (PVD) couples. *J. Sex. Med.* 7 (11): 3715–3724.
- 33 Rosen, N.O., Muise, A., Bergeron, S. et al. (2015). Approach and avoidance sexual goals in couples with provoked vestibulodynia: associations with sexual, relational, and psychological well-being. *J. Sex. Med.* 12 (8): 1781–1790.
- 34 Yong, P.J., Sadownik, L., and Brotto, L.A. (2015). Concurrent deep-superficial dyspareunia: prevalence, associations, and outcomes in a multidisciplinary vulvodynia program. *J. Sex. Med.* 12 (1): 219–227.
- 35 Goldstein, A.T., Pukall, C.F., Brown, C. et al. (2016). Vulvodynia: assessment and treatment. *J. Sex. Med.* 13 (4): 572–590.