UCSF
UC San Francisco Electronic Theses and Dissertations

**Title**
A Disease Itself: The Transformation of Pain After 1945

**Permalink**
https://escholarship.org/uc/item/8x54c8r1

**Author**
Beitler, Stephen David

**Publication Date**
2016

Peer reviewed|Thesis/dissertation

eScholarship.org Powered by the California Digital Library
University of California

# A Disease Itself: The Transformation of Pain After 1945

by

Stephen Beitler

DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

in

History of Health Sciences

in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

I'm very grateful for the generous help and encouragement that my committee members provided throughout the process. I also appreciate the support that my fellow students and numerous UCSF faculty members gave to an improbable student. *A Disease Itself* is dedicated to my wife Noel. Her unwavering belief in the project, and in me, made the dissertation both possible and eminently worth doing.

# A Disease Itself: The Transformation of Pain After 1945

## By Stephen Beitler

A Disease Itself examines a fundamental shift in the understanding and clinical status of pain in the United States after 1945. Pain was transformed from a simple, rote, well understood, and largely treatable event into a clinical syndrome defined by variability, chronicity, and complexity. Pain became subjective, rooted in individual experience, beliefs, and circumstances as much as in organic illness and injury. An insurgent model of pain refashioned the primary clinical challenge as chronic pain, asserted dense interconnections among pain's psychological and physical dimensions, and advocated multidisciplinary treatment. Together, these changes refashioned how people experienced pain, how clinicians treated it, legislative actions, and the fortunes of dozens of pharmaceutical companies. They reflected as well substantial cultural shifts in ideas and practices of identity, selfhood, authority, and autonomy.

A Disease Itself explores the history of how pain has been measured, managed, and organized professionally in order to track the origins and contours of this fundamental change. The dissertation begins with a historical review of the development of scientific, medical, and cultural understandings of pain from 1800 to 1945. It then examines the measurement, management, and professionalization of pain through three in-depth case studies. The first case study examines how a new model of pain was operationalized clinically in an assessment instrument, the McGill Pain Questionnaire (MPQ), published in 1975. The second explores how wider debates over risk and reward in treatment were reflected in enduring clinical ambiguities surrounding a highly successful pain reliever, Darvon, between its debut in 1957 and its removal from the market by the Food and Drug Administration (FDA) beginning in 2010. The third case study depicts how a new pain paradigm was central to the launch of International Association for the Study of Pain (IASP) after 1973. A Disease Itself draws on an extensive array of research studies on the MPQ, government and industry documents on Darvon, and the published works of early leaders of the IASP in its portrayal of a fundamental shift in the understanding and clinical status of pain.

# Table of Contents


| | |
|---|---|
| Introduction | 1 |
| Pre-histories of Pain's Transformation | 20 |
| Understanding Pain Through Measurement | 42 |
| Darvon – A Lucrative Ambiguity | 92 |
| Reformulating Pain: Model and Practice in Formative Tension | 140 |
| Conclusion | 170 |
| Bibliography | 184 |

# Introduction

At a September 2013 workshop on back pain, anesthesiologist and pain researcher Sean Mackey raised a historical question that is at the heart of *A Disease Itself: The Transformation of Pain After 1945*. In describing new findings on electrochemical and genetic processes in pain, Mackey noted that a Cartesian model, which had dominated medical thinking about pain for 300 years, had, over the last 50 years, been proven substantially wrong. Pain had turned out to be far less rote and mechanistic than Descartes portrayed it. But if time and science had shown that Descartes had gotten it so wrong, what accounted for his model's centuries of dominance? What had happened to change this, and how did it come about? My dissertation addresses these questions by exploring some of the historical circumstances and forces behind a fundamental shift in the understanding and experience of bodily pain.[1]

1. Sean Mackey, M.D., Ph.D., is Chief of the Division of Pain Medicine and Redlich Professor of Anesthesiology, Perioperative and Pain Medicine, Neurosciences and Neurology at Stanford University. He is the Immediate Past President of the American Academy of Pain Medicine. Mackey was a key contributor to the Institute of Medicine's comprehensive 2011 report on pain in America. He was far from alone or early in noting the limitations of a model that Descartes first spelled out in 1664, or in exploring how ideas about pain had evolved. See Institute of Medicine, *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research* (Washington, DC: National Academies Press, 2011); Manfred Zimmermann, "The History of Pain Concepts and Treatment before IASP," in *The Paths of Pain, 1975-2005,* ed. Harold Merskey et al. (Seattle: IASP Press, 2005) 5; Fernando Cervero, *Understanding Pain: Exploring the Perception of Pain* (Cambridge: The MIT Press, 2012), 6-7; Thomas Dormandy, *The Worst of Evils: The Fight Against Pain* (New Haven: Yale University Press, 2006), 121; Ronald Melzack and Patrick Wall, *The Challenge of Pain, Updated Second Edition* (New York: Penguin Books, 1991),151; Zimmermann in Merskey et al., 10; Thomas Dormandy, *The Worst of Evils* (New Haven: Yale University Press, 2007), 314; Harold Merskey, "Some Features of the History of the Idea of Pain," *Pain* 9 (1980): 3-8; Edward R. Perl, "Ideas about pain: a historical view," *Nature Reviews/Neuroscience* Volume 8 (January 2007): 71-80; James D. Hardy, Harold G. Wolff, and Helen Goodell, *Pain Sensations and Reactions* (Baltimore: The Williams and Wilkins Company, 1952), 3; John J.

Mackey's tone suggested that the eclipse of Descartes's model had been, in hindsight, a predictable outcome of scientific advance. While *A Disease Itself* locates significant origins of this change in greater understanding of the neuroanatomy of the nervous system after about 1800, these advances were not sufficient to explain what occurred. After 1945, the understanding and clinical status of pain became rooted in an inclusive, personalized model whose ascent to medical and cultural priority changed how people experienced pain, how the medical profession treated it, dynamics between patients and doctors, legislative actions, and the fortunes of dozens of pharmaceutical companies. It also reflected substantial cultural shifts in ideas and practices of identity, selfhood, authority, and autonomy. Pain was reconfigured from a rote event in the nervous system, largely symptomatic, understood, and increasingly treatable, to become a distinct clinical condition defined by complexity, variability, and chronicity. This insurgent model refashioned the primary clinical challenge as chronic pain, asserted crucial interconnections among pain's psychological and personal dimensions, and advocated multidisciplinary treatment as crucial. After the middle of the twentieth century, a long-simmering challenge to a dominant model of pain, given direction by the gate-control theory of pain (1965), promoted pain and its treatment as a distinct clinical specialty; an urgent, cross-disciplinary professional focus; and defined by chronicity, variability, and fundamental subjectivity. The core identity of pain was refashioned.

My case studies show some of the ways in which this change was articulated, promoted, contested, shaped, and ratified in the histories of how pain has been measured, managed, and organized. A new paradigm was central to the launch of International Association for the Study of Pain (IASP) after 1973; the IASP gave structure to long-standing debates about how to assess and treat pain. A new model was operationalized clinically in a pain assessment instrument, the McGill Pain Questionnaire (MPQ), published in 1975. The MPQ attempted to put psychological and

---

Bonica, "Pain research and therapy: past and current status and future needs," in *Pain, Discomfort and Humanitarian Care*, ed. LKY Ng and John J. Bonica (New York: Elsevier-North Holland, 1980),1-46.

personal factors on a par with organic illness and injury in helping clinicians assess what might have caused, and might be aggravating, patients' pain. Wider debates over risk and reward in pain treatments, and the variability of pain, were reflected in the enduring medical and social ambiguities of a highly successful pain reliever, Darvon, between its US debut in 1957 and its removal from that market by the Food and Drug Administration (FDA) beginning in 2010. The ascent of the new model of pain was certified by the US medical profession in the establishment of pain medicine as a recognized sub-specialty by the American Medical Association (AMA) starting in 1993.

Descartes' model had been the starting point from which a biomedical concept of pain as simple, rote, symptomatic, understood, and increasingly treatable had developed and become entrenched by the mid-twentieth century. This model understood pain as acute or transient, an often-predictable accompaniment to a range of clinical conditions and events. *A Disease Itself* focuses on the United States after 1945 and integrates histories of how pain has been measured, managed, and organized in order to show how this model was displaced as the prevailing framework for understanding pain among clinicians and patients. After 1945, developments in all three histories challenged prevailing notions of pain while leaving longer-standing quandaries intact. For example, dozens of scales and techniques to measure pain, while helpful in diverse clinical presentations of pain, fell short of providing a clinically useful "pain thermometer" or anything close to a widely deployable method. While pharmacological and complementary treatments proliferated after World War II, the clinical prevalence of pain was rising, as chronic pain emerged as a substantial issue. Even new measurement tools and therapies did not relegate pain's ambiguities to the sidelines. Instead they gave new forms to enduring quandaries.[2]

2. The "triumph" of a model of pain as complex and subjective has not been total, just as the dominance of a stimulus-and-response model had coexisted and prevailed among theoretical challenges and clinical quandaries. Thomas Hadjistavropoulos and Kenneth D. Craig, editors, *Pain: Psychological Perspectives* (Mahwah, NJ: Lawrence Erlbaum Associates, 2004), 333-338; Akiko Okifuil, "Interdisciplinary Pain

The ascent of a new model to prevalence sought to revise pain's traditional marginality within medicine by establishing it as a distinct medical entity rooted in complexity, chronicity, and subjectivity. Dislodging this status was not simple; its roots went back several centuries in numerous directions. These included pain's importance as a symptom, which was denied by few, even among dissenters from pain orthodoxy. But this value had, prior to the middle of the twentieth century, made pain less intriguing to clinicians and researchers. At the same time, many clinicians at mid-century believed pain had mostly been "solved," which was at least defensible if pain meant only acute pain. After 1945, a growing number of treatments for transitory pains made it harder to establish chronic pain as urgent. Its familiarity in many medical specialties but its home in none gave pain an organizational ambiguity. The inability to measure pain reliably worked against physicians' focus on it as a discrete condition. Pain's scant treatment in medical training; traditionally low levels of federal research support; and its ties to addiction all worked to marginalize pain among American clinicians.[3]

---

Management with Pain Patients: Evidence for Its Effectiveness," *Seminars in Pain Medicine* Vol. 1, No. 2 (2003): 110-119; Melzack and Wall, *Challenge of Pain*, 149-154, 157-158, 162-164. Clinicians, historians, and social scientists increasingly have examined the origins and forms of a decisive shift in the understanding of pain after 1945. Keith Wailoo. *Pain: A Political History* (Baltimore: Johns Hopkins University Press, 2014); Joanna Bourke, *The Story of Pain: From Prayer to Painkillers* (Oxford: Oxford University Press, 2014); Richard C. Chapman and John D. Loeser, ed., *Advances in Pain Research and Therapy: Issues in Measurement, Volume 12* (New York: Raven Press, 1989), 2, 63-65, 231-234, 438-440; Noemi Tousignant, "Pain and Pursuit of Objectivity: Pain-Measuring Technologies in the United States, c. 1890-1975," McGill University Ph.D. dissertation, 2006; Javier Moscoso, *Pain: A Cultural History*, trans. Sarah Thomas and Paul House (London: Palgrave Macmillan, 2012); Daniel M. Doleys, *Pain: Dynamics and Complexities* (Oxford: Oxford University Press, 2014); David B. Morris, *Illness and Culture: Pain in the Postmodern Era* (Berkeley: University of California Press, 2004).

3. Early leaders of the challenge to a prevailing model of pain had often noted its marginality within clinical practice and an overall lack of research interest as a problem in itself prior to the mid-20th century. See John Bonica, "Evolution and Current Status of Pain Programs," Journal of Pain and Symptom Management, Vol. 5., No. 6 (December 1990): 368-374; Melzack and Wall, *Challenge of Pain*, ix; Patrick D. Wall, *Pain: The Science of Suffering* (New York: Columbia University Press, 2000); *Oral History Interview with Kathleen Foley*, 25 June 1996 (Ms. Coll. No. 127.14), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise B. Darling Biomedical Library, University of California, Los Angeles; *Oral History Interview with B. Berthold Wolff*, 5-6 November 1993 (Ms. Coll. No. 127.39), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise B. Darling Biomedical Library, University of California, Los Angeles.

In putting forward a concept of pain defined by chronicity and subjectivity, promoters of an "insurgent" model challenged more than medical orthodoxy in two main ways. An effort to revise pain's clinical status suggested limits for a biomedical model that focused on identifiable, direct causes of specific diseases with known symptoms, courses, and treatments. In addition, the centrality of patient reports in the new model's methods, scales, and techniques of pain assessment questioned reliance on, or even the existence of, exclusive knowledge, skills, and experience among professionals when it came to pain. If pain was as decisively subjective as the new model portrayed it to be, what did it mean for a clinician to treat pain? What should or could pain medicine consist of? How should a clinician use and evaluate patient input in assessing that person's pain? How should a clinician approach a patient whose pain cannot be tracked to its sources?

While it is not a focus of the dissertation, the 1965 publication of the gate control theory (GCT) of pain was a galvanizing event in the transformation that my project examines. The GCT proposed mechanisms of the nervous system by which psychological and personal factors were electrochemically integrated into the organism's responses to painful stimuli. Its developers, neuroanatomist Patrick Wall and experimental psychologist Ronald Melzack, believed that the scope and impact of complex modulations of "pain signals" in the brain and spine were dimly understood but critical to unlocking pain's secrets. The GCT provoked a flood of research, commentary, and controversy over the accuracy of its predicted mechanisms and its larger challenge to how pain was understood. The GCT offered a more flexible, inclusive scheme for how pain, especially chronic pain, worked.[4]

4. The GCT's status as the most significant contribution to pain theory in the twentieth century is secure. Its political resonance was depicted by Keith Wailoo in *Pain: A Political History* (Baltimore: Johns Hopkins University Press, 2014). Wailoo said that one of the GCT's main effects was to move the field of pain "deliberately, relentlessly, toward appreciating the power of the subjective, the mind, psychology, and perception in pain and its control." He argued that Melzack and Wall's theory "reinforced many of the tendencies of the era [1960s and 1970s] … the theory resonated on multiple levels with the era's legal battles, cultural critiques pain relief practices, and liberalizing political commitments." He showed how issues of wartime and workplace disability in the US drove policy and legislative debates that reflected the cultural

If advances in neuroanatomy and physiology were not sufficient to explain a change in pain's clinical standing, where might historians look? One direction is to the intense cultural upheaval, around issues of authority and trust, that unfolded in the US in the 1970s. A model of pain as complex and subjective fit well with this turmoil, for which Vietnam, Watergate, women's liberation, and Patti Hearst have become symbols and reminders of political and social disruption. Dozens of professions, including medicine, endured severe contests over their authority, legitimacy, and expertise. Key drivers of these struggles were evolving notions of selfhood, individuality, and identity after 1945. The emergence of a prevailing model of pain as variable and subjective built on ontological foundations that were recast in post-war America. After 1945, a growing number of Americans wrestled with new ideas about the individual as self-directed and able to draw on personal experiences and beliefs as useful sources of authority and autonomy.[5]

While the fundamental turn in pain happened after 1945, critical events between 1800 and 1945 had created the conditions for this change. My analysis includes four significant pre-histories that shaped a transformation in pain's status: advances in neuroanatomy of the nervous system after 1800; the development of anesthesiology as a medical discipline; a collaboration among the federal government, academia, and industry to understand morphine and its derivatives; and the wartime experiences of anesthesiologists Henry Beecher and John Bonica. These activities and events built scientific, clinical, organizational, and conceptual foundations for the reshaping of pain as complex,

---

upheavals of post-war America. See Wailoo, *Pain: A Political History*, 77-79; D. C. Turk, "Chronic Pain: Models and Treatment Approaches," in *International Encyclopedia of the Social and Behavioral Sciences* (New York: Elsevier Science Ltd., 2001), 1782-9; Christopher Spanswick and Chris Main, *Pain Management: An Interdisciplinary Approach* (London: Palgrave Macmillan, 2000).

5. Historians have combed over the inexhaustible 1970s as a period of intense cultural contests and upheavals that reverberate down to the present. Rick Perlstein's political and social histories are detailed and insightful. See Rick Perlstein, *Nixonland: The Rise of a President and the Fracturing of America* (New York: Scribner, 2009); Rick Perlstein, *The Invisible Bridge: The Fall of Nixon and the Rise of Reagan* (New York: Simon and Schuster, 2014); Francis Wheen, *Strange Days Indeed: The 1970s – The Golden Age of Paranoia*. (New York: Public Affairs, 2009); Dominick Sandbrook, *Mad as Hell: The Crisis of the 1970s and the Rise of the Populist Right* (New York: Anchor Books, 2011); Mike Saks, "Medicine and the Counter Culture," *in Medicine in the Twentieth Century*, ed. Roger Cooter and John Pickstone (Sydney: Harwood Academic Publishers, 2000), 113-124.

indivisible along physiological and psychological lines, shaped by an individual's history, and, after 1973, organized to encourage dialogue and collaboration across specialties.

In 1943 surgeon and University of Oregon professor of surgery William K. Livingston summarized physicians' prevailing understanding of pain and a dilemma it posed:

> I was brought up in a medical generation in which the reflex arc of two, or possibly three, neuron units was not interpreted as a symbol of a very complex function, but as an actuality. I received the impression that pain was a primary sensation dependent upon the stimulation of a specific sensory ending by a stimulus of a certain intensity, and conducted along a fixed pathway to ring a special bell in consciousness. Pain was as simple as that … The idea that anything might happen to sensory impulses within the nervous system to alter their character, destination, or the sensation they registered in consciousness was utterly foreign to my concept. But in practice I found that it was incredibly difficult to make this concept consistent with clinical observation.[6]

*A Disease Itself* tells the story of how the concept of pain that Livingston had learned was challenged and supplanted.

**From the Ancients to Descartes**

The roots of both a Cartesian model and the paradigm that would supplant it can be detected in early debates over the origins, nature, and mechanisms of pain. These took shape well before the Common Era, at a time when physiology was seen as a microcosm of how the wider world worked. Pain was attributed to the actions of evil spirits, devious substances, and thin-skinned gods. Other concepts of pain were more abstract. About 500 BCE Buddha ascribed the universality of pain to the frustration of desires that were derived from people's sensory impressions. In privileging the

6. William Livingston, *Pain Mechanisms* (New York: Macmillan, 1943), 61.

body's sensate reality as the basis of a universal experience, the Buddha attributed a highly individualistic foundation to pain. In Christianity pain and suffering were accepted as fundamental to the natural order and as a sign of negative divine reaction to a person's behavior and thoughts.[7]

At about the same time the Buddha was seeking to understand pain, inquiries about how the body "registered" pain were taking shape. A disciple of Pythagoras from southern Italy, Alcmaeon of Croton, suggested that the brain, not the heart, was the center of sensation and reason. He asked whether sensory perception required a direct connection between the brain and the sense organs. To find out, Alcmaeon cut the optic nerves of live animals and observed the ensuing loss of vision. Alcmaeon concluded that all sense organs were connected to the brain by nerves, and that these connections were necessary for the perception of each individual sensation. His model thus linked each sense organ to a specific sensation by means of a connection between the brain and diverse organs.[8]

Alcmaeon's concept contributed to the idea of five distinct senses that Aristotle (384-322 BC) put forward. For Aristotle, pain was not a discrete sense like sight or hearing. It was fundamentally an emotion that resulted from the abnormal or inappropriate stimulation of any of the senses. Aristotle dismissed the brain as irrelevant to sensation and emotion, seeing it as an inert collection of bone marrow inside the skull. The spinal cord was not any more important, since it was a thread made of fat on which vertebral bones happened to hang. Aristotle saw pain and pleasure as

7. It would be an oversimplification to assert that bodily pain has shed all remnants of these earlier conceptions. See Doleys, *Pain: Dynamics and Complexities*, 13; Kenneth Keele, *Anatomies of Pain* (Springfield, IL: Charles C. Thomas, 1957), 7, 19; Dormandy, *Worst of Evils*, 280-298; Moscoso, *A Cultural History of Pain*, 85-96, 113-117; Bourke, *Story of Pain*, 81, 91-102.
8. Cervero, *Understanding Pain*, 35-6; Keele, *Anatomies*, 16.

positive and negative motivators of human behavior. They were twinned "passions of the soul" whose true centers were in the heart.[9]

Some physicians diverged from the Aristotelean view. For Galen (AD 130-201) pain was fundamentally a sensation, with the brain as the central organ of sensory perception. He distinguished sensory and motor nerves as well as others of lesser sensitivity associated with pain. In this way the central nervous system can be said to have re-emerged with Galen. He pointed to dissections performed in the second and third centuries BCE to bolster his view of the brain as the organ of sensation. These procedures had shown that the brain was connected to nerves that traveled from the periphery through the spinal cord. Even with these challenges, Aristotle's view held sway for a long time; he had summarized much of physiological thought before the structures of the nervous system began to appear.[10]

Aristotle's influence meant it would take almost another 2,000 years to establish the nervous system's sensory function. Starting from a view of physiology that deviated only modestly from Galen's, Rene Descartes provided an initial statement of a model of pain that became entrenched in clinical medicine and that William Livingston described in 1943. For his example Descartes depicted a boy whose foot inches too close to a fire. Descartes' explanation was that the "particles" of the fire stimulated the small ends of sensory nerves in the skin and started the transmission of impulses up to the brain. There, reflected in the pineal gland as if by a mirror, the impulses stimulated the motor nerves that pulled the boy's leg muscles so that he removed his foot from the

9. Cervero, *Understanding Pain*, 9-10; Keele, *Anatomies,* 12, 31, 34; Merskey, "Some Features," 3-5; Doleys, *Pain: Dynamics and Complexities*, 15; Edward E. Perl, "Ideas about pain: a historical view," *Nature Reviews/Neuroscience*, Vol. 8 (January 2007): 71-80.
10. Keele, *Anatomies*, 43, 46, 52; Doleys, *Pain: Dynamics and Complexities*, 15; Perl, "Ideas about Pain," 72-77; Cervero, *Understanding Pain*, 9-11.

fire. Descartes thus sketched the first contemporary model of pain as a stimulus-and-response, mechanistic but undeniably physiological event.[11]

Descartes's location of the "seat" of pain in biology was a "launch point" from which a biomedical model of pain would emerge. While he may have set the study of pain on a course that Mackey would later assess as proven to have been amiss, an enduring contribution of Descartes's model was to situate pain within biology and physiology just as these disciplines were developing as organized experimental sciences. Starting in the 1600s, the transmission of nerve impulses came slowly to be seen as a physical, not spiritual, event. Pain was becoming more natural, linked somehow to physiology, and not the mischief of the divine.[12]

**The Historiography of Pain**

The emergence of chronic pain as a clinical syndrome has roughly paralleled an expanding focus on the history of pain across scholarly disciplines, within the study of history, and in the topics and issues that have received scrutiny. Over the past seventy years, as pain was redefined as a distinct medical syndrome or condition, historians have increasingly added to the work of scholars in the physical, social, and behavioral sciences, as well as that of clinical researchers, in their studies of

---

11. In 2012, IASP President and anesthesiologist Fernando Cervero said that, despite pain's enhanced stature within clinical medicine, many current textbooks still described pain as the result of a straight pathway from the periphery to the brain. See Cervero, *Understanding Pain*, 64; Keele, *Anatomies*, 38, 55, 69, 72, 73; See also Daniel de Moulin, "A Historical-Phenomenological Study of Bodily Pain in Western Man," *Bulletin of the History of Medicine*, 48:4 (1974: Winter): 540-570; Roselynn Rey, *The History of Pain* (Cambridge: Harvard University Press, 1998); Melzack and Wall, *Challenge of Pain*, 149; Mariet A. E. Vrancken, "Schools of Thought on Pain," *Social Sciences and Medicine*, Vol. 29, No. 3 (1989): 435-444; David B. Morris, *Illness and Culture in the Postmodern Age* (Berkeley: University of California Press, 2000); Michael R. Bond, *Pain: Its Nature, Analysis and Treatment, Second Edition* (Edinburgh: Churchill Livingstone, 1984); Sarah Coakley and Kay Kaufman Shelemay, editors, *Pain and Its Transformations: The Interface of Biology and Culture* (Cambridge: Harvard University Press, 2007); Elaine Scarry, *The Body in Pain* (New York: Oxford University Press, 1985); Mary-Jo Delvechhio Good, et al., ed., *Pain as Human Experience: An Anthropological Perspective* (Berkeley: University of California Press, 1992).

12. Donald B. Caton, an anesthesiologist, wrote in 1985: "Some time between Locke [1632-1704] and Mill [J.S., 1806-1873], pain changes from a divine to a natural phenomenon and from a beneficial to a destructive process." See Donald Caton, "The Secularization of Pain," *Anesthesiology* (62: 1985):493-501; Edward R. Perl, "Ideas about pain; a historical view," *Nature Reviews/ Neuroscience* 8 (January 2007): 71-80; K. D. Keele, *Anatomies of Pain (*Springfield, IL: Charles C. Thomas, 1957); H. Merskey, "Some Features of the History of the Idea of Pain," *Pain*, 9(1980): 3-8; Dormandy, *Worst of Evils*, 67, 86.

pain. Historians have examined scientific, clinical, and social influences on the development of pain theories and treatments and have confronted the diversity of clinical approaches. Narratives have focused on debates over the origins and nature of pain as well as mind/body issues and the nature of perception, awareness, and learning; the roles of social and cultural factors in the individual experience of pain; and how politics and commerce have shaped understandings and the treatment of pain since 1945. Historians have analyzed how social forces have shaped the experience and understanding of pain; how pain became a venue for political contests and public policy debates; the growth of pain relief as an economic activity; pain's ties to addiction in terms of medical practice and public policy; and how the interplay of science and commerce after 1945 in the United States affected how people understood, experienced, and treated pain.

By the middle of the nineteenth century, foundational discourses had developed on three topics: how to relieve symptomatic, acute pain; the mitigation of severe pain in those suffering from progressive diseases, such as cancer and arthritis; and how to address intractable, persistent pain from disorders such as migraine headache as well as illnesses or injuries that had ended or been cured. Discourses in the post-1945 history of medicine have focused on the behaviors and impacts of the pharmaceutical industry and the growth of pain relief as an economic activity; the expansion of complementary and alternative treatments; and the rise of chronic pain as a clinical challenge. Historians increasingly examined clinical medicine as a dimension of culture and economics. Like many other professions, medicine had endured vigorous political and social "cross-examination" in the 1960s and 1970s. Both medical practice and history increasingly focused on the rise of chronic diseases, including chronic pain.[13]

13. Over the last 75 years historians have increased their contributions to the scholarly literature on pain that prior to that had been dominated by scholars in clinical and academic medicine; psychology, anthropology, and sociology; and public health. This work has also been the focus of historiographical inquiries. See Roselynn Rey. *The History of Pain*, trans. Louise Elliott Wallace, J. A. Cadden, and S. W. Cadden (Cambridge: Harvard University Press, 1998); Mariet A. E. Vrancken, "Schools of Thought on Pain," *Social Sciences and Medicine*, Vol. 29, No. 3 (1989): 435-444; David B. Morris, *Illness and Culture in the Postmodern*

*A Disease Itself* extends this historiography by showing how developments in pain measurement, management, and institutional histories helped shape a basic transformation in the clinical status of pain after 1945. My dissertation complements work on changes in how pain has been understood, represented, treated, and administered by focusing on this decisive shift. A Disease Itself identifies meaningful connections across the histories of how pain has been measured, managed, and organized as researchers sought to isolate constitutive elements of the experience, understand the neurochemical foundations of the body's reactions to noxious stimuli, and develop pharmacological and other treatments based on these findings. Connections across these historical domains helped refashion pain as clinically chronic and decisively subjective. An insurgent model of pain supplanted the Cartesian model with a more inclusive, holistic, and complex concept of what pain was and how it worked.

Historians have drawn on a massive clinical and scientific literature on pain's origins, nature, treatment, and broader social and cultural dimensions. They have incorporated work by anthropologists, sociologists, and psychologists to understand cultural influences on the perception and experience of pain, its social meanings and individual variability in the condition and its relief. An important contribution to post-1945 discourses has been sociology's focus on the foundations

---

*Age*. (Berkeley: University of California Press, 2000); Michael R. Bond, *Pain: Its Nature, Analysis and Treatment, Second Edition*. (Edinburgh: Churchill Livingstone, 1984); Sarah Coakley and Kay Kaufman Shelemay, ed., *Pain and Its Transformations: The Interface of Biology and Culture*. (Cambridge: Harvard University Press, 2007); Elaine Scarry, *The Body in Pain*. (New York: Oxford University Press, 1985); Mary-Jo Delvechhio Good, et al., ed., *Pain as Human Experience: An Anthropological Perspective*. (Berkeley: University of California Press, 1992); George Rosen, "Disease and Social Criticism: A Contribution to the Theory of Medical History," *Bulletin of the History of Medicine* (January 1941): 5-15; George Rosen, "Levels of Integration in Medical Historiography: A Review," *Journal of the History of Medicine* (Autumn 1949): 460-467; Frank Huisman and John Harley Warner, ed., *Locating Medical History: The Stories and Their Meanings*. (Baltimore: The Johns Hopkins University Press, 2004); Roger Cooter and John Pickstone, ed., *Medicine in the Twentieth Century*. (Sydney: Harwood Academic Publishers, 2000); Nancy D. Campbell, *Discovering Addiction: The Science and Politics of Substance Abuse Research*. (Ann Arbor: The University of Michigan Press, 2007); Gert Brieger, "The Historiography of Medicine," in Bynum and Porter, ed., *Companion Encyclopedia of the History of Medicine*, 24-45; Noemi Tousignant, "The Rise and Fall of the Dolorimeter: Pain, Analgesics, and the Management of Subjectivity in Mid-twentieth-Century United States," *Journal of the History of Medicine*, Vol. 66 (April 2011): 145-179; Javier Moscoso. *Pain: A Cultural History*. London: Palgrave Macmillan, 2012; Karl M. Dallenbach, "Pain: History and Present Status," *The American Journal of Psychology*, Vol. 52, No. 3 (July 1939): 331-347; Edwin G. Boring. *Sensation and Perception in the History of Experimental Psychology*. (New York: Appleton Century Crofts, Inc., 1942): 9.

of, and contests over, professional authority and legitimacy among medical providers and patients. Sociologists have looked at how professions define themselves and establish social legitimacy. They have examined questions of professional authority and autonomy, how they are given meaning and validity and how both can be challenged by new models. How have clinicians focused on pain fought for legitimate professional authority? How has pain medicine acquired technical and cultural standing since the middle of the 20th century, and what drove this change? In an experience increasingly defined as individual and circumstantial, who has expertise about my pain, what does that expertise comprise, and who decides? Whose perspectives count most decisively in the assessment and treatment of pain? Sociologists have employed several approaches to their analysis of authority and legitimacy in professions. Taxonomies have sought to identify attributes that define a profession, while dynamic analyses have looked at what forces affect the ability of occupational participants to organize and present themselves in socially approved, and rewarded, ways. Process approaches have focused on developmental patterns in economics, science, technology, and commerce that have shaped professions. Structural-functionalists have seen professions as occupations that require specialized skills and abstract knowledge and thus merit special recognition in terms of free-market supply and demand. Power theory has depicted professions as occupations that can wrest recognition as professions from society. Together, these analytical approaches have helped historians grasp issues of status, professional recognition, the power to set requirements and standards, and the organizational structure of a scientific discipline.[14]

14. Ronald L. Numbers, "The Fall and Rise of the American Medical Profession," in *The Professions in American History*, ed. Nathan O. Hatch (Notre Dame, IN: University of Notre Dame Press, 1988), 51-72; Paul Starr, *The Social Transformation of American Medicine* (New York: Basic Books, 1982), 4, 5, 7, 9, 13; Douglas Klegon, "The Sociology of Professions: An Emerging Perspective," *Sociology of Work and Occupations*, Vol. 5., No. 3 (August 1978): 267-268, 271, 274; Frederic W. Hafferty and Donald W. Light, "Professional Dynamics and the Changing Nature of Medical Work," *Journal of Health and Social Behavior*, Vol. 35, Extra Issue: *Forty Years of Medical Sociology: The State of the Art and Directions for the Future* (1995): 132-153; Patrick B. Forsyth and Thomas J. Danisiewicz, "Toward a Theory of Profesionalization," *Work and Occupations*, Vol. 12, No. 1 (February 1985): 59-76; Robert Dingwall. *Essays on Professions* (Burlington, VT: Ashgate Publishing

The sociological analysis of professions has been part of the historiographical record that has tracked how pain became secular and clinical before it could be understood as chronic and subjective. How this happened is a theme that ties together the pre-histories in Chapter 1. After 1800, the study and treatment of pain slowly became more medical, clinical, and professional, with these developments accelerating after 1945. These changes had enormous consequences for patients, clinicians, pharmaceutical companies, and society as a whole. Before pain could become a clinical entity and specialty, it had to become a medical problem, wrested from the domain of divine focus and spiritual indicator. A change in pain's core identity from spiritual to physical gradually unfolded and accelerated after about 1800 in the West; the secularization of pain, articulated first by Descartes, helped to move bodily pain beyond the spiritual realm. After 1945, another reformulation "positioned" pain as complex, individual, and variable.[15]

The introduction of surgical anesthesia in 1846 was a turning point in pain's secularization and in pain becoming defined as clinical and then distinct condition. As 19th century clinicians and clerics recognized quickly, anesthesia raised difficult questions about the practice of medicine, the nature of awareness and perception, and suggested possibilities for the management of pain that had previously not been feasible. The resistance to it within medicine and society reflected both the salience and complexities of these issues as well as how deeply embedded were concepts of pain as divine comment and reaction, as a necessary evil. But if pain could be so effectively eliminated, without harm or undue risk, how might such capabilities be deployed beyond the

---

Company, 1985); Peter Conrad, "Eliot Freidson's revolution in medical sociology," *Health: An Interdisciplinary Journal for the Study of Health, Illness, and Medicine,* Vol. 11(2): 1141-1144; Everett Hughes. *Men and Their Work* (New York: The Free Press of Glencoe, 1958), 78-80; Eliot Freidson. *Profession of Medicine: A Study of the Sociology of Applied Knowledge* (New York: Dodd, Mead & Company, 1970), xviii, xix, xxi, 11, 21, 304, 312, 357, 368-370.

15. Martin S. Pernick. *A Calculus of Suffering: Pain, Professionalism, and Anesthesia in Nineteenth Century America* (New York: Columbia University Press, 1985); Jan R. McTavish. *Pain and Profits: The History of the Headache and Its Remedies in America* (New Brunswick, NJ: Rutgers University Press, 2004); Rey, *History of Pain*, 3, 5, 89-91; Doleys, *Pain: Dynamics and Complexities*, 17-22; Bourke, *Story of Pain*, 123-130.

surgical theater? Anesthesia challenged the inevitability of pain and in doing that challenged the idea that pain was beneficial or meaningful spiritually.[16]

Anesthesia was a critical development in a gradual decline in the belief in the positive benefits of pain, both medically and spiritually; support for the idea of clinical and human benefits of pain endured within medicine and beyond well after anesthesia had become more routine. Pain in childbirth had been ordained by Scripture and was held to be crucial for inculcating proper ways of being a mother. Pain told its sufferers that God felt they needed to change. These attributes bolstered reticence about addressing pain relief as a medical goal. They would also provide some of the residual resistance to the idea of pain as a distinct condition, some of which was shared by the insurgent model's biggest supporters, such as neuroanatomist and pain theorist Patrick Wall.[17]

Historical debates over the value and nature of pain reflect its centrality to cultural and spiritual domains. Several dimensions of its history have shaped this centrality: pain's status as a universal, eternal human event; its standing as a foundational problem across the history of medicine; its evolution as a growing public-health and policy challenge in the 21st century; its importance as a metaphor and focus of major religious and spiritual traditions; and its significance as a subject and metaphor within literature, painting, photography, and other representational arts.

This multifaceted significance has contrasted with pain's marginality within the practice of medicine in the US before about 1970. In their mid-1990s reminiscences about the contemporary history of pain, it was a commonplace among early participants in the IASP (launched in 1973) that pain as a clinical problem in itself had received scant attention in research and teaching in the

16. Bourke, *Story of Pain*, 124, 292, 296-297; Pernick, *A Calculus of Suffering*, 42-58; Rey, *History of Pain*, 152-182.

17. L. A. Reynolds and E. M. Tansey, ed., *Innovation in Pain Management*: the transcript of a Witness Seminar, Wellcome Trust Centre for the History of Medicine, 2004, held at University College London (UCL), December 12, 2002. Joanna Bourke has seconded Pernick's and McTavish's conclusions that, prior to about 1900, many people were skeptical about the concept of pain relief. She described as "persuasive" Pernick's argument that decisions not to use anesthesia in surgery were often based on "ideas about differential sensitiveness to pain" among racial and ethnic groups as well as women and children. See Bourke, *Story of Pain*, 275.

immediate post-war period. After 1900, researchers such as neurophysiologist Charles Sherrington and Henry Head, as well as surgeons Thomas Lewis and William Livingston, began to focus on pain from different clinical and cultural backgrounds, had studied the mechanisms of the nervous system and bolstered a challenge to prevailing concept of pain as straightforward and rote. Their speculations about the complexities of pain within the nervous system initially did little to change the marginality of pain, particularly in chronic forms, within clinical medicine prior to the 1970s. This marginality had derived from pain's status as a symptom; its familiarity in many medical specialties but its "home" in none; its enduring ties to addiction; the inability of pain to be measured in a clinically useful way; and a growing belief among clinicians after 1945 that pain had largely been "solved," or was about to be, by an array of treatments for acute or transient pain. The story of how changes in measurement, management, and organization of pain helped refashion this marginality is the story that *A Disease Itself* endeavors to tell.[18]

**Chapter Organization**

The dissertation focuses on the histories of how pain has been understood, treated, and professionally organized in order to track and characterize the transformation it proposes. What shift took place? Why did it matter? How did developments in measurement, management, and institutions propel this change?

Chapter 1 sketches four pre-histories that enabled and shaped a basic transformation after 1945. These events and developments – research in the physiology of the nervous system after 1800; the rise of anesthesiology as a clinical discipline; an inter-war collaboration among federal government agencies, academia, and pharmaceutical companies; and the wartime experiences of surgeon

18. Wall interview, UCLA History of Pain Collection, 9-10, 15-18; Foley interview, UCLA History of Pain Collection, 12, 16-22, 38-40; *Oral History Interview with Benjamin L. Crue, Jr*., 9-10 May 1996 (Ms. Coll. No. 127.11), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Library Special Collections, Louise M. Darling Biomedical Library, University of California, Los Angeles; Melzack and Wall, *Challenge of Pain*, 134-138; Thomas Lewis. *Pain* (New York: Macmillan and Company, 1942); Livingston, *Pain Mechanisms*, 61.

William Livingston, anesthesiologist Henry K. Beecher and anesthesiologist John J. Bonica -- contributed to a reformulation of pain's clinical standing by creating scientific and conceptual foundations, institutional settings, professional and commercial networks, and organizational leadership that gave structure and direction to a transformation in the clinical status of pain. These were enabling conditions and developments that guided, shaped, and organized a transformation in pain's medical status.

Chapter 2 examines the history of pain measurement and looks at the McGill Pain Questionnaire (1975), a six-page assessment tool that was published in 1975 and was used in a wide range of clinical settings between 1975 and about 1995. The MPQ sought to operationalize an inclusive model of pain, and what about it needed to be measured, by quantifying personal and psychological factors within the process of clinical assessment; it assumed the fundamental inseparability and diagnostic parity of these factors; it put patient input at the center of the pain-assessment process; and it implemented a concept that what needed to be included in pain assessment were personal history and current circumstances that might be contributing to pain experience. The MPQ was far from a perfect or complete pain assessment instrument. Its history sheds light on how elusive the quantification of pain has been for clinicians and researchers. The profusion of scales, methods, and tools for pain measurement after 1945 itself attests to pain's variability and complexities.

Chapter 3 explores the history of pain management and focuses on Darvon, a synthetic opiate pain reliever introduced in the United States in 1957. Darvon's long and commercially successful career was marked by clinical and social ambiguity, driven by uncertainty about its stand-alone effectiveness and safety. This ambiguity, and the debates within research communities and the federal government that it generated, revealed more detailed contours of broader contests over pain's origins, nature, and treatment. With unusual sharpness, an enduring Darvon debate has reflected the diversity of painful conditions and variability of responses to treatment; how

differently effectiveness and safety can plausibly be defined and evaluated; and the role of pharmaceutical company marketing and promotion in creating perceptions of Darvon and influencing the dialogues about it. In 2010, in announcing its phased withdrawal from the US market, federal regulators acknowledged the openness of even the most recent data to differing interpretations. In this they followed in footsteps of bureaucratic predecessors, starting in the late 1970s; they also replicated their regulatory forebears in handing down close-call decisions in favor of Darvon after comparably exhaustive reviews.

Chapter 4 covers organizational and institutional changes that affected the understanding and clinical status of pain. In 1973, the International Association for the Study of Pain (IASP) was founded as a multidisciplinary, global, and energetic professional home to diverse clinicians and scientists who were interested in pain. It promoted an inclusive model of pain by opening membership and leadership chances to practitioners from many specialties and disciplines; from its 1973 founding the IASP cultivated participation and leadership from various branches of psychology and championed research that investigated psychological shapers and expressions of pain. It steadily expanded the various subdivisions of psychology – clinical, social, psychiatric – among its membership and publications; they developed relationships with the WHO and the US pharmaceutical industry in order to promote the understanding of pain it promoted as a global clinical challenge that was misunderstood, rampant, and a first duty of the medical profession. It has exerted significant influence on the development of pain taxonomies, research, multidisciplinary treatment, and the development of global networks across medical and scientific disciplines.

*A Disease Itself* asserts a fundamental shift in the understanding and clinical status of pain after 1945 and locates this reconfiguration in the histories of measurement, management, and institutional development. The forces that drove this reformulation did not begin as WWII came to

an end. Their roots were in scientific investigations in anatomy and physiology; the development of anesthesiology as a medical specialty at the precise moment in the 1920s, 1930s, and 1940s when American clinicians and their professional organizations, across many medical disciplines, were deciding what it meant to be a specialty and to certify people in it; an extended research collaboration among government, academia, and the pharmaceutical industry that sought to understand pain, addiction, and their treatment; and the experiences of key clinicians in World War II, which would impel post-war efforts to move the study and treatment of pain out of the margins and into the mainstream. To see how these events helped create a fundamental transformation and created conditions under which pain's clinical marginality would be challenged, the next chapter looks at important pre-histories.

**Chapter 1 – Pre-histories of pain's transformation**

A transformation of pain's clinical status did not materialize suddenly. It grew from diverse historical antecedents -- scientific, medical, and organizational developments that enabled and nurtured this change. Pain's clinical and institutional marginality comprised the historical setting from which, after 1945, a successful challenge to a prevailing model of pain and its status within medical research, training, and practice emerged. Between 1800 and 1945, developments in science and medical practice gradually eroded the hegemony of an established Cartesian framework for pain and built a foundation for pain's revised clinical status. After 1945 an insurgent model of pain as complex, chronic, and subjective slowly supplanted an established paradigm of pain as mechanical, repetitive, and well understood.

This chapter examines four of the historical antecedents that drove the shift. Its goal is to show how each pre-history helped erode the scientific, clinical, and organizational marginality of pain. These pre-histories were sometimes discrete phenomena and were sometimes linked and mutually formative. They shaped the content and articulation of a new paradigm that transformed pain's historical marginality in diverse ways.

After 1800, findings in the neuroanatomy and physiology of the nervous system provided scientific grounding for a revised understanding of pain as complex and shaped by personal factors. As research on the structures, functions, and interconnections across the nervous system accumulated, a model of pain as straightforward and "hard-wired" was less able to account for the diversity and variability of what clinicians observed.[1]

1. Keele, *Anatomies*, 12, 64, 85; Melzack and Wall, *Challenge of Pain*, 149-164; Rey, *History of Pain*, 132-154.

Anesthesiology's steadily expanding engagement with pain management as a clinical problem, along with its concurrent organizational development, helped establish pain as a distinct clinical focus. In addition, anesthesiology's achievement of specialty status within the American Medical Association (AMA) in 1940 prefigured the emergence of pain medicine as an official sub-specialty several decades later. Between 1900 and 1940, anesthesiologists mapped out the clinical and educational content of their practice within dozens of local, state, regional, and national groups as well as at universities and hospitals. These efforts helped to create professional networks that contributed to the emergence of pain as a distinct clinical syndrome and to the organizational development of pain medicine.[2]

Between 1929 and 1945 a research collaboration among government, academia, and the philanthropic community on structure-function relationships of the morphine molecule and its derivatives had substantial long-term impacts on the transformation of pain's clinical status. This collaboration advanced the pharmacology of pain relief and stimulated development of numerous pain relievers, such as meperidine, that became commercially available after 1945. After 1935, compounds that showed therapeutic promise in animal studies were tested on inmates at the federal government's narcotic prison at Lexington, Kentucky. This effort also nurtured American professional and commercial networks in which the biochemical workings of pain relief and addiction received ongoing scrutiny and informed debates over the origins and mechanisms of addiction and pain. This program helped establish the federal government's fiscal and political involvement in public policy issues in which addiction and pain relief, including the elusive

2. Harold R. Griffith, "History of the World Federation of Anesthesiologists," *Anesthesia & Analgesia* 42 (1963): 389-397; Gaston L. Labat, "Regional Anaesthesia," *Annals of Surgery* 73 (1921): 165-169; Surjya Sen, David P. Martin, Douglas R. Bacon, "Exploring Origins: Was John Bonica's Model of Modern-Day Pain Management Influenced by John Lundy's Earlier Work?" *Regional Anesthesia and Pain Medicine*, Volume 32, Number 3 (May-June 2007): 258-262; "ABA Timeline," from The American Board of Anesthesiology web site, www.theaba.org/ABOUT/Test-History, accessed 9-19-15.

boundaries between medical and non-medical use of morphine and its derivatives, were at the center.[3]

The experiences of three clinicians during World War II gave significant direction and leadership to the content, professional standing, and wider cultural resonance of the post-war transformation that *A Disease Itself* explores. Anesthesiologists Henry K. Beecher and John Bonica and surgeon William K. Livingston were among hundreds of clinicians who encountered pain's many varieties in combat zones and medical units during World War II. While their theaters of operations varied, all three interacted with thousands of wounded soldiers; at its peak, the naval hospital in California at which Livingston worked had 12,000 beds. The perspectives that this amount of clinical material provided were among the influences that shaped their post-war speculations and organizational leadership in an emerging field of pain management.[4]

For Beecher, Bonica, and Livingston, pain's entrenched marginality within medicine was a collective denial of the urgency of an elemental medical problem and evidence of a moral shortcoming within the profession. Theirs was, in this sense, a conservative critique that sought to restore pain to what they saw as its former and appropriate centrality in healing. This chapter

3. Related to this topic has been the gradual bifurcation of addiction medicine from pain medicine between 1930 and 1990. I'm grateful to Caroline Jean Acker for encouraging me to incorporate this change in exploring how the understanding of pain shifted. This demarcation forced both disciplines to define themselves as distinct from the other. Caroline Jean Acker, "Planning and Serendipity in the Search for a Nonaddicting Opiate Analgesic," in *The Inside Story of Medicines; A Symposium*, ed. Gregory J. Higby and Elaine C. Stroud (Madison: American Institute of the History of Pharmacy, 1997): 143; Caroline Jean Acker, "Take as Directed: The Dilemmas of Regulating Addictive Analgesics and Other Psychoactive Drugs," in *Opioids and Pain Relief: A Historical Perspective. Progress in Pain Research and Management, Vol. 25*, ed. Marcia L. Meldrum (Seattle: IASP Press, 2003): 35-55; Nancy D. Campbell. *Discovering Addiction: The Science and Politics of Substance Abuse Research* (Ann Arbor: The University of Michigan Press, 2007); Nathan B. Eddy and Everette L. May, "The Search for a Better Analgesic," *Science*, Vol. 181, 3 (August 1973): 407-414; Nathan B. Eddy, "The Search for New Analgesics," *Journal of Chronic Disease*, Volume 4, Number 1 (July 1956): 59-71; Nancy Campbell, J.P. Olsen, and Luke Walden, *The Narcotic Farm: The Rise and Fall of America's First Prison for Drug Addicts* (New York: Abrams, 2008); William L. White, *Slaying the Dragon: The History of Addiction Treatment and Recovery in America* (Normal, IL: Chestnut Health Systems/Lighthouse Institute, 1998), 260-1.

4. The basics of Beecher's and Bonica's stories have been described in numerous accounts. See Baszanger, *Inventing Pain Medicine*, 3, 65-66, 69; Marni Jackson. *Pain: The Science and Culture of Why We Hurt* (London: Bloomsbury, 2002), 274-277; Cervero, *Understanding Pain*, 14, 16, 133-134; Melzack and Wall, *Challenge of Pain*, 7, 26, 36, 239, 258, 263, 265, 275; Livingston, *Pain and Suffering*, xi-xiii.

examines how each pre-history challenged this marginality and the fundamental view of pain it was based on. Together, the activities sketched in the pre-histories helped spur the emergence of pain as a distinct clinical entity and a recognized specialty by articulating the clinical urgency of pain as a problem in its own right. The pre-histories show how an insurgent view of pain was more than a challenge to a Cartesian model. It met with resistance and skepticism in part because this concept of pain questioned a biomedical model of disease that emphasized the isolation of distinct, repeatable etiologies; consistent symptom profiles; predictable responses to therapies; and the possibility of cures that worked reliably across population groups and cultures. A notion of chronic pain as a defining and urgent set of clinical problems posed a fundamental challenge to a biomedical model's explanatory power.

The roots of pain's historical marginality extended much further back than 1900 and had several components. Among the earliest sources were enduring clinical quandaries, such as pain in the absence of illness or injury, as in headaches; the persistence of pain after cure or recovery; and the wide variability of reactions to comparable events and therapies. Across the 19th century, as mechanized technologies of warfare proliferated, medical interest in phantom-limb pain and causalgia, a severe, burning pain caused by injuries to nerves, attracted growing interest among clinicians. Phantom-limb pain and causalgia raised difficult questions about how the nervous system produced and perpetuated these conditions.[5]

5. Pain's marginality had led to its lack of appeal as a research focus prior to 1965, as described by several of the field's early leaders. Foley, Wall, and Crue Oral History interviews, UCLA Liebeskind History of Pain Collection; Merskey, "Some Features," 3-8; Joanna Bourke, "The History of Medicine as the History of Pain," *History Today*, Volume 61, Issue 4 (April 2011); Dormandy, *Worst of Evils*, 121; Melzack and Wall, *Challenge of Pain*, 147-165; Rey, *History of Pain*, 34; Patrick D. Wall. Pain: *The Science of Suffering* (New York: Columbia University Press, 2000). William Livingston was greatly influenced by the work of neurologist Silas Weir Mitchell, who had observed and written extensively on phantom-limb pain and causalgia based on his experiences during the American Civil War. Livingston's post-doctoral student, Ronald Melzack, recalled that Livingston could recite large sections of Mitchell's extensive writings almost by heart. See Livingston, *Pain and Suffering*, xi-xv.

At the same time, pain's resistance to replicable measurement made it clinically problematic. The ability to quantify bodily states in agreed-upon units, along with the quest to measure the effects of treatments, had become a hallmark of advanced biomedical science by the mid-20th century in the United States. As Chapter 2 shows, the inability to measure pain in a clinically replicable way did not hinder the creation and use of dozens of scales, tools, tests, and methods for assessing the intensities of pain, the effectiveness of analgesics, and the existence of innate bodily capacities that affected individual pain tolerance, thresholds, and responses to therapies. But a generalized scale or method for the assessment of pain foundered in the face of pain's variability.[6]

In addition, pain's ties to addiction had by 1945 created further obstacles to clinical engagement. In the United States the history of opiate use and its socio-chemical cousin, the use of pain relievers more widely, have been deeply entangled since the start of the 20th century. This history reveals a series of peaks in opiate use both within medical practice and beyond its purview (1900-1920, 1948-1960, 1971-1980). Each peak has spawned political activity and public policy debate over whether addiction was a social product or a character flaw, the outcome of circumstances or genetic slippage.[7]

---

6. Although the exact mechanisms are elusive, it seems plausible that the failure to measure pain definitively (at least as defined by clinicians) contributed to the ascent of a notion of pain as decisively subjective. See Donald D. Price and Stephen W. Harkins, "Combined Use of Experimental Pain and Visual Analogue Scales in Providing Standardized Measurement of Clinical Pain," *The Clinical Journal of Pain*, 3 (1987):1-8; Donald D. Price, Francis M. Bush, Stephen Long, and Stephen W. Harkins, "A comparison of pain measurement characteristics of mechanical visual analogue and simple numerical rating scales," *Pain*, 56 (1994): 217-226; Melzack and Wall, *Challenge of Pain*, 39-42, 260, 276, 278-9; C. Richard Chapman and John D. Loeser, ed., *Advances in Pain Research and Therapy, Volume 12: Issues in Pain Measurement* (New York: Raven Press, 1989); Harold Merskey, "The Perception and Measurement of Pain," *Journal of Psychosomatic Research*, Vol. 17 (1973): 251-255; Joanne Pearce and Stephen Morley, "An experimental investigation of the construct validity of the McGill Pain Questionnaire," *Pain*, 39 (1989): 115-121; Ian McDowell, *Measuring Health: A Guide to Rating Scales and Questionnaires* (Oxford: Oxford University Press, 2006), 483-491; Ronald Melzack, "The McGill pain questionnaire: major properties and scoring methods," *Pain* 1:3 (1975): 277-99; Ronald Melzack and Joel Katz. "Pain Measurement in Adult Patients," in Stephen McMahon, Irene Tracey, and Dennis C. Turk, ed., *Melzack and Wall's Textbook of Pain, Sixth Edition*. (New York: Elsevier, 2013), 305-314.

7. The persistence of deep social and clinical entanglement between pain relief and non-medical use of opiates is clear from historical analyses of opiate use in America. David T. Courtwright, *Dark Paradise: A History of Opiate Addiction in America* (Cambridge, MA: Harvard University Press, 2001); David T. Courtwright, *Forces of Habit: Drugs and the Making of the Modern World* (Cambridge, MA: Harvard University

Other attributes reinforced pain's marginality in several ways. By the middle of the 20th century, most clinicians understood pain as a reliable symptom of many conditions and the product of diverse procedures, Pain was a marker on the road leading to the target – identification of the root cause of a disease as indispensable to finding a cure. Pain was thus familiar in many disciplines, but as a symptom it lacked an organizational "home" within any one specialty as well as the clinical gravitas that dozens of diseases had attained. As late as 2011, a detailed profile of pain in America described treatment as having suffered from this lack of institutional "ownership" within medicine. Pain's status as a symptom thus had more than clinical effects. It impeded organizational activity and coherence as well as the establishment of pain as a distinct specialty.[8]

In addition, by the middle of the 20th century most American physicians understood pain to mean acute pain, that is, a largely predictable outcome of conditions and procedures. After 1900, success against acute pain had been considerable. The synthesis of heroin and aspirin in last months of 19th century in Germany had stimulated this progress. These advances against acute pain made the significance of chronic pain harder to convey within medicine. But in clinicians' offices, hospitals, and living rooms across America, chronic pain became more prevalent after World War II. The rise of chronic pain was driven by a large cohort of physically and psychologically wounded from two global wars, an aging population, and steady stream of

---

Press, 2001); Campbell, *Discovering Addiction*, 4-9, 12-28, 30, 32, 40, 66, 78; David F. Musto, *The American Disease: Origins of Narcotic Control, Third Edition* (Oxford: Oxford University Press, 1999). One way in which Courtwright has upended popular and historical perceptions of opiate use has been to show how, contrary to widespread belief among late-20th-century drug-policy reformers, heroin addiction had already started to decline by the 1914 passage of the Harrison Act, the first federal legislation to attempt regulation of opiates. Courtwright contended persuasively that by 1914 physicians had become increasingly wary of the dangers of opiate-based preparations and medically induced addiction.

8. Institute of Medicine, *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research* (Washington, DC: National Academies Press, 2011).

industrial and vehicular accidents. It was thus more than the beliefs and wartime experiences of clinicians that was turning chronic pain into urgent clinical issue.[9]

The growing importance of chronic pain in the post-World War II era would contribute to the erosion of pain's marginality within clinical medicine. The following pre-histories show how formative conditions for a change in pain's status had begun to take shape many decades prior to that war.

**Anatomy and Physiology after 1800 -- Pain as Complex**

Research in anatomy and physiology after 1800 helped erode pain's marginality by providing a biomedical foundation for a model of pain as complex, variable, individual, and chronic. This work loosened the dominance within medicine of a concept of pain as rote and well understood. After 1800, as neuroanatomy and physiology developed as experimental sciences, the nervous system became a defining intellectual challenge that expanded interest in pain. Across the nineteenth century, the demarcation of the central, peripheral, autonomic, and sympathetic sub-systems, as well as understanding of the different roles of various nerve fibers, the details of transmission mechanisms, and the modulation of noxious input within the spinal cord and brain gradually filled in a picture of pain as complex. The existence and mechanisms of ascending and descending pathways from the brain and spinal cord gradually came into view. These findings fueled debates about the roles and relative importance of the peripheral and central nervous systems as well as how the electrochemical workings of nerves, spine, and brain were turned into the perception and experience of pain. Scientists and clinicians within both camps perceived an inexorable pattern of increased complexity as a consistent and significant outcome of studies in anatomy and physiology. Complexity came to include the neurochemical encoding and modification of affective dimensions

9. The emergence of chronic pain as a defining medical issue was part of a broader trend in which chronic diseases moved to the forefront of clinicians' attention. See Baszanger, *Inventing Pain Medicine*, 72-79, 88-96, 190-191, 301-302; Joseph Earle Moore and David Seegal, editors, "Announcement," *The Journal of Chronic Diseases*, Vol. 1, No. 1 (January 1955): 1-11.

of pain; the active involvement of multiple areas and functions of the brain; the increasing differentiation and specificity of structure and function across the nervous system; and the inseparability of anatomical, physiological, chemical, and electrical dimensions within the experience and analysis of pain.[10]

These advances had quiet beginnings. In 1811, Scottish surgeon Charles Bell privately published a short pamphlet in which he described two types of nerve fibers. Motor nerves carried commands from the brain to muscles and other peripheral organs, while sensory nerves carried information from the body's periphery to the brain. In peripheral nerves the two fibers were often found together. Each took different routes through the spinal cord; Bell surmised that the sensory and motor tracts remained separate on their way to the brain. Bell and Francois Magendie identified the respective motor and sensory functions of the spine's ventral and dorsal nerve roots. The Bell-Magendie Law held that sensory nerves lead to the posterior roots of the spinal cord while motor nerves lead from the anterior roots. In addition, it was the posterior roots that conveyed sensation, including pain. Bell and Magendie had launched a project -- mapping motor and sensory structures and patterns in the nervous system -- that would occupy the rest of the nineteenth century, as anatomists and physiologists sought to describe perceptual events in sensory-motor terms.[11]

Across the nineteenth century, numerous researchers built on the work of Bell and Magendie to paint an increasingly dense picture of how the nervous system worked. Other discoveries included identification of the spine's dorsal horn in 1822 and, in the 1870s, findings on the role of pathways

10. Wall, Wellcome Seminar, 77-79; Keele, *Anatomies*, 103-135; William D. Willis, Jr., "Physiology and Anatomy of the Spinal Cord Pain System," in *Paths of Pain*, Merskey, Loeser, and Dubner, ed., 89; Patrick D. Wall, "Modulation of pain by nonpainful events," in *Proceedings of the First World Congress on Pain, Advances in Pain Research and Therapy, Volume 1*, John J. Bonica and Denise G. Albe-Fessard, ed., (New York: Raven Press, 1976), 1-16.

11. Pathologist and historian Thomas Dormandy noted that Bell had achieved this with no more than "the naked eye and the scalpel." See Dormandy, *Worst of Evils*, 301, 426; Keele, *Anatomies*,55, 63, 103-112, 124, 130, 156; Rey, *History of Pain*,162-165, 182-184, 190-192, 209, 162-165; Baszanger, *Inventing Pain Medicine*, 48.

from the spinal cord to the brain. Receptors specialized for the sensation of pain began to be isolated by the end of the 19th century, and increasingly detailed descriptions of the electrochemical duality of nerve impulses were being made by 1900. In the 1860s Emil duBois-Reymond described the electrochemical structure and function of the nerve impulse. He also designed the alagometer, which generated galvanic current and was the first device for measuring sensitivity to pain; duBois-Reymond used it to test the effect of various drugs on skin sensitivity. Theodore Schiff investigated spinal cord pathways, and Theodor Schwann examined the difference between nerve fibers and their covering, known now as myelin. Charles-Edouard Brown-Sequard mapped the pathways that nerve fibers and impulses took, showing how different conditions or events, such as stroke, could alter the course of nerves and nerve tracts in the central nervous system. Based on animal experiments and clinical observation, he argued that nerve fibers from the left side of the brain crossed to the right side of the spinal cord and vice versa.[12]

In 1840 Johannes Muller published his theory of specific sensory modalities, and, just as the gate control theory would 125 years later, Muller's ideas stimulated extensive research. Other investigators fleshed out a detailed theory of specific end organs, peripheral nerve fibers and nerve tracts that underlay perception of different sensations, including pain. Muller's doctrine of specific nerve energies asserted that each individual sensory mode (sight, hearing, etc.) depended on the stimulation of a particular form of nerve ending and was carried from these endings by corresponding nerves. Muller thus saw the ability to perceive the outside world as limited. What we took in through our senses was just that part for which we have the right sense organ. Muller's doctrine of specific nerve energies set a course for physiological research that was followed for

12. Research during the 19th century frequently sought to establish a physiological basis for Descartes's notion of pain as a reflex process within the nervous system. See Keele, *Anatomies*, 12, 64, 85; Doleys, *Pain: Dynamics and Complexities*, 17-22; Oral History Interview with Patrick Wall, John C. Liebeskind History of Pain Collection, Ms. Coll. No. 127.2, Louise M. Darling Biomedical Library, UCLA, Conducted August 10, 1993; Lewis, *Pain,* 11-22, 34-38; Milton J. Lewis, *Medicine and the Care of the Dying: A Modern History* (Oxford: Oxford University Press, 2007); Warren R. Nielson, "The Concept of Pain," *The Clinical Journal of Pain*, Vol. 17, No. 4 (Supplement 2001): S5-S7; Cervero, *Understanding Pain*, 136.

more than a century. Muller's theory raised a difficult question. If each of our senses had dedicated nerves, where were the sense organs for pain?[13]

In the 1890s physician Max von Frey was a critical figure in establishing the concept of a fixed neural substrate for pain that was firmly in place by the late 19th century. Von Frey proposed a rigid neurological architecture in which a direct link between sensations evoked from the skin and the type of nerve endings conveyed impulses as noxious or hurtful input. Von Frey mapped distinct areas of the skin as pressure, warmth, cold, and pain spots. He formulated laws of stimulation for pressure and pain and said pain was a special sense with its own dedicated network tied to a spot in the brain that managed that sensation. Von Frey's model greatly expanded Muller's concept of specific nerve energies. His ideas were a literal and influential interpretation of the doctrine of specific nerve energies and were the basis of specificity theories of pain.[14]

By the end of the 1800s, perspectives on how pain worked were dominated by this specificity model, following Muller and von Frey, which assigned specific receptors and pathways to pain. But discoveries about brain and spine function had also cleared epistemological space for a more inclusive notion of pain as a product of densely interwoven chemical and electrical workings of the nervous system. Growing detail about the structures and functioning of nerve fibers and cells made hard-wired specificity increasingly less plausible. To some researchers, the nervous system clearly did more than relay input that was untouched and unaffected. Some began to surmise that there were patterns in how noxious input was modulated and transmitted to produce sensations of discomfort and pain.

---

13. Anesthesiologist and historian Fernando Cervero has described Muller's theory as "one of the most significant developments in the scientific study of sensory perception." He wrote that the concept of specific nerve energies would launch "an intense search for the links between anatomical structures in the nervous system and sensory modes, amongst which pain was to play a prominent part." See Cervero, *Understanding Pain*, 36-38; Lewis, *Pain*, 34.

14. Von Frey "established pain as a special sense, defined by its special quality, and set it up definitely as something different from unpleasantness and the reactions that usually, but not always, accompany pain." Cervero, *Understanding Pain*, 39-40; Keele, *Anatomies*, 132.

Physiologist Alfred Goldscheider and others advanced a belief that the spinal cord and brain were crucial in aggregating and modulating painful stimuli and organizing the body's response. This break with specificity theory led to pattern theories of pain and was originally stated by Goldscheider in 1894. He stressed the importance of the intensity of a stimulus, as well as integrative and aggregative activities by the central nervous system, as crucial to the pain experience. Goldscheider's study of tabes dorsalis, a condition that affected late-stage syphilis sufferers, convinced him that patterns of nerve impulses that lead to pain were produced by summation of peripheral sensory input at the dorsal horn in the spinal cord. Pain was the outcome of noxious stimulation that exceeded a threshold level and that followed excessive stimulation of receptors that were normally fired by non-noxious heat or touch stimuli or by pathological conditions that enhance the aggregation of inputs produced by normally non-hurtful stimuli. Goldscheider's approach led to other theories, such as Livingston's central summation theory, proposed in 1943, that was founded on the premise that specific central neural mechanisms aggregated noxious stimuli. Given what Goldscheider considered a lack of evidence for a one-to-one relationship between pain perception and the intensity of the stimulus, he argued that the sensation of pain resulted from special patterns of stimuli intensity and interpretation in the brain. Pain resulted when the total output of the skin's sensory cells exceeded a critical level."[15]

A neurophysiological basis for aggregation and summation of stimuli by the nervous system was articulated by neurophysiologist Charles Sherrington. In 1900 he had defined pain as a psychical dimension of a built-in reflex designed to protect the body. Building on the findings of Bell and Magendie, he traced pathways between muscles and the spinal cord to the brain and back. Sherrington's studies led to two conclusions that questioned a rigid, straight-through model of how the body responded to harmful input. First was his concept of the brain as a progressively complex

15. Perl, "Ideas about History of Pain," 72; Dormandy, *Worst of Evils*, 399-403; Keele, *Anatomies,* 103, 108-113, 119, 130-134, 141, 156, 183, 184; Cervero*, Understanding Pain*, 2-4; Bourke, *Story of Pain*, 10; Lewis, *Pain*, 3-12; Baszanger, *Inventing Pain Medicine*, 51. Kotarba, *Pain: Psychological Dimensions*, 30.

structure built of increasingly dense networks of nerve cells that communicated across synapses – a word he had coined. For Sherrington even simple voluntary and reflex actions were thus profoundly complex events. In addition, he conceptually separated pain processing from its interpretation. At the start of the 20th century, Sherrington spelled out an alternative to specificity theory that was the basis of a challenge to a prevailing pain model. He put the brain at the center of the pain experience and proposed inherent complexity in the structures and processes of the nervous system. In separating the physiological processing of noxious stimuli from how those were perceived and experienced, Sherrington accorded conceptual and operational equality to physiology and psychology in his model. The processing of painful stimuli could take place at numerous points within the nervous system, with pain perception guided by the involvement of numerous sectors of the brain, including those that were involved in affective and emotional dimensions of experience. Sherrington's was an early challenge to a notion of the nervous system as predicated on fixed hardwiring. He thus anticipated a broader challenge to specificity theory in the modeling of how pain worked.[16]

**Anesthesiology, 1900-1945 -- pain as a clinical focus**

The development of anesthesiology as a medical discipline contributed to the erosion of pain's marginality in two main ways. Clinical and scientific developments, including new anesthetic agents and techniques, expanded the discipline's engagement with pain beyond pre- and post-surgery to encompass the management of chronic pain. In addition, organizational activities, starting in 1905, helped create professional networks and define the clinical content of the specialty. The combined effect of these developments was to launch a reconceptualization of pain within anesthesiology. More than 70 years before the American Board of Anesthesiology (ABA) certified the first group of physicians in pain medicine in 1993, anesthesiologists had begun to

16. Dormandy, *Worst of Evils*, 399-403; Rey, *History of Pain*, 279, 294, 297-298; Lewis, *Pain*, 3-12.

define a specialty in which pain featured prominently. The development of anesthesiology as a bounded discipline helped refashion pain as a distinct syndrome characterized by variability, diverse presentations, and inconsistency in the effects of comparable or identical therapies.

After its introduction in 1846, anesthesiology had developed as an adjunct of surgery, and before World War I procedures were limited, simple, and usually performed by a surgical intern or an operating nurse. The war had created a large number of chronic pain patients, many of whom were enduring physical and emotional trauma, and clinicians felt the need to develop better treatments. The war stimulated the use of nitrous oxide and oxygen as anesthetic agents, and in the 1920s the development of gas, local, and spinal anesthesia expanded the field. Articles published during the 1930s by [Ernest] Woodbridge, Henry Ruth, and Emery Rovenstine posited the importance of pain to the practice of anesthesiology. After 1920, anesthesiology addressed shifting clinical definitions, new technologies and methods, accumulating research findings, and sometimes unclear boundaries of practice and its management. These activities anticipated a path that pain medicine would both take and leave in becoming a medical entity.[17]

As in the history of pain, what became a large "field" started in the concerns and interests of a small number of clinicians. In October 1905 nine physician-anesthetists met at the Long Island College Hospital at the invitation of Dr. A. Frederick Erdmann. This group became the New York

17. Harold R. Griffith, "History of the World Federation of Anesthesiologists," *Anesthesia & Analgesia* 42 (1963):389-397; Labat, "Regional Anaesthesia," 165-169; Surjya Sen, David P. Martin, Douglas R. Bacon, "Exploring Origins: Was John Bonica's Model of Modern-Day Pain Management Influenced by John Lundy's Earlier Work?" *Regional Anesthesia and Pain Medicine*, Volume 32, Number 3 (May-June 2007): 258-262; "ABA Timeline," from The American Board of Anesthesiology web site, www.theaba.org/ABOUT/Test-History, accessed 9-19-15; Keith Sykes with John Bunker, contributing ed., *Anaesthesia and the Practice of Medicine: Historical Perspectives* (London: The Royal Society of Medicine Press, 2007), 97; Philip D. Woodbridge, "Therapeutic Nerve Block with Procaine and Alcohol," *American Journal of Surgery* (August 1939): 278-288; Henry S. Ruth, "Diagnostic, Prognostic and Therapeutic Nerve Blocks," *The Journal of the American Medical Association*, Vol. 102, No. 6 (February 10, 1934): 419-425; E. A. Rovenstine and H. M. Wertheim, "Therapeutic Nerve Block," *The Journal of the American Medical Association*, Vol. 117, No. 19 (Nov. 8, 1941): 1599-1603.

Society of Anesthetists in 1911, by which time there were 23 members. By 1916 there were more frequent meetings, clinically and business oriented, in New York hospitals.[18]

After 1920, new techniques and chemical agents, such as lidocaine, created opportunities in pre- and post-operative pain and spurred the growth of anesthesiology groups. In 1919, Frances H. McMechan founded the National Anesthesia Research Society, and in 1925 its name was changed to the International Anesthesia Research Society. In 1922, the first issue of its journal, Current Researches in Anesthesia and Analgesia, was published. The Boston Society of Anesthetists was founded in 1920, and in the same year the California State Medical Association recognized a Section on Anesthesia. The Southern Association of Anesthetists and the Pacific Coast Society of Anesthetists were formed in 1922. The Eastern Society of Anesthetists made its debut in 1923, as did the American Society of Regional Anesthesia, with the latter founded to honor French neurologist Gaston Labat.[19]

Labat and his students were central figures in anesthesiology after 1920. Labat's techniques and his textbook, published in 1922, were promoted in his travels in the US and became a touchstone of regional anesthesia for his students, including John Lundy, Rovenstine, and Ralph Waters. Charles Mayo had recruited Labat to the Mayo Clinic to teach methods that had been pioneered in Europe. In 1924 Lundy became head of division on regional anesthesia at the Mayo Clinic, where he developed a three-month training course.[20]

---

18. History of Anesthesiology Reprint Series, Vol. 26: *Anesthesia Organizations* (Park Ridge, IL: American Society of Anesthesiology, 1999); C. Ronald Stephen, "Anaesthetists' Travel Club, 1929-1952: An Historical Review," (St. Louis: Academy of Anesthesiology, 1992); Albert M. Betcher, "Historical Development of the American Society of Anesthesiologists, Inc.," in P. P. Volpitto and L. D. Vandam, ed., *The Genesis of Contemporary American Anesthesiology* (Springfield, IL: Charles C. Thomas, 1982), 85-121.
19. History of Anesthesiology Reprint Series, Anesthesia Organizations, 1999; Douglas R. Bacon, "Gaston Labat, John Lundy, Emery Rovenstine, and the Mayo Clinic: The Spread of Regional Anesthesia Between the World Wars," *Journal of Clinical Anesthesia* 14 (2002): 315-320.
20. Michel Y. Dubois and Kenneth A. Follett, "Pain Medicine: The Case for an Independent Medical Specialty and Training Programs," *Academic Medicine*, Vol. 89, No. 6 (June 2014): 863-868; M. Swerdlow, M. D. Mehta,

During the 1930s anesthesiologists debated the contours of a specialty and worked for recognition by the AMA. The now-New York Society of Anesthetists convened a two-day conference in 1930 to mark the group's 25th anniversary. In 1936 the organization became the American Society of Anesthetists, and over the next decade it led joint meetings with state groups in Connecticut, Texas, Ohio, and New England. In 1936 the American Society of Anesthesiologists authorized Lundy to work with the AMA for recognition of anesthesiology as a specialty. Lundy had long been working for such recognition and for a Section on Anesthesia within the AMA. This effort was hampered by the unwillingness of other organizations, such as the Associated Anesthetists of the United States and Canada and the International Anesthesia Research Society, to submit statements supporting the recognition of anesthesiology as a specialty. In 1937 a group from several societies of anesthetists met with people from the AMA's Section on Surgery with the goal of creating an organization that would certify doctors in their practice of anesthesiology. The American Board of Anesthesiology formed in 1937. Over the next four years the Advisory Board for Medical Specialties and the AMA's Council on Medical Education recognized ABA as an affiliate of the surgery board and as a separate primary board. In June 1940 the AMA formally recognized anesthesiology as a specialty.[21]

While new chemical agents and techniques opened clinical space and organizational opportunity for physician anesthesiologists, the inability of multiple groups in the late 1930s to support a single effort at recognition by the AMA suggested deeper divisions in the field. The efforts of Lundy and others sought to establish anesthesiology as a discipline by bringing the practice within the

---

and S. Lipton, "The role of the anesthetist in chronic pain management," *Anaesthesia*, Volume 33 (1978):250-257.

21. This description does not cover the impact on anesthesiology of efforts in the first decades of the twentieth century to establish standards and procedures for what comprised a specialty within American medicine. See Betcher, "*Historical Development*," 191-194 in *History of Anesthesiology Reprint Series, Vol. 26*; Rollin M. Gallagher and Scott M. Fishman, "Pain Medicine: History, Emergence as a Medical Specialty, and Evolution of the Multidisciplinary Approach," in *Neural Blockade in Clinical Anesthesia and Pain Medicine, Fourth Edition*, Michael J. Cousin et al., ed. (Philadelphia: Wolters Kluwer/Lippincott William & Wilkins, 2009): 633.

purview of licensing and credentialing bodies within the profession. This strategy sought to address several challenges to physicians' exclusive rights to practice anesthesiology. In addition to ongoing efforts to win professional standing with hospital administrators and surgeons, there was contention with nurse anesthetists, who were established as helpers to surgeons and were frequently better trained and more experienced in administering anesthesiology than the average physician. To some, physician anesthetists seemed unnecessary. Nurse anesthetists formed a national association in 1932, while medical anesthetists formed the American Society of Anesthetists in 1935. The AMA's position was that only physicians and dentists should provide anesthesia, but it knew that enforcement was problematic. Through the 1930s nurse anesthesia continued as direct competition to physician anesthesiologists.[22]

The history of anesthesiology between 1900 and 1940 helped create conditions for the refashioning of pain's marginality that would coalesce after 1945. Efforts to define a specialty through organizational development, collaboration, and competition helped organize clinical and research debates in a field that was increasingly addressing pain as a discrete clinical entity. Publications, meetings, and advocacy helped produce networks and structures of professional self-management in a medical discipline in which pain was a distinct, and growing, focus.

**Studying pain and addiction, 1929-1945 -- the intersection of science and commerce**

Between 1929 and 1945 a research collaboration of the federal government, academia, and the philanthropic/business community challenged pain's marginality through the scope and duration of its research, its nurturance of professional networks, and its establishment of scientific foundations for pain relief as a large commercial endeavor, advanced the clinical demarcation of

22. Bacon, "Labat, Lundy, and Rovenstine," 315-318; Rosemary Stevens. *American Medicine and the Public Interest, Updated Edition with a New Introduction* (Berkeley: University of California Press, 1998), xxiv, 255-257. Stevens noted an "increased focus on recognition and treatment of pain and suffering as problems to be dealt with as a normal part of the medical encounter" as part of a changing landscape in American medicine after 1970.

pain management and addiction medicine, and expanded the arsenal of opium-based pain relievers. The research focus was the relationships between morphine's molecular structure and its functional mechanisms for the mitigation of pain and the creation of physical and psychological dependence and addiction. An important locale for the testing of prospective analgesics as well as a wide array of pharmaceutical and "street" drugs was the Addiction Research Center (ARC) at the federal narcotics prison in Lexington, Kentucky, which opened in 1935. While much consequential work that grew out of this collaboration took place after 1945, such as the first testing of methadone, the ARC's first decade was an important pre-history to pain's transformation.[23]

In 1929, the National Research Council (NRC), which had been established during World War I to coordinate war-related research, merged its Committee on Pharmacological Research with the Committee on Drug Addiction, which was part of the Bureau of Social Hygiene, a Rockefeller-funded organization. The Bureau offered a three-year grant of US$286,000 for the NRC to lead a study of opiate addiction. The NRC's goal was to identify and test compounds for pain-relief capability and toxicity, as well as to figure out how to detach the pain-relief capability, structurally and functionally, from the molecule's ability to engender dependence and addiction.[24]

---

23. Caroline Jean Acker and Nancy Campbell have led the exploration of the ways in which, in Acker's words, "concerns about opiate addiction as a social problem [in the early decades of the twentieth century] created an opportunity for the advancement of drug development pharmacology in the United States." See Caroline Jean Acker, "Addiction and the Laboratory: The Work of the National Research Council's Committee on Drug Addiction, 1928-1939," *Isis*, Vol. 86, No. 2 (June 1995): 167-193.

24. Nancy Campbell's study is an excellent portrayal of the importance of this work in creating what she called "overlapping networks of pain and addiction research." See Campbell, *Discovering Addiction*, 15; Keele, *Anatomies*, 103, Dormandy, *Worst of Evils*, 32, 169; Rey, *History of Pain*, 121, 135; Nathan B. Eddy and Everette L. May, "The Search for a Better Analgesic," *Science*, Vol. 181, (3 August 1973): 407-414; Nathan B. Eddy, "The Search for New Analgesics," *Journal of Chronic Disease*, Volume 4, Number 1 (July 1956): 59-71; Caroline Jean Acker, "Planning and Serendipity in the Search for a Nonaddicting Opiate Analgesic," in Gregory J. Higby and Elaine C. Stroud, editors, *The Inside Story of Medicines; A Symposium* (Madison, WI:: American Institute of the History of Pharmacy, 1997), 143; Caroline Jean Acker, "Take as Directed: The Dilemmas of Regulating Addictive Analgesics and Other Psychoactive Drugs," in *Opioids and Pain Relief: A Historical Perspective. Progress in Pain Research and Management, Vol. 25* ed. Marcia L. Meldrum (Seattle: IASP Press, 2003), 35-55; Caroline Jean Acker, "From All Purpose Anodyne to Marker of Deviance: Physicians' Attitudes Towards Opiates in the US From 1890 to 1940," in *Drugs and Narcotics in History,* Roy Porter and Mikulas Teich, ed., (Cambridge: Cambridge University Press, 1995), 114-132.

The NRC hired Lyndon F. Small, an organic chemist at Harvard who had worked in the Munich lab of Heinrich Wieland on the chemistry of opium alkaloids, to lead this work. Small and the NRC arranged with the University of Virginia, where Small taught, to set up a lab. The team set an ambitious course. They studied the complete set of structural variations on the morphine molecule and identified a range of physiological effects these compounds produced in animals. In Ann Arbor, Michigan, pharmacologist Nathan B. Eddy's group tested compounds produced in Small's lab for therapeutic and toxic effects, including addiction potential. Between 1929 and 1939, the Committee coordinated the study of more than 150 derivatives of morphine and more than 300 synthetic products at the universities of Michigan and Virginia. Small worked on the morphine molecule, breaking it down and adding new groups at different places to create new derivatives; Erich Mosettig focused on synthetic derivatives of morphine, starting with phenanthrene, a coal-tar product that matched the structural core of morphine.[25]

As the NRC project unfolded, a third critical link in this research chain began operations. In 1929 Congress authorized construction of two "narcotics farms," and in 1932 groundbreaking took place in Lexington, Kentucky. Lexington opened in 1935, and a "sister" facility in Fort Worth, Texas joined it two years later. The federal narcotics prisons brought physicians, scientists, and support staff together with thousands of former and current addicts, a selectively winnowed population of experienced and frequently articulate chroniclers of diverse drug experiences, for wide-ranging basic research and drug development focused on addiction and pain. After 1929, promising compounds developed in Small's lab were tested at a federal prison annex at Ft. Leavenworth, Kansas; after 1935, this activity switched to Lexington. Over the next four decades Lexington was a trial site for dozens of pharmaceutical and street drugs, including propoxyphene (the chemical

25. The testing of compounds for potentially addictive properties was far from an established procedure. Acker has noted that "there was no known reliable method for determining whether a drug was addictive before launching it into medical practice." See Acker in Higby and Stroud, *Inside Story*, 143; Eddy and May, "Search for a Better Analgesic," 409.

heart of Darvon). Its clients and partners included the United States government, pharmaceutical firms, and the United Nations. By the mid-1950s, Lilly, Merck, Squibb, Wyeth, Schering, and others had studied barbiturates, mescaline, heroin, alcohol, codeine, methadone, Miltown, LSD, Demerol, and many others at the arc.[26]

The "narcotic farm," set on a thousand acres outside Lexington, embodied the activism and ambition of the early New Deal. Its goals were to effect the social rehabilitation of America's drug addicts and to find a permanent cure for drug addiction. One impetus was the growth of the population of addicts between 1900 and 1930, a consequence of the enforcement of the Harrison Act of 1914, several legal decisions on enforcement of the Act, and the closure of maintenance clinics in New York and other urban centers after 1923. "Narco," as it was known by locals, was a blend of a prison and hospital to which some people committed themselves voluntarily. It brought together a diverse collection of people united by their experience with drug addiction. It housed jazz musicians (who practiced and performed for other inmates), doctors and nurses, street hustlers, prostitutes from cities across America, and "drugstore cowboys" who had run afoul of a growing roster of synthetic forms of morphine such as Dilaudid.[27]

The ARC never lacked willing and qualified research subjects. About a half dozen Public Health Service doctors worked there. Early studies questioned prevailing concepts of addicts and

---

26. Campbell's study is one of the few historical forays into a rich convergence of science, medicine, and law enforcement that evolved over almost 40 years. There was a state narcotics prison in California, at or called Spadra, during the 1950's; my own efforts to locate further data on this prison have so far been unsuccessful. Campbell, *Discovering Addiction*, 81, 91; Nancy D. Campbell, JP Olsen, and Luke Walden, *The Narcotic Farm: The Rise and Fall of America's First Prison for Drug Addicts* (New York: Abrams, 2008), 12, 15; US Department of Commerce Report #981, 1946; Tom Carnwath and Ian Smith, *Heroin Century* (New York: Routledge, 2002), 41, 57; Alfred W. McCoy, *The Politics of Heroin: CIA Complicity in the Global Drug Trade, Revised Edition* (Chicago: Lawrence Hill Books, 2003).

27. The work of Campbell and her co-authors on the Lexington facility is a fascinating chapter in the intersection of medicine and public policy. A stint at Narco "became a rite of passage for countless young addicts as well as the central gathering place for America's growing drug subculture." Many of the research practices employed at Lexington were outlawed after the early 1970s. The authors note that "medical research on prisoners was both legal and common in America in the 1930s through the 1960s, and the ARC's practices, publicized in newspapers, magazines, top-flight scientific journals, and on television, went virtually unquestioned by the general public." See Campbell, Olsen, and Walden, *Narcotic Farm*, 12-15, 23.

addiction, namely that addicts were less intelligent and more psychopathic than other people and that physical features conveyed clues as to who would become addicted and who wouldn't. Researchers came to understand that standard portrayals of drug addicts as hapless "dope fiends" were often oversimplified and inaccurately negative. Numerous research subjects were articulate and thoughtful about which drugs they liked and why. They talked about their lives before jail and their involvement with drugs, their backgrounds, and the paths that had led them to Lexington. Researchers were fascinated by these stories for the insights they gave about the cultural, sociological, and psychological dimensions of a social group that, in the middle decades of the twentieth century, was still little-known and poorly understood. These encounters led researchers to ask why and how some people became addicted and not others. Was it "wiring," circumstances, or some hybrid of them? Why was relapse so common?[28]

The goals of the ARC extended beyond the roots and forms of individual addiction; researchers saw themselves as performing an important public health function. The testing of new and known compounds sought to keep addictive compounds from reaching the market and medical practice. Heroin was the threat to public health that drove the ARC's work in pre-market testing in an era before clinical trials were standard or required. Darvon, Demerol, Dilaudid, and Miltown, as well as preparations that contained codeine, barbiturates, and amphetamines, were among the hundreds that ARC researchers investigated. Over its entire career of four decades, inmates volunteered for experiments involving hundreds of famous, obscure, and work-in-progress drugs. Another important goal had motivated research since morphine had been isolated in the first years of the

28. Harris Isbell, et al., "Studies on Lysergic Acid Diethylamide (LSD-25)." Part 1, "Effects in Former Morphine Addicts and Development of Tolerance during Chronic Intoxication," *Archives of Neurology and Psychiatry* 76 (1956): 468-478. One of the less savory legacies of Lexington were unimaginably long exposures to high doses of powerful drugs that some of the experiments entailed. One study kept a subject on on-and-off weekly cycles of LSD for almost three months. See Campbell, *Discovering Addiction*, 165. Even adjusting for less refined photographic technologies in the 1950s, images of the Lexington facility are both stark and expansive. The shots of research in progress convey a stark, no-frills atmosphere, with few distractions. At the same time the facility appears to have spacious grounds and a warm layout. See Campbell, Olsen, and Walden, *Narcotic Farm*, 15-22, 33, 148-149.

nineteenth century: to find a painkiller with morphine's analgesic power but without its addictive properties.[29]

Coordinated research on morphine's and its derivatives' analgesic and addictive properties contributed significantly to the pre-history of pain's clinical transformation. This effort expanded knowledge of morphine's properties, accelerated development of pain relievers, and stimulated the growth of professional research networks among academic centers and government facilities. This work advanced the articulation of pain management as distinct from addiction medicine while it strengthened the interest and commitment of the pharmaceutical industry to pain relief as an attractive market.

**Roots of leadership and direction, 1941-1945 -- pain as a professional entity**

The wartime experiences of anesthesiologists John Bonica and Henry Beecher, as well as surgeon William Livingston, helped undermine pain's marginality by providing theoretical and organizational leadership, structure, and direction to a challenge to pain's clinical status and understanding among their colleagues. Their experiences during the war convinced them of the urgent need for their profession to re-think an elemental issue and for colleagues to question their assumptions and beliefs about pain. All three came to appreciate the clinical value of bringing different medical perspectives to bear on pain's treatment. The war catalyzed the ability and commitment of Bonica, Beecher, and Livingston to shape an insurgent model of pain as defined by

29. The ARC was at the center of a "government program to evaluate the addiction potential of new pharmaceuticals so that addictive drugs could be kept off the market or legally controlled." After 1945 scientists at the ARC worked with the US government, the United Nations, the World Health Organization, and non-US governments in sharing data on the abuse potential of diverse substances. Other post-war studies included the first tests on methadone in a 1948 trial involving 115 men. As Congressional investigations in the 1970s would reveal, another was the extensive testing of LSD, with direct collaboration of the CIA, which was interested in the chemical as a potential "truth serum" and Cold War weapon. See Campbell, Olsen, and Walden, *Narcotic Farm*, 25-29, 164. Starting points for a more complete history of LSD include Jay Stevens, *Storming Heaven: LSD and the American Dream* (New York: Grove Press, 1987), and Martin A. Lee and Bruce Schlain, *Acid Dreams: The Complete Social History of LSD; The CIA, the Sixties, and Beyond* (New York: Grove Weidenfeld, 1985).

chronicity, variability, and the impact of personal dimensions and psychological dynamics. They provided conceptual and organizational leadership to pain treatment becoming more multidisciplinary, integrated, inclusive, and personalized. All were influenced by the enormous number and diversity of painful conditions that the war presented.[30]

At a 7700-bed hospital at Fort Lewis in Washington state, John Bonica was called to the operating room several dozen times on a typical day. As staff doctor in charge of pain control, Bonica encountered a staggering array of wounds, and he frequently consulted colleagues in various specialties on an assortment of cases. He came to believe that an interdisciplinary approach gave the best hope of effective treatment. For Bonica, diverse perspectives were not a hindrance; what impeded progress were difficulties in collaborating across specialties. Fort Lewis was where Bonica's belief in the value then in the necessity of multidisciplinary treatment approaches to combat pain's diversity, mutability, and persistence.[31]

Bonica was born in Italy in 1917, and his family came to the United States in 1924. When his father died eight years later, Bonica's financial situation became tenuous. He took numerous jobs to help finance his medical studies, including work as a professional wrestler under the name Johnny (Bull) Walker. Bonica became light-heavyweight champion of Canada in 1939 and World Champion in 1941. His unorthodox preparation for a career in medicine would turn out to be relevant. The wrestling injuries Bonica endured turned into chronic joint and muscle pain, for which he

30. Beecher would go on to do significant work in the development of the double-blind, randomized clinical trial as well as in medical ethics, while Bonica hewed closely to his focus on pain. See Henry K. Beecher, "Ethics and Clinical Research," *New England Journal of Medicine* 74 (1966): 1354-1360, and Henry K. Beecher. *Research and the Individual* (Boston: Little, Brown, 1970); Baszanger, *Inventing Pain Medicine*, 2, 3-5, 13, 58; Campbell, *Discovering Addiction*, 45, 81-85.

31. John Bonica, *The Management of Pain* (Philadelphia: Lea and Feibiger, 1953), 5; John J. Bonica et al., editors, *Advances in Pain Research and Therapy, Volume 1: Proceedings of the First World Congress on Pain* (New York: Raven Press, 1976), xxvii-xxx.

underwent nerve blocks and other procedures throughout his life. His travails, along with what he saw his wife endure in childbirth, impelled Bonica to study pain with ferocious energy.[32]

He had been trained to use nerve blocks in relieving pain of various kinds, and they were an important part of what he did at Fort Lewis. After several weeks of managing 11 operating rooms with two nurses and some corpsmen with no medical training, he recalled hearing from Emery "Rovie" Rovenstine about the capabilities of regional anesthesia in mitigating pain, and Bonica slowly added these procedures to his arsenal. Bonica also served under surgeon Joel Deuterman, who had trained at the Mayo Clinic with John Lundy, and Deuterman's background in regional anesthesia may have influenced Bonica. After the war Bonica's views continued to evolve to appreciate both the limits of nerve blocks and the efficacy of other methods, including behavioral and cognitive therapies, acupuncture, hypnosis, and relaxation.[33]

After the war Bonica wrote *The Management of Pain* (1953), a 1500-page book that reflected his increasingly expansive views on pain management and that would help define the field in the post-war era. It conveyed an inclusive model of pain by including a range of treatments, such as behavioral methods, hypnosis, and physical medicine, alongside extensive discussions of therapeutic nerve blocks and surgical remedies for pain. The book called for multidisciplinary approaches to treatment as crucial in addressing pain's many forms and origins. Two decades later Bonica founded and drove the launch of the International Association for the Study of Pain (IASP). His wartime experiences in a massively crowded operating theater were the roots of his

32. Sykes with Bunker, contributing ed., *Anaesthesia and the Practice of Medicine,* 90-103.
33. Surjya Sen, David P. Martin, and Douglas R. Bacon, "Exploring Origins: Was John Bonica's Model of Modern-Day Pain Management Influenced by John Lundy's Earlier Work?" *Regional Anesthesia and Pain Medicine*, Volume 32, Number 3 (May-June 2007): 258-262.

commitment to the multidisciplinary treatment of pain and his lifelong belief that his profession had neglected pain, especially in its chronic forms.[34]

Henry K. Beecher was born in 1904 in Peck, Kansas. His family name was Unangst, but when he learned that he was descended from theologian Henry Ward Beecher and Harriet Beecher Stowe, author of Uncle Tom's Cabin, he began to use Beecher as his family name. In 1928 Beecher enrolled in Harvard Medical School, where he trained as an anesthesiologist. He graduated in 1932, and in 1933 he started two years' residency with Edward Churchill, professor of surgery at Harvard and on staff at Massachusetts General Hospital. In 1935 Beecher traveled to Denmark to work in the physiology laboratory of Nobel Laureate August Krogh.[35]

Churchill and Beecher served in Italy in 1944 and 1945. As wounded soldiers arrived at the medical tent, Beecher would ask if they wanted help for their pain. To his astonishment, many soldiers, including a third of the most grievously wounded, declined. This did not fit with what Beecher and his medical-school generation had been taught, which was that pain varied directly with the severity of an organic injury.[36]

Beecher began to track soldiers' responses to his offers of pain relief, and in 1946 he published an article based on his wartime experience. Among seriously wounded soldiers who were questioned within 12 hours of receiving their wounds, 25 percent reported only slight pain and 32 percent reported no pain at all. He concluded that the idea that pain varied directly with the extent of a wound had to be reconsidered. Beecher postulated a critical role for circumstances and attitudes in shaping individual responses to pain. In highlighting the role of situational and personal factors in the pain experience, Beecher questioned the universality of a biomedical model

34. Bonica, *Management of Pain*, 5-18.
35. Baszanger, *Inventing Pain Medicine*, 50, 55, 57; Campbell, *Discovering Addiction*, 90-98; David B. Morris., *The Culture of Pain: Illness in the Postmodern World* (Berkeley: University of California Press, 1988), 42-43.
36. Baszanger, *Inventing Pain Medicine*,50, 55, 57; Cervero, *Understanding Pain*, 133-134; Marcia L. Meldrum, "A Capsule History of Pain Management," *Journal of the American Medical Association*, Vol. 290, No. 18 (November 12, 2003): 2470-2475.

in understanding and treating pain. Soldiers wounded in Italy had been injured but had also been removed from extreme danger, anxiety, and fear. Their release from combat seemed to mitigate the physical effects of their painful wounds. Beecher's observations were an early statement of the centrality of meaning and context in the experience of pain. He came to believe that what people perceive as pain emerged from the coordinated interplay of multiple organic, psychological, and social factors. Beecher's 1946 article, in which he described his experiences at Anzio and what he felt they meant, expressed a key element of the post-war challenge to a prevailing model of pain. His elevation of individual and environmental factors in the personal reaction to organic damage opened a conceptual door to the integration of physical and psychological dimensions in explaining pain and in treating it. Beecher did not theorize on the implications of his ideas. He left that to dozens of clinicians and scientists who would take the lead he had provided.[37]

On his 50th birthday in October 1942, surgeon and University of Oregon professor of surgery William K. Livingston received two telegrams; one from publisher Macmillan saying that his book had been accepted for publication, and the other from the Surgeon General's office ordering him to report for duty at the Oakland Naval Hospital, where he served for the entire duration of the war. He was initially assigned to general surgery and was in charge of a 40-bed ward and had very little contact with peripheral nerve cases. He slowly began to see more cases of major and minor causalgia. As he went through the galley proofs of his book, some of which covered cases similar to those that Silas Weir Mitchell had seen during the Civil War, Livingston found himself wrestling with three particular cases that one of his great teachers would have recognized at once.[38]

During World War II Livingston's work at an Oakland, California naval hospital brought him into contact with hundreds of wounded soldiers who were in pain. He found that the experiences of his

37. Henry K. Beecher, "The Pain of Men Wounded in Battle," *Annals of Surgery* 123:1 (1946): 96-105; Campbell, *Discovering Addiction*, 90-98; Baszanger, *Inventing Pain Medicine*, 40-53.
38. Livingston*, Pain and Suffering,* 94-98.

patients with nerve injury did not fit well with his understanding of pain, and he began to look for other concepts. He explored ideas about neuromodulation, inhibition and gating, and the temporal, spatial and summation patterning of stimuli. He kept meticulous records as he tried to categorize patterns and anomalies in what he saw. In 1943 he brought together these observations in Pain Mechanisms. Like Beecher and Bonica, he was puzzled by the diversity of conditions that confounded what he thought he had learned in medical school. Livingston proposed the existence of nervous-system mechanisms to account for the observed aggregation of pain impulses in conditions such as trigeminal neuralgia and phantom limb pain. He believed that irregular patterns of nerve "firings" led to unwanted reverberating circuits in the dorsal horns of the spinal cord. These circuits sent messages to the brain that produced pain.[39]

Livingston was working through these issues while he was surrounded by immediate clinical challenges that rivaled what Bonica was seeing in scope and complexity. The capacity of the Oakland Naval Hospital expanded rapidly and soon reached 12,000 beds. It was one of four naval centers designated for the study and treatment of peripheral nerve injuries, and the staff soon included general surgeons, neurosurgeons, neurologists, psychologists, and "intern" equivalents in nerve surgery. They kept detailed records on all their patients beyond the standard hospital records and made punch cards for all the cases; in 1966 Livingston could consult almost 1300 of these detailed case histories, more than 900 of which were cases of nerve injury due to wounds from high-velocity missiles. Livingston concurred with Beecher in his assessment of a gap between what his training had led him to expect and what he was seeing. A strict correlation between the severity of a wound and the pain experienced by their victims simply did not exist, even though

39. Livingston's ideas are descended from Goldscheider's earlier depiction of pattern theories of pain, that is, models that stress the interactions of different cell types, brain areas, and neurochemicals in shaping a person's responses to painful stimuli. Specificity theory is the corresponding term for models that emphasize hard-wired, straight-line mechanisms that Livingston and others contested. See Melzack and Wall, *Challenge*,158-160; Chris J. Main and Chris C. Spanswick, *Pain Management: An Interdisciplinary Approach* (Edinburgh: Churchill Livingstone, 2000), 7; John J. Bonica, "Pain research and therapy: past and current status and future needs," in *Pain, Discomfort and Humanitarian Care*, LKY Ng and John J. Bonica, ed., (New York: Elsevier-North Holland, 1980), 1-46; Reynolds and Tansey, editors, 2004, xx.

peripheral nerves were among the most sensitive in the body. There had to be other factors that shaped what people perceived.[40]

These four pre-histories – neurophysiological research, the development of anesthesiology, a research collaboration, and the experiences of several clinicians -- are creation stories in a basic shift in the clinical status of pain took place after 1945. The pre-histories describe the creation of scientific, clinical, professional, and organizational conditions that led to a refashioning of pain within medicine after 1945. Central to this shift was a change in how pain was understood by clinicians and patients.

40. Livingston, *Pain and Suffering*, 94-101. "As peripheral nerves are such sensitive structures and the carriers of all sensory impressions, it would be natural to expect that missile wounds of nerves would be the most painful of all wounds. Our records indicated that severe pain is the exception rather than the rule in such cases. Approximately 70 percent of our patients stated flatly that they had experienced no pain of any consequence at the time of wounding and none directly referable to the injured nerve during their period of convalescence."

## Chapter 2 – Understanding through Measurement

In 1954, William Livingston, head of the department of surgery at the University of Oregon Medical School, ventured east to visit laboratories whose work was of interest to researchers who, under Livingston's direction, were conducting animal studies on the neurobiology of pain. He visited psychologist Donald Hebb's lab at McGill University, where he saw an experiment led by Peter Milner and James Olds. The young psychologists believed they had identified a "pleasure center" in the rat, based on the animal's reactions to electrical stimulation at numerous points in the brain. Subsequent work showed that there was not one such center, but a network of neural connections that, when stimulated electrically, produced effects that the rat perceived as rewarding. Livingston's account did not mention Ronald Melzack, a student of Hebb's who received his doctorate in 1954 and would spend the next three years as a post-doc in Livingston's lab.[1]

Chapter 1's pre-histories looked at long-term and proximate activities, events, and developments that drove a scientific, professional, and clinical refashioning of how pain was understood by clinicians and patients after 1945. The first section of this chapter sketches how Livingston and Hebb articulated core principles of this change. The second section focuses on how the MPQ attempted to operationalize a model of pain that these ideas comprised. This chapter examines the first of three crucial dimensions of that transformation – a change in the fundamental understanding of pain's nature, origins, mechanisms, and effects.

Hebb's fundamental interest was the neurological bases of behavior and learning; Livingston's was the surgical and broader challenge of pain relief. From divergent interests and approaches, Hebb and Livingston articulated key features of what became, after 1965, a new model of pain.

1. Livingston, *Pain and Suffering,* 197-200. Livingston completed the manuscript shortly before he passed away in March 1966. He had been compiling and working on what became the book for two decades.

They speculated on possible neurophysiological mechanisms for the kinds of pain they saw: complex, deeply enmeshed with personal attributes and history, and widely variable within distinct conditions and among people. They envisioned the central nervous system as more than a passive administrator of electrochemical events and substances. The brain and spine actively shaped the pain experience. Pain was dynamic, mutable, and far more complex than a stimulus-and-response model -- either in physiology or psychology -- could account for. Hebb and Livingston put forward ideas on how the nervous system could electrochemically store and retrieve elements of personal experience in forms of memory and learning that affected how people felt pain. Their ideas contributed to concepts of brain plasticity, the modulation of noxious stimuli, and the centrality of the brain in the experience of pain.[2]

Both Livingston and Hebb anticipated later research directions in the questions they asked and possibilities they raised. Livingston's observations and speculations on the role of multiple ascending and descending pathways in pain perception, the role of central sensitization, the impact of inflammation in activating visceral nociceptors, and the importance of learning, attention, and expectation on the perception of pain intensity exerted substantial influence on research directions and theoretical speculations. Hebb's concept of the cell assembly, a cluster of neuronal connections forged in pre- and post-synaptic activities, patterns, and effects, has been widely applied in research in cognitive neuroscience, computer systems theory, and neural networking. Both men believed in the brain's ability to encode elements of personal history, beliefs, and attitudes in the body's responses to pain through the involvement of areas in the brain known to be involved in these

2. Hebb and Livingston shared a belief in learning as a component of the pain experience. Livingston wrote that experiments with a range of animals "suggest that habituation, like other forms of learning, is a manifestation of some fundamental property of nervous tissue. … "Personally, I believe that the conditioning a child receives from parental influences can change the severity of the pains he will experience for the remainder of his life." See Livingston, *Pain and Suffering*, 194, 220.

affective dimensions. Livingston and Hebb both emphasized learning and adaptation as attributes of the nervous system.[3]

**William Livingston -- pain as complex**

William Livingston once said that the most significant discovery on pain in his lifetime had been that the brain can to modulate its own sensory input, and that it's conceivable that this capability extends to the furthest reaches of the peripheral nervous system. He was born in Wisconsin in 1892 and was raised in that state and in Oregon. After medical training and residency on the east coast, he returned to Oregon in 1922 to start in private practice. He served as a state medical officer with responsibility for assessing workers' claims to compensation for job-related injuries. In these years he encountered a staggering number and varieties of phantom limb pain, nerve pain, and cases he could not explain. During World War II Livingston worked at the Oakland (California) Naval Hospital's department of peripheral nerve injuries. Livingston was a skilled chronicler of clinical events and conditions; and he was fascinated by the quandaries of experimental design and implementation -- two attributes that he brought to his engagement with pain across his career.[4]

Livingston's *Pain Mechanisms* (1943) was an early and ambitious critique of a prevailing model of pain as straightforward and rote. It addressed the traditional specificity theory of pain and expressed ideas that sparked a major expansion of pain research after 1945. Livingston spelled out what he saw as the weaknesses of traditional specificity theory's model of a straight-through, hard-wired transmission system. In *Pain Mechanisms* he explored new concepts: the temporal and

3. Raymond M. Klein, "Donald Olding Hebb," at www/scholarpedia.org/article/Donald_Olding_Hebb, accessed 6-15-16; Howard L. Fields, introductory note to Livingston, *Pain and Suffering*, xv-xvi.
4. Ronald Melzack, foreword to Livingston, *Pain and Suffering*, viii-ix, 8-10, 96-97. Livingston, Bonica, and Beecher were among the many clinicians whose World War II experiences in treating pain were decisive in their post-war directions. Livingston agreed with the findings of Beecher's studies on how circumstances could be central to an individual's pain perception and experience. Livingston wrote that "In some instances the men actually welcomed their wounds as representing a means of escape from conditions they felt were increasingly intolerable, as on Guadalcanal. To them a wound meant rest, protection, and perhaps a return home. Many of the men said they would gladly have 'settled' for a serious wound if only they could have been sure that it would not kill them or cause them too much suffering."

spatial patterning of pain, the importance of integrative and summation mechanisms of the central nervous system, the potential for reverberating neural circuits to account for persistent pathological pain states, the importance of groups of specific neurons in the spinal cord in the gating of sensory and motor input, and the use of anesthetic blocks and stimulation techniques to relieve pain. He was unambiguous in his belief in the abilities of the body and the environment to alter input at any point in the nervous system. He was struck by how closely psychic states could mimic organic disease, and he believed that psychological elements were part of every patient's pain woes.[5]

5. Livingston, *Pain Mechanisms*, 30, 43, 45, 49-50, 138; Livingston, *Pain and Suffering*, vii, xv-xvi. He described the main thesis of *Pain Mechanisms* as follows. "A peripherally situated trigger point is capable of initiating a pathological state characterized by spreading reflexes, and probably dependent upon a disturbed physiologic status of the spinal centers." His critique of specificity theory was precise. "Having subscribed to the law of specific nerve energies as it may apply to the sensory nerves of the skin, it remains to decide more exactly to what degree they are specific, and what is to be considered as the specific unit. Are there specific receptors for each of four sensations that can be derived from skin stimulation, and no more? What is to be taken as the specific unit: the end-organ, the fiber, the neuron as a whole, or the entire conducting mechanism for each kind of sensation?" "By countless repetition of harmful stimuli of different types applied to the exposed surfaces of the body, the skin has acquired many receptor units capable of responding to different stimuli." "I believe that the eventual sensation resulting from peripheral stimulation can be modified by changes in the peripheral environment, alteration in the status of the receiving centers, and probably by influences exerted on the train of impulses anywhere along their route from the skin to the brain." For Livingston, and others, a moral and professional imperative was at the heart of his critique of how clinicians engaged with pain. At the small pain clinic Livingston had set up in order to push researchers out of the lab to see for themselves what pain was like, Melzack described how Livingston interacted with patients whose pains were the most debilitating. "Livingston treated those patients with a special compassion and kindness, and his brilliant questions (often asked for my benefit) revealed to me what he knew so well – that prolonged pain is debilitating, demoralizing, devastating. It grinds people down and makes life a burden. Patients doubt themselves and think they must be crazy if so many operations and treatments do not take their pain away. And, Livingston pointed out to me, in their frustration over their inability to help their patient, physicians sometimes reinforced that view with great psychological harm to the patient." Livingston emphasized the "tremendous complexity of the problems relating to pain and all sensory perceptions with which this work is concerned." His student Melzack recalled in his Foreword to *Pain and Suffering* that "*Pain Mechanisms* received good reviews but little real recognition beyond lip service. Melzack characterized the response by saying that the book simply wasn't understood. "The 1940s and 1950s were the heyday of specificity, when textbooks and research entrenched the concept that the degree of pain experience is proportional to the extent of injury and that the way to block pain is to cut pain nerves and pathways. A common model for how the nervous system functioned was a telephone exchange that automatically sent intact messages from one point to another via long fiber tracts. But soon Livingston encountered "a more dynamic concept of pain than I had learned." It featured modulation by and within the nervous system, in multiple directions and at different sites. He (and others) believed that impulses from a diseased organ could embed abnormal neuronal activity within the spinal cord.

Livingston thus expressed a fundamental notion of pain as rooted in neurophysiological processes and complexities. He believed that pain could be shaped by inputs at all levels of the central nervous system. He described pain as a transactional process comprising ongoing interactions and feedback loops. He was impressed with what he termed the dynamic abilities of pain, its near-willfulness and persistence, its capacity to carve new pathways, take new forms, and evade therapies. He expressed frustration at the failures of his repeated and diverse attempts to relieve pain, which suggested to him an evil persistence in the clinical dilemma. In these moments pain took on the attributes of a "spoiled and stubborn child which fiercely resents interference and punishment, and deliberately goes ahead seeking means to break over restraint." Livingston asserted that brain functioning was far more complicated than a 'from-here-to-there affair." He came to view pain as a transactional event of vast complexity that unfolded in a discernible time sequence and in conformity with what he termed a "definite teleological design."[6]

For Livingston an especially critical group of neurons were the spinal cord cells that sent impulses to and from the brain and cord and were involved in reflex activity. These internuncial neurons established different routes by which an incoming impulse reaches the motor cells in the spine. He believed that these neurons' role was key to how the brain was involved in modifying pain. The internuncial pools were the nervous system's receiving station, and they had a lot of responsibility for which impulses were sent over which pathways and the distribution of motor impulses to the periphery.[7]

---

6. Livingston, *Pain Mechanisms*, 11, 26; Livingston, *Pain and Suffering*, xvi, 162.
7. Livingston, *Pain Mechanisms*, 55, 58-9, 72-73, 76; Livingston, *Pain and Suffering*, 205, 207-8, 219, 228. By the 1940s Livingston had been convinced of the importance of the detailed, dispersed processing of noxious stimuli that was managed centrally in ways still not clear. "Head reached the opinion, many years ago, that the neurons of the posterior horns of the spinal cord were more than simple relay stations. He believed that they were capable of either facilitating or inhibiting the sensory impulse before it reached the secondary neuron, and that they were actively engaged in integrative functions affecting all normal sensory impulses. And it was his view that this central integration was not confined to the spinal segment at which the sensory impulse entered the cord, but continued to modify the pattern of impulses at each functional level between the spinal segment and the sensorium." "The afferent impressions produced by the actions of an external

**Donald O. Hebb -- pain as learned**

Donald Hebb was the son of two physicians and was raised in Nova Scotia. His first ambition was to write novels, and immediately after undergraduate school he taught high school and was a principal. By age 30 Hebb was at a crossroads. His wife had died in a car accident on Hebb's 29th birthday, and his work as principal at a Montreal high school was floundering. He began a Ph.D. program in psychology at the University of Chicago in 1934, with Karl Lashley, a physiological psychologist, as his main teacher. In 1937 Hebb applied to work at the Montreal Neurological Institute, where, under the tutelage of surgeon Wilder Penfield, Hebb studied the effects of injury and surgery on the brain. In 1942 Hebb reunited with Lashley, who was then Director of the Yerkes National Primate Research center in Orange Park, Florida. At Yerkes, Lashley's goal was to develop ways to assess learning and problem-solving among chimpanzees, while Hebb would study the animals' personalities and emotional makeup. But the chimpanzees proved less amenable to training than Lashley had envisioned. One result was that planned studies of the effects of post-surgical brain lesions were not carried out. Still, Hebb said that he had learned more about human personality and behavior during his time at Yerkes than at any other five-year period, with the exception of his own first five years.[8]

---

stimulus are highly complex, and are subject to the integrative action of the central nervous system, before they can become fitted to subserve sensation. "I am beginning to feel that the central disturbance is the essential factor in many diseases." Head: "We believe that the physical forces of the external universe produce within us a number of impressions, which are in many cases incompatible with one another from the sensory point of view. These are sorted, combined, and controlled within the central nervous system until they are sufficiently integrated to underlie sensation; the final product being simpler than its constituent elements." Sensory perception as a "central interpretation synthesized from a composite of many different afferent impulses and apperceptions."

8. Peter M. Milner, "Obituary, Donald Olding Hebb (1904-1985)," Elsevier August 1986 347-351; "The Brain and Behavior: Donald O. Hebb," at https://brain-health-neurology.knoji.com/the-brain-and-behavior-donald-o-hebb, accessed 6-15-16; Peter M. Milner, "The Mind and Donald O. Hebb," *Scientific American* (January 1993): 124-129; D. O. Hebb, "On Human Thought," *Canadian Journal of Psychology*, (1/1/1953): 7, 99-110; D. O. Hebb, "Neuropsychology: Retrospect and Prospect," *Canadian Journal of Psychology* 37 (1) (1983): 4-7; D. O. Hebb, "Drives and the C.N.S. (Conceptual Nervous System)," *The Psychological Review*, Vol. 62, No. 4 (July 1955): 243-254. This was Hebb's Presidential address, Division 3, at the September 1954 meeting of the American Psychological Association in New York.

In 1949, Hebb published *The Organization of Behavior*, the book that established his reputation. Hebb devoted only 10 pages of the book to pain. He believed that pain was the result of the spatial and temporal disruption of organized activity in the brain stem and cortex. For Hebb this interference per se was the physiological basis of pain. He believed that specificity theory was far too narrow and that some form of patterning had to be a more fruitful model for pain in the nervous system. Pain was capable of affecting learning but could also energize behavior, and in some circumstances it appears to facilitate learning directly. For Hebb, any theory of pain had to try to explain how and why an increase of pain frequently resulted from greater than normal activity in neuronal structures.[9]

But his comments on pain were a small part of a much larger work on how the nervous system organized neuronal activities to produce human perception and experience. Hebb did not see how individual cells could work in isolation or how individual cells could carry a particular perception or ability. He believed that activities in and around synapses in the cerebral cortex were modified by experience in order to store information. For many years his ideas have been summarized as neurons that fire together wire together. The book "postulated that associative memories are formed in the brain by a process of synaptic modification that strengthens connections when presynaptic activity correlates with postsynaptic firing." Hebb believed that as a person's environment changes and new information is stored, cells gain responsiveness to some stimuli and lose responsiveness to others. In this way neuronal receptive fields could be altered, in their structures and capabilities, by experience. Synaptic areas that had been fortified by coordinated activity would thrive and grow new branches; other areas with uncoordinated or deficient activity

9. Hebb, *Organization of Behavior*, 109-119, 181-190. Hebb's inclusion of Lashley's statement that "pain is often an accompaniment of injury to the somesthetic system all the way from peripheral nerve to thalamus" suggested that Hebb agreed that pain was a complex, variable event that involved numerous parts of the spine and brain. Mark F. Bear, "Bidirectional Synaptic Plasticity: From Theory to Reality," *Philosophical Transactions: Biological Sciences*, Vol. 358, No. 1432 (April 29, 2003): 649-655; Doleys, *Pain: Dynamics and Mechanisms*, 36.

would languish. Over time, complex behaviors were formed from sets of cell assemblies or configurations that Hebb called phase sequences. Long-term potentiation (LTP) was defined as a lasting increase in synaptic strength that was affected by pre-, post-, and a combination of both kinds of synaptic mechanisms.[10]

A contributing factor to Hebb's impact was the timing of his ideas in relation to broader trends in psychology. Hebb's book attempted to show how, in his view, psychology had over-emphasized stimulus and response as the fundamental, dominant mechanism of learning and behavior. Hebb asserted that psychology as a science had to be rooted in biology, and that psychologists and neurophysiologists shared common goals even though their methods differed substantially. Hebb's interest was in the neurological organization of behavior, the mechanisms by which the central nervous system accomplished this organization over time, and how behaviors arose from neurological activity, including learning. "Organization" for Hebb denoted a synthesis of molecular and system-level activities and sought to bring together mechanistic and systems perspectives; in this view, neurological forms, structures, characteristics, and workings were expressions of such organization. Hebb believed that research after 1930 had shown that nerve cells were far from physiologically inert and did not need to be excited from the outside to discharge. In this view the nervous system was alive and active; Hebb cited epilepsy as an example of what the nervous system could generate on its own initiative. In addition, Hebb believed that studying how behavior was organized neurologically enabled scientists to ask the most pertinent and intriguing questions about the nervous system.[11]

---

10. Steven J. Cooper, "Donald O. Hebb's synapse and learning rule: a history and commentary," *Neuroscience and Behavioral Reviews* 28 (2005): 851-874.
11. Peter T. Manicas, *A History & Philosophy of the Social Sciences* (Oxford: Basil Blackwell, 1988), 236; Boring, *Sensation and Perception*, 494; D. O. Hebb, "What Psychology is About," *American Psychologist* (February 1974). Hebb described himself as a "determinist – I assume that what I am and what I think are entirely the products of my heredity and my environmental history. I have no freedom about what I am. But that is not what free will is about. The question is whether my behavior is entirely controlled by present circumstances."

Perhaps more influential than Hebb's specific ideas about pain was the stance his book took in relation to broader trends in academic psychology. In addition to being a physiological psychologist, Hebb was also a developmentalist who believed that learning and change, in the environment, the person's responses to it, and the nervous system's ability to adjust; he was an early conceptualizer of brain plasticity. In 1913 John B. Watson had created an inflection point with publication of his talk, "Psychology as the Behaviorist Views It," which was given at Columbia University in 1913, and behaviorism began to become an influential and pervasive "school" within psychology. One of Watson's targets was what he considered a fatal flaw of introspection -- its inability to contribute to putting psychology on a scientific footing. But just as Livingston rejected what he felt was an overly narrow concept of pain, so did Hebb spurn what he saw as a massive over-simplification that behaviorism promoted.[12]

Hebb readily acknowledged the influence and reach of Watson's ideas. He described Watson's proposal as having two key elements. First, psychological method had to become objective by using behavioral instead of introspective evidence. The second tenet, an objective theory based on methods for making deductions and inferences from observed behavior in response to stimuli, had, in Hebb's view, turned out to be useful in limited ways but at bottom greatly lacking. Hebb saw behaviorism as a fundamentalist psychology that sought to strip behavior and its origins to what it proposed as scientific psychology's bare essentials: whatever we can ourselves observe. For Hebb there were, in this approach, strong parallels with Taylorite scientific management, which sought to reduce manufacturing and other workplace behavior to repetitive, visible routines designed to optimize productivity and efficiency. Overtones of social control and industrial discipline in

12. John M. O'Donnell, *The Origins of Behaviorism: American Psychology*, 1870-1920 (New York: New York University Press, 1985), 12-13, 137, 157, 191-211, 213-214; George Mandler, *A History of Modern Experimental Psychology: From James and Wundt to Cognitive Science* (Cambridge, MA: The MIT Press, 2007), 65, 99-106, 139-143, 175-177; Donald S. Napoli, *Architects of Adjustment: The History of the Psychological Profession in the United States* (Port Washington, NY: Kennikat Press, 1981), 42-48; Asenath Petrie, *Individuality in Pain and Suffering, Second Edition* (Chicago: The University of Chicago Press, 1978).

Watson's approach appear to have irked Hebb more as a matter of temperament than views on control.[13]

For Hebb, the fatal flaw of behaviorism was its narrowness. Psychology, including problems of mind, consciousness, and behavior, had no choice but to anchor itself in biology, because awareness and perception and the human traits that make pain so urgent were rooted in the neurophysiology of the brain. What happened inside the skull was crucial and largely unknown, except for Hebb's firm certainty that the brain was the key to the most significant mysteries. Critical problems in psychology were thus neurophysiological but deeply clinical and social as well. All that we observe was a product of a dense mix of genetics and environment, or the interplay of a person's makeup with his or her experience. Hebb's was a deeply physiological psychology in which personal experiences were encoded electrochemically within the nervous system.[14]

One expression of Hebb's attempt to marry physiology and psychology was a series of letters he exchanged with George Bishop, professor of neurosurgery at Washington University in St. Louis. The Hebb-Bishop letters, exchanged between December 1950 and April 1957, articulated fundamental issues in neurophysiology that sought to account for pain's variability and intractability. These dialogues sketched a more inclusive, holistic approach to pain that later theorists and researchers, such as Melzack, Bonica, and other early leaders of the IASP, would refine and promote. The letters probed how physiology and psychology interacted in pain; the roles of the peripheral and central nervous systems; and how the brain was involved. They show how two advanced scientists were inquiring into similar issues from very different medical perspectives.

---

13. Hebb remained impressed with the hold that behaviorism had exercised over so much of American psychology. He said in 1981 that the perceived value of the "subjective introspective report has become more than doubtful … All serious work in psychology depends essentially on the objective data of behavior (which, of course, includes spoken language). This makes psychology a biological science and mind a biological issue." See D. O. Hebb, "Consider Mind as a Biological Problem," *Neuroscience*, Vol. 6, No. 12 (1981): 2419-2422; Hebb, *Organization of Behavior*, 99-100, 101-103; "Watson's stimulus-and-response theory was not as incompetent as it seemed and it was not easy to refute it conclusively by hard evidence."
14. D. O. Hebb, "What Psychology is About," *American Psychologist*, February 1974.

They articulated clinical and research problems at the intersections of psychology and physiology that challenged a prevailing understanding of pain. How did the brain respond to or address noxious input? How did all the potential dimensions of the pain experience, with its many qualities of sensation and feeling, emerge from the neurophysiology of the nervous system?[15]

Hebb believed that brain development sequences in the first years of life, as well as early experiences with pain, could have strong influences on later behavior by adults. If that was the case, how might pain be learned? Hebb tentatively offered that "we can't take the central end for granted, and this is what I was trying to raise in my book. Pain has no special centers in the CNS, but it has very special effects." Bishop speculated on how much, and what elements of, people's reactions to pain had been some form of learned association with the effects of other painful events. Few clinicians who treated pain doubted the effects of mental states and emotions -- anxiety or apprehension or fear -- could produce pain or make it worse. Hebb and Bishop were both interested in central mechanisms, rooted in the electrochemical workings of the brain, through which these emotional states were perceived, expressed, and incorporated into the pain experience. Hebb further proposed that "'secondary pain' – an emotional elaboration which I think you are talking about, involving learning and ideas about pain -- might be the activation of particular pathways ('cell assemblies'??), organized by a learning process."[16]

Livingston and Hebb together created conceptual framework for Melzack and Wall's gate control theory of pain, which they published in 1965, as well as for the McGill Pain Questionnaire (MPQ) that followed ten years later. They envisioned pain as complex, multifactorial, and idiosyncratic. Its variability was rooted in the structure and operations of the nervous system. This inclusive concept put the brain at center of pain's formation and mysteries, privileged patients' self-reports,

15. Harold Merskey, ed., *Thoughts and Findings on Pain: The Hebb-Bishop correspondence and a selection of papers*. (Vancouver: The Canadian Pain Society and the American Pain Society. 1996), vii, 7-13;
16. Merskey, ed., *Thoughts and Findings*, 10, 12-14, 22; George Riddoch, "Central Pain," *Lancet*, 1 (1938):1150-1156 and 1205-1209; George Riddoch, "Phantom Limbs and Body Shape," *Brain*, 64 (1941):197-222.

and rooted experience and personal history in the electro-chemical workings of the brain. It was this model of pain that the MPQ sought to measure, assess, characterize, in clinically useful and repeatable ways, by reconciling physiological and psychological dimensions in a single assessment tool. The MPQ sought to operationalize a notion of pain as complex, both personal and social, that Livingston and Hebb expressed.

Changes in how pain was assessed after 1945 were part of a larger shift in medical orthodoxy on pain among physicians, scientists, and patients. The roots of this change extended back to debates over whether pain was a sensation or an emotion. Across the twentieth century a growing number of clinicians challenged a dominant concept of pain as straightforward, rote, and well understood in favor of a notion of pain as multidimensional, individual, and circumstantial. Within the medical and social science communities, this challenge was led by anesthesiologists, surgeons, neurologists, and psychologists. One product of this shift was a proliferation of scales, questionnaires, observational methods, and experimental techniques to quantify pain.

Between its publication in 1975 and a decline in its use after about 1995, the MPQ was widely deployed and studied. It was both a culmination of decades of pain measurement activity and a departure from what had preceded it. It sought to integrate physical and psychological factors; it tried to quantify the impact of personal history and current circumstances; and it put patient report at the center of clinical evaluation. While the MPQ was not the only pain measurement tool that sought to bring patients' reports to the center of clinical assessment, its long career arc, its direct ties to the GCT, and its explicit effort to integrate physiological and psychological components of pain have made it a powerful lens for the history of pain measurement. The MPQ was the most

ambitious and successful attempt to operationalize a model of pain that Livingston and Hebb first formulated.[17]

The MPQ challenged a prevailing model of pain and helped refashion the understanding of pain among clinicians and patients in several ways: The MPQ incorporated and sought to quantify an "insurgent" understanding of pain by operationalizing ideas of Hebb and Livingston -- inclusion, complexity, plasticity, and learning -- in a pain assessment tool. It sought to incorporate an individual's prior experience in electrochemical encoding by the nervous system; it assigned a significant role to learning and personal history in the experience of pain; and it portrayed the body's responses to noxious stimuli as a networking event in which clusters of neurons interacted and worked together in cell assemblies and phase sequences. Livingston's notion of complexity, of circuitry gone awry as a source of intermittent or chronic pain; of different pathways for modulation, a special role for internuncial pools or collections of spinal neurons; says that every patient's complaint of pain has a psychological dimension.

The MPQ put psychological and personal dimensions of the pain experience on an equal clinical footing with physiological factors [in several ways]. The MPQ situated patient report at the center of pain assessment. It did this by the specific questions it asked and topics it raised; by the relative

17. David Biro, *The Language of Pain: Finding Words, Compassion and Relief* (New York: W. W. Norton & Company, 2010), 80-83, 158; Merskey, Loeser, and Dubner, ed., *Paths of Pain,* 273, 279-280; C. Richard Chapman and John D. Loeser, ed., *Advances in Pain Research and Therapy, Volume 12: Issues in Pain Measurement* (New York: Raven Press, 1989), 175-176, 298-304; Richard H. Gracely, "Evaluation of Pain Sensations," in Merskey, Loeser, and Dubner, ed., *Paths of Pain*, 279; Bill Noble, David Clark, Marcia Meldrum, Henk ten Have, Jane Seymour, Michelle Winslow, and Silvia Paz, "The Measurement of Pain, 1945-2000," *Journal of Pain and Symptom Management*, Vol. 29, No. 1 (January 2005): 14-21; Ian McDowell, *Measuring Health: A Guide to Rating Scales and Questionnaires* (Oxford: Oxford University Press, 2006), 16; Harold G. Wolff and James D. Hardy, "On the Nature of Pain," *Physiological Reviews*, Vol. 27, No. 2 (April 1947): 167-199; Dennis C. Turk, Thomas E. Rudy, Peter Salovey, "The McGill Pain Questionnaire Reconsidered: Confirming the Factor Structure and Examining Appropriate Uses," *Pain* 21 (1985): 385-397; Kenneth A. Holroyd, et al., "A multi-center evaluation of the McGill Pain Questionnaire: results from more than 1700 chronic pain patients," *Pain* 48 (1992): 301-311; Diana J. Wilkie, et al., "Use of the McGill Pain Questionnaire to Measure Pain: A Meta-Analysis," *Nursing Research*, Vol. 39, No. 1 (January/February 1990): 36-41.

weight it assigned to each of the three dimensions it probed – sensory, affective, and pain intensity. These factors went from scant acknowledgment in assessment of pain to full standing. It situated patients at center by making their input the raw data from which pain was quantified.

The MPQ stimulated extensive research and debate into its applications, reliability, and cross-cultural utility. These studies applied the MPQ to a wide range of clinical conditions, medical settings, and with different population groups. Why did it stimulate so much research? The imprimatur of its developer was a factor, as was the concurrent emergence of findings on the body's endogenous pain-modulation capabilities. Researchers understood that the inability to measure pain had made it problematic to many clinicians and that a robust solution would be a major advance. Even though the MPQ fell short of becoming a "pain thermometer" or even an enduring tool in the clinician's arsenal, its relevance to the history of pain measurement seems clear. Its elevation of psychological and personal factors in pain assessment; its belief that pain was at once subjective and measurable; and its placement of patient report at the center of pain assessment contributed to the MPQ's challenge to the clinical marginality of pain.

**A Bold and Imperfect Unity -- The MPQ**

In 1989 Dennis Turk compared attempts to measure pain to the quest of a hunter pursuing an animal no one has ever seen. In the terms of Turk's analogy, the McGill Pain Questionnaire (MPQ) has been an historically rich safari. For twenty years after it was introduced in 1975, the MPQ was deployed widely in hospitals, doctors' offices, clinics, and research laboratories. Its clinical use declined after the mid-1990s, but interest endured, and the MPQ now stands as the most widely used and researched pain-measurement instrument in history. More than 500 studies have probed its content and structure; its linguistic and psychological premises; and its applicability across

medical conditions, cultures, treatment settings, and patient groups. The MPQ has been shortened, tweaked, and translated into more than 60 languages.[18]

This chapter shows how the MPQ helped to end the marginality of psychological factors in the assessment of pain after World War II and thus contributed to a transformation in the clinical status of pain. The MPQ's career, research breadth, and global reach enabled it to create a singular niche in the history of pain measurement. At the same time, the MPQ, and pain measurement more broadly, have been critical enabling technologies in the history of medical understandings of pain's nature and treatment.[19]

This chapter argues that the MPQ has been a pivotal and revealing technology in the history of how pain came to be understood and managed as decisively subjective in the second half of the twentieth century. After the middle of the twentieth century, pain's subjectification took place within an increasingly dense network of professional activities that stimulated the growth of pain management as a medical specialty. Pain slowly became a discrete condition, with an expanded array of discourses, patient communities, and practices. Together these developments signaled a redefinition of pain as defined by variability, chronicity, and decisive subjectivity.[20]

---

18. In 2014 historian Joanna Bourke described the literature on the McGill Pain Questionnaire as vast and debates over the MPQ as unlikely to subside. See Bourke, *Story of Pain*, 147-154; Melzack. *Puzzle of Pain*, 93-95; Biro, *Language of Pain*, 80-83, 158; Merskey, Loeser, and Dubner, ed., *Paths of Pain*, 273, 279-280; Chapman and Loeser, ed., *Advances in Pain Research*, 175-176, 298-304; Richard H. Gracely, "Evaluation of Pain Sensations," in Merskey et al., 279.

19. Clinicians, historians, and social scientists increasingly have examined the origins and forms of a decisive shift in the understanding of pain after 1945. See Wailoo, *Pain: A Political History*; Cervero, *Understanding Pain*, 2012; Loeser and Chapman, ed., *Advances in Pain Research*, 2, 63-65, 438-440, 231-234; Noemi Tousignant, "Pain and Pursuit of Objectivity: Pain-Measuring Technologies in the United States, c. 1890-1975," McGill University Ph.D. dissertation, 2006; Moscoso, *Pain: A Cultural History*, 2012; Doleys, *Pain: Dynamics and Complexities*, 2014; David B. Morris. *Illness and Culture in the Postmodern Age*. Berkeley: University of California Press, 2000.

20. Baszanger, *Inventing Pain Medicine*, 52. Journalistic accounts of pain's post-1945 emergence as a discrete medical syndrome include Judy Foreman, *A Nation in Pain: Solving America's Biggest Public Health Problem* (Oxford: Oxford University Press, 2014); Melanie Thernstrom, *The Pain Chronicles: Cures, Myths, Mysteries, Prayers, Diaries, Brain Scans, Healing, and The Science of Suffering* (New York: Farrar, Straus and Giroux, 2010); Marni Jackson, *Pain: The Science and Culture of Why We Hurt* (London: Bloomsbury, 2003); Jean E.

The MPQ played a critical role in pain's subjectification in several ways. Its content and structure depicted pain as at once subjective and quantifiable. It put patients' descriptions at the heart of clinical assessment and on an uneasy par with clinicians' perspectives. It articulated a concept of pain as firmly tied to a person's circumstances, attitudes, and beliefs. In these ways the MPQ sought to reconcile pain's physiological elements with its psychological, social, and cultural dimensions. The MPQ is a rich case study in pain's subjectification because of its pioneering attempt to operationalize the measurement of its concept of pain in a way that would have clinical relevance.[21]

The MPQ was not a static tool. Melzack encouraged modifications and adaptations and contributed to the development of shorter versions and some that were honed for specific conditions. Alongside research on the original version, content and structural changes began to emerge a few years after publication. In hopes of putting the MPQ into a broader historical setting, this section looks briefly at two other pain measurement tools, the Pain Perception Profile (PPP, 1982) and the Brief Pain Inventory (BPI, 1982). Both sought to improve the MPQ's clinical utility by addressing perceived shortcomings in its original form.[22]

Melzack was far from alone in his studies of pain, but he has made a singular contribution. He was co-developer, with neurophysiologist Patrick Wall (1925-2001), of the gate control theory of pain (GCT), published in 1965 and widely acknowledged as a milestone of the contemporary pain era. Starting in the 1990s Melzack would develop the neuromatrix theory of pain, the product of

---

Jackson*,"Camp Pain:" Talking with Chronic Pain Patients* (Philadelphia: University of Pennsylvania Press, 2000).

21. Melzack and Wall, *Challenge of Pain*, 39-42; 278-9; Cervero, *Understanding Pain*, 26-27; Merskey et al., *Paths of Pain*, 273, 279-280.

22. Randall L. Daut, Charles S. Cleeland, and Randall C. Flanery, "Development of the Wisconsin Brief Pain Questionnaire to Assess Pain in Cancer and Other Diseases," *Pain* 17 (1983): 197-210; Bernard Tursky, Larry D. Jamner, and Richard Friedman, "The Pain Perception Profile: A Psychophysical Approach to the Assessment of Pain Report," *Behavior Therapy* 13, 376-394 (1982): McDowell, *Measuring Health*, 491-6, 514-7;

four decades of trying to reconcile the physiology and psychology of pain. This section also looks at the MPQ within the broader history of these theoretical contributions.[23]

Two key elements link the GCT and neuromatrix theory to the MPQ. The first is their shared goal of unifying theory and practice, the lab and the clinic, psychology and physiology, in the understanding and treatment of pain. The second is their focus on chronic pain. After 1945 in the United States, the injured from two world wars, increasing life expectancy, and the rise of automobile accidents were making chronic pain a widespread clinical problem. For Melzack and others, chronic pain was among the persistent anomalies that rendered a stimulus-and-response model of pain questionable. Other such quandaries included headache (pain in the apparent absence of injury or illness), phantom limb pain (from a body part that was no longer there), and the placebo effect (pain relief in the absence of a biochemical agent). The diverse forms of chronic pain would expand this list of confounding anomalies and would lead the definition of the post-1945 world of pain.[24]

After an overview of the MPQ, this section looks at issues that clinicians, researchers, and historians have raised about it. This is followed by a brief discussion of research that illustrates

---

23. Manfred Zimmermann, "The History of Pain Concepts and Treatment before IASP," in Merskey et al., *Paths of Pain*, 19; The neuromatrix theory has yet to receive the attention from clinicians and historians that the gate control theory has received. Ronald Melzack, "From the gate to the neuromatrix," *Pain*, Supplement 6 (1999) S121-S126; Ronald Melzack, "Evolution of the Neuromatrix Theory of Pain: The Prithvi Raj Lecture, Presented at the Third World Congress of World Institute of Pain," *Pain Practice*, Volume 5, Issue 2 (2005): 85-94; Kimberly K. Trout, "The Neuromatrix Theory of Pain: Implications for Selected Nonpharmacologic Methods of Pain Relief," *Journal of Midwifery & Women's Health*, Volume 49, Number 6 (November/December 2004): 482-488; Anthony E. Reading, "Pain Measurement and Experience," *Journal of Psychosomatic Research*, Vol. 27, No. 5 (1983): 415-420.

24. Chronic pain has received growing attention from diverse clinicians, researchers, and social scientists since the 1970s. See Thomas Hadjistavropoulos and Kenneth D. Craig, editors, *Pain: Psychological Perspectives* (Mahwah, NJ: Lawrence Erlbaum Associates, 2004), 114-126, 271-301; Steven M. Brena, editor, *Chronic Pain: America's Hidden Epidemic* (New York: Atheneum/SMI, 1978); Isabelle Baszanger, "Deciphering chronic pain," *Sociology of Health & Illness*, Vol. 14, No. 2 (1992): 181-214; S. N. Mohamed, G. M. Weisz, and E. M. Waring, "The Relationship of Chronic Pain to Depression, Marital Adjustment, and Family Dynamics," *Pain*, 5 (1978): 285-292; Ulf Lindblom and Richard Tegner, "Are the Endorphins Active in Clinical Pain States? Narcotic Antagonism in Chronic Pain Patients," *Pain*, 7 (1979): 65-68; Michael Strumpf, Anne Willweber-Strumpf, and Michael Zenz, "Economic considerations in chronic pain," *Bailliere's Clinical Anesthesiology*, Vol. 12, No. 1 (March 1998): 89-102.

how these issues have been explored. The final part of this section sketches the broader history of pain measurement as well as the MPQ's links to the gate control and neuromatrix theories in order to put the MPQ into a richer historical setting.

**MPQ Overview**

The MPQ was a milestone in pain assessment, but Melzack was not the first to explore the complex role of language in pain. Avicenna (980-1037), Arabic physician and philosopher, viewed pain as a stand-alone sensation that resulted from a disturbance of the optimal mixture of the body's four temperaments: heat, cold, dryness, and moistness. He identified 15 varieties of pain and used descriptors such as compressing, incisive, and stabbing to categorize them.[25]

In the 1850s, physician Constantine Hering advised colleagues on how to assist patients who lived far away. He suggested asking these patients to report on aspects of their discomfort, such as where it hurt, how long it had hurt, any changes in the pain, what helped, and what didn't. Hering provided a list of words that doctors could use to guide their patients to a depiction of their conditions.[26]

In 1971, Melzack and statistician Warren Torgerson drew on earlier lists of pain words in a seminal paper on language and pain. In 1920 psychologist Edward Titchener had proposed four categories of the pain experience: prick, clear pain, quick pain, and ache. In 1939 psychologist Kenneth Dallenbach published a list of 44 words that described different qualities of pain and listed five groupings for these words: temporal, such as throbbing; spatial, such as radiating; its

25. Doleys, *Pain: Complexities and Dynamics*, 16.
26. Bourke, *Story of Pain*, 134.

relationship to pressure, such as pressing; its affect, such as ugly; and a catch-all for qualitative attributes, such as dull or pricking.[27]

In late 1975 the debut issue of the journal *Pain* included the article that introduced the MPQ. Melzack's goal was to create a way to assess clinical pain that could be replicated and that produced data that could be compared statistically. Data for the questionnaire had been obtained from 297 patients who had pain from arthritis, cancer, sciatica, phantom limbs, obstetric conditions, and as a result of surgery.[28]

The 1975 paper described significant weaknesses of existing measurement tools and contended that these drawbacks stemmed in part from the narrowness of the concept of pain that the tools embodied. The prevailing approach was to measure and treat pain as a discrete sensory quality that varied only in intensity. Melzack characterized "pain" as a generic descriptor, a label that encompassed an almost limitless assortment of qualities. Clinical realities, laboratory studies, and common experience confirmed the vast diversity of pain, with the difference between the pain of a broken leg and a toothache as a simple example. Melzack compared the description of pain strictly in terms of intensity to a portrayal of the visual world solely in terms of the flow of light, without regard to patterns, colors, textures, and other elements of the visual experience.[29]

The MPQ is a six-page questionnaire. It uses structured word groups, pictures, and questions to help patients describe what they are experiencing. Its word clusters and questions embody three dimensions of the pain experience: sensory (what it feels like), affective (how it makes the person

27. Ronald Melzack and Warren S. Torgerson, "On the Language of Pain," *Anesthesiology*, Volume 34, Number 1 (1971): 50-59; Edward B. Titchener, "Notes from the psychological laboratory of Cornell University," *American Journal of Psychology*, 31:212 (1920); Kenneth M. Dallenbach, "Somesthesis," in Edward G. Boring, H. S. Langfeld, and H. P. Weld, ed., *Introduction to Psychology (*New York: Wiley and Sons, 1939), 608-625.
28. Ronald Melzack, "The McGill Pain Questionnaire: Major Properties and Scoring Methods," *Pain*, 1 (1975), 277-299.
29. Melzack and Torgerson, "Language of Pain," 53-55; Dallenbach, "Somesthesis," in Boring, Langfeld, and H. P. Weld, ed., *Introduction to Psychology,* 610-615.

feel), and evaluative (how intense the pain is). This multi-tiered model was a break with the prevailing unitary conception of pain.[30]

The MPQ has five sections. An unnumbered segment elicits information on the patient's age, diagnosis, and current pain relief regimen. Part 1 was a back- and front-view outline sketch of a gender-neutral adult body designed to help the patient show where he or she was feeling pain and whether the pain was internal, external, or both. Part 2, titled "What Does Your Pain Feel Like?" contained 20 groups of two to six descriptor words each and asked the patient to choose the one word within each group that best described his or her present pain. Part 3 asked "How Does Your Pain Change With Time?" and included questions about temporal patterns and what increased or relieved the pain. Part 4 sought an answer to "How Strong Is Your Pain?" It affirmed the importance of the intensity dimension of pain and included a one-to-five scale and six questions that could be answered only with the five words: mild, discomforting, distressing, horrible, and excruciating. The 1975 paper also included a description of an experiment designed to establish pain intensities implied by the words within each of the twenty word groups in Part 2.[31]

The MPQ word groups asked about the three dimensions of pain that the questionnaire proposed. The sensory qualities of pain included temporal, spatial, pressure, and thermal properties; affective dimensions referred to feelings of tension, fear, and autonomic responses; evaluative words described the overall intensity of the experience. For example, one affective subclass included the words "tender, taut, rasping, splitting," while the constrictive pressure sub-segment of the sensory category included "pinching, pressing, gnawing, cramping, crushing." The word groups are the crux of the MPQ's articulation of pain as subjective. By asking individuals to pick from a standardized collection of 78 words, the MPQ provided an open, albeit limited, canvas from which patients suffering from a wide range of conditions could work with clinicians to reach a

30. Melzack, "McGill Pain Questionnaire," 278.
31. Melzack, "McGill Pain Questionnaire," 277, 283.

shared understanding of what the patient was experiencing. It also stimulated debate on the choices and ordering of words within the groups; the variability of a word's meaning and connotations for English speakers and others; whether pain had the three dimensions Melzack proposed; and whether the theory of pain that the MPQ embodied was accurate and complete.[32]

Four key measurements could be derived from the word clusters as well as the MPQ's intensity scale. The pain rating index (PRI) consisted of the total of the numerical values of all words chosen in each of the three categories or the total for all categories. For example, "pinching, pressing, gnawing, cramping, crushing" are listed in 1-to-5 order of least pain to worst. Adding the values of all words chosen produces a score for each category and a total score. A third measurement is the number of words a patient selects, since users could choose to leave a word group unmarked. Finally, present pain intensity (PPI) is an overall measure from one to five that was derived from the combination of words and numbers chosen by patients in Part 4.[33]

The use of 78 descriptive adjectives organized into 20 subgroups gave patients and clinicians a presumably comparable framework as they worked to achieve a shared assessment of a patient's pain. The MPQ's words, questions, pictures, and methods for scoring put the patient in substantial control of a procedure that aspired to clinical credibility. For Melzack, pain was quantifiable and deeply subjective. The centrality of patient input for clinical assessment, while not new with the MPQ, was an important way in which the subjectivity of pain was given primacy.

To understand more fully how the MPQ took the form it did, it is helpful to look at the path to the MPQ that Melzack took. This backstory shows how he came to focus on pain and how his early training as an experimental psychologist shaped his later views. Melack's path also conveys the power of the prevailing stimulus-and-response model of pain and how this model came to be questioned. In 2004, Melzack and psychologist Joel Katz wrote that during the 1950s there had

32. Melzack, "McGill Pain Questionnaire," 279, 281.
33. Melzack, "McGill Pain Questionnaire," 277, 283.

been no space for contributions to pain from psychology's extensive work on attention, past experience, anxiety, or the meaning of the situation to the individual. The story of the MPQ's development shows the interplay of theory and practice in the assessment of pain and puts the MPQ into a wider historical frame.[34]

The path that led to the MPQ began while Melzack was a student at McGill University. As the earlier section of this chapter described, Melzack's teacher, experimental psychologist Donald Hebb, was studying dogs who had been raised in isolation with the goal of understanding how this experience might have affected their decision-making skills. Hebb encouraged his students to engage with theory as a guide to research and as a way to unify diverse and often perplexing findings. Hebb emphasized the centrality of the brain in perceptual experience, even though understanding of how this worked was limited. Hebb's ideas would have a significant influence on Melzack and the MPQ.[35]

Melzack noticed that Hebb's dogs, who had been well cared for while isolated, did not seem to feel pain the way other dogs did. Years later he recalled this as one of the first times it had occurred to him to study pain more seriously. Research in this period assumed that animal subjects did not feel pain, a belief that Melzack said he knew could not be accurate. Over time, he came to believe that psychology as a whole had taken a wrong turn in its emphasis on stimulus and response as a dominant model of behavior and learning.[36]

In 1954 Melzack earned his doctorate in psychology from McGill. As he was about to finish his degree Melzack approached his neurophysiology professor, Herbert Jasper (1906-1999), who knew Melzack was interested in pain, for suggestions on a post-doctoral position. Jasper suggested his

34. Marcia Meldrum, personal communication, July 16, 2013; Ronald Melzack and Joel Katz, "The Gate Control Theory: Reaching for the Brain," in *Pain: Psychological Perspectives,* Hadjistavropoulos and Craig, ed., 13-35.
35. Ronald Melzack Interview, October 16, 1995, John C. Liebeskind Collection in the History of Pain, Louise Darling Biomedical Library at UCLA, 10, 12.
36. Mark Shainbaum, "The king of (understanding) pain," *McGill Reporter*, November 17, 2008.

friend Bill Livingston, chair of the surgery department at the University of Oregon whose book *Pain Mechanisms* (1943) Melzack admired. Livingston was supervising residents and post-docs and had opened a clinic for people with chronic pain. Research at Oregon had suggested the existence of multiple nerve pathways and roles for several brain regions in the pain experience. In the late 1950s, Melzack was finding it increasingly hard to believe that the brain's only role was to evoke a simple, one-dimensional sensation.[37]

In his first year in Livingston's lab Melzack continued his work on the brain neurophysiology of pain responses in animals. As his second year began Livingston told him that while he could continue on this track "until the cows come home," Livingston believed it was time for Melzack to start meeting patients who were suffering intractable pain. These contacts, Livingston said, would put Melzack's physiologic research into a broader perspective. On Tuesdays Livingston and anesthesiologist Frederick Haugen were seeing patients, and Melzack began to join them. Livingston told Melzack not to expect to be able to do a lot for these people. For his part, Melzack realized that he had very little understanding of how pain actually worked.[38]

At the clinic he saw people whose pain had not gone away after an injury healed or an illness ended. One such person was Mrs. Hull, who Melzack described as an energetic and spirited woman of high intelligence in her mid-70s. Mrs. Hull was diabetic and had lost her legs to gangrene, but this had not diminished her descriptive abilities. She was experiencing severe pain in her legs that had been amputated. Melzack would take Mrs. Hull and her husband Willy on Sunday afternoon drives, during which Mrs. Hull would describe her pain as burning, shooting, excruciating, and more. Melzack noticed how Mrs. Hull's adjectives conveyed the intensity and character of her pain

37. In the Preface to *The Puzzle of Pain* (1973), Melzack thanked Hebb for introducing him to the problem of pain and Livingston for "leading me through the subtleties and complexities of the problem." See Ronald D. Melzack. *The Puzzle of Pain* (New York: Penguin Books, 1973), xii; Melzack, "The McGill Pain Questionnaire," 199-202.
38. Jackson, *Pain: Culture and Science*, 332-333.

as well as the feelings it evoked. Years later, Melzack would look back at meeting Mrs. Hull as the start of the sequence of events that would lead to the MPQ.[39]

Melzack began to keep notes on the words Mrs. Hull used, believing that they might be of use. In the early 1960s he began to see how he could sort the descriptors to reflect sensory, affective, and evaluative dimensions of pain in a questionnaire to help patients convey what they were experiencing to clinicians.[40]

After three years Melzack left Oregon to take a faculty position at the Massachusetts Institute of Technology (MIT). Here he met Patrick Wall (1925-2001), an Oxford-trained neurophysiologist with whom Melzack would have ongoing discussions, sometimes heated, about the mechanisms of pain, the role of the brain, and the workings of the nervous system. These conversations would lead to the development of the gate control theory (1965). Although Wall approached pain from a very different perspective, he and Melzack shared a belief that the simple stimulus-response model was inadequate to explain the diversity of what physicians encountered.[41]

Through the early 1960s, Melzack's clusters of pain words received their collector's sporadic attention. At MIT Melzack was a member of the Pretzel Club, a group of academic psychologists who met irregularly over beers and snacks to discuss their research. One talk in particular piqued Melzack's interest. Statistician Warren Torgerson (1925-1999) described his work in an emerging field called multiple group discriminant analysis. In one experiment Torgerson had asked participants to put line scribbles into groups made up of scribbles that were similar to each other. Melzack wondered if Torgerson's statistical methods could be applied to his pain words. He spoke with "Torgie," as club members knew him, who said he would mull over what Melzack had described. At the next meeting, Torgerson said he was interested in working with Melzack. Over

39. Melzack and Katz, "The Gate Control Theory," 201.
40. Melzack and Katz, "The Gate Control Theory," 201.
41. Melzack and Katz, "The Gate Control Theory," 201.

the next several years, they conducted experiments that produced a significant amount of data on how different kinds of patients responded to the pain words.[42]

Melzack eventually left MIT to join the McGill faculty, and Torgerson went to Johns Hopkins. They continued to work on a paper, published in 1971, that contained many of the concepts, and introduced the structure, of what would become the MPQ. They characterized existing pain measurement tools as flawed by an assumption that pain varied only in intensity. Melzack and Torgerson proposed that pain was capable of taking many forms and exhibiting a wide array of qualities, and their paper attempted to specify these qualities. Their analysis included the three dimensions of pain that became the major classes within which the MPQ organized pain words.[43]

The 1971 paper described an experiment with 20 subjects who were asked to evaluate how accurately Melzack and Torgerson had organized 13 subclasses of pain words. Another experiment involved 140 introductory psychology students, 20 physicians, and 20 patients living in the Montreal area. They started from the premise that pain, like sight and hearing, was complex. Their word list reflected this complexity and, they believed, the ability of the brain to evaluate the nature and significance of the pain stimulus. They asserted that their data showed that English contains many words that describe pain; that there was agreement among their experimental subjects that these words comprise meaningful groups and subgroups that stand for broad attributes of pain; and that many of the words represent shared descriptions of the intensity of pain, regardless of their subjects' backgrounds. Melzack and Torgerson proposed that the word groups could serve as the heart of a questionnaire to help clinicians determine the properties and nature of specific pain conditions in diverse individuals. The article's tables are an early draft of what would be published as the MPQ four years later.[44]

42. Melzack and Katz, "The Gate Control Theory," 201.
43. Melzack and Torgerson, "On the Language of Pain," 50-59.
44. Melzack and Torgerson, "On the Language of Pain," 58-59.

Melzack's early experiments, the accretion of pain words, and his work with Torgerson were reflected in the 1975 publication of the MPQ. Its ability to help patients articulate, and practitioners understand, an individual's pain experience has been a significant contribution. No measurement tool has been more thoroughly vetted across conditions, patients, and cultures by clinicians, researchers, social scientists, and historians. The questionnaire's development, clinical career, and research history have spurred debate over the concepts and theory of pain that the MPQ embodies; its psychological, linguistic, and cultural assumptions and implications; clinical and operational strengths and drawbacks; and ontological questions about the changing nature of medical knowledge.

Extensive research and deployment of the MPQ in diverse clinical settings have raised linguistic, epistemological, operational, and clinical questions about the assumptions, word categories, scoring methods, cross-cultural utility, and impacts of the MPQ. In 1985 Chapman et al. reviewed linguistic questions that the MPQ's first decade had raised. The authors asked whether the questionnaire's word scales required an unrealistic level of linguistic ability among experimental subjects and users. Assuming that patients gave a full effort, the authors argued that results could still reflect the limitations of a person's vocabulary as much as they might capture the nature of the pain. Some studies had found empirical support for the semantic homogeneity of the words in the 20 subgroups, while other findings were less supportive of the 1-to-5 number scales within these groups. The researchers asked if the MPQ's structure put too much emphasis on sensory aspects (which have the most subgroups) at the expense of the affective and evaluative dimensions.[45]

The clinical reality of the three dimensions of pain that the MPQ postulated has been challenged in several studies. A 1985 experiment concluded that subjects had difficulty in consistently distinguishing the sensory, affective, and evaluative word groups. This made the scores generated

45. C. R. Chapman, et al., "Pain Measurement: An Overview," *Pain* 22 (1985): 1-31; Bourke, *Story of Pain*, 151; McDowell, *Measuring Health*, 471, 488-9; Biro, *Language of Pain*, 46, 196.

by patients' responses unreliable. The analysis of the MPQ's structure with two patient groups argued for use only of the total PRI score in assessing pain. A (1994) survey of more than 1700 chronic pain patients looked at whether the PRI really did assess three distinct components when other experiments had proposed as many as seven that the PRI itself could detect. The authors wrote that variances in statistical methods and patient samples explained a significant portion of these differences.[46]

The question of whether the MPQ produced consistent scores for comparable medical conditions has been investigated. Was pain so individual that personal history and circumstances would consistently "trump" physiological patterns? Research in 1990 generated normative scores for similar medical conditions, with such scores based on large samples and intended to represent the population either as a whole or in defined subgroups. The subjects were from 51 studies of people in pain after surgery and from dental, obstetrical, experimental, headache, and lower-back conditions. The review supported the validity of the MPQ in gauging pain intensity and qualities. Across a subject group of 3600 people, all the estimated normative MPQ scores never exceeded 50 percent of the maximum. The authors attributed this to a skew in the measurements that was rooted in the inaccessibility of some of the descriptors. Only a quarter of the 78 MPQ words were used frequently by more than 20 percent of the people. The authors suggested that this consistency could make word-selection patterns a fruitful way to use the MPQ to differentiate painful conditions.[47]

Clinical usefulness has been an explicit goal of the MPQ since its debut, and several studies between 1996 and 2001 sought to further such utility by reducing the number of words patients could pick from. Three research projects looked at the MPQ descriptors' ability to articulate pain

46. Dennis C. Turk, Thomas E. Rudy, Peter Salovey, "The McGill Pain Questionnaire Reconsidered: Confirming the Factor Structure and Examining Appropriate Uses," *Pain* 21 (1985) 385-397; Holroyd et al., "A multi-center evaluation," 301-311.
47. Diana J. Wilkie, et al., "Use of the McGill Pain Questionnaire to Measure Pain: A Meta-Analysis," *Nursing Research*, Vol. 39, No. 1 (January/February 1990): 36-41.

sensation. The study found that about 32 of the 84 sensory adjectives could not be classified by the researchers within any of the MPQ's sensory subcategories because of subjects' unfamiliarity with the words or variability in how the words were used. The other 52 words could be placed in the same sensory subgroups and were given the same intensity ratings as in the original MPQ. The authors argued for this smaller set of MPQ descriptors as more clinically precise and diagnostically useful than the original group. In a follow-up, the researchers doubled the sample size to about 140 people. Twenty-eight of the 32 words retained in the first study also satisfied criteria for inclusion in this study, with four words not part of the first study added here. The authors concluded again that these 32 words would sharpen the clinical utility of the MPQ. Five years later the authors examined the affective and evaluative categories, citing research that found inconsistencies in how these words were organized. This 2001 study found that only 6 of 18 affective words, and 5 of 11 in the evaluative category could be classified in their original subgroups. They concluded that a shorter list would improve the diagnostic utility of the MPQ.[48]

The large number of MPQ translations has prompted examination of its cross-cultural strengths and limitations. An analysis of the MPQ in Polish studied translations that the authors described as made by literal translations of adjectives from English. They asked if reliance on adjectives as descriptors would be appropriate in cultures in which adjectives were not the main way that speakers talked about pain. They concurred with Chapman et al. (1985) that the questionnaire contained words that people don't typically use to describe their pain. More broadly, culturally relevant influences on the experience of pain raise complex questions about the importance of

48. Ephrem Fernandez and Stuart Towery, "A parsimonious set of verbal descriptors of pain sensation derived from the McGill Pain Questionnaire," *Pain*, 66 (1996): 31-37; Stuart Towery and Ephrem Fernandez, "Reclassification and rescaling of McGill Pain Questionnaire verbal descriptors of pain sensation: a replication," *Clinical Journal of Pain*, 12(4) (December 1996): 270-6; Ephrem Fernandez and Gregory J. Boyle, "Affective and Evaluative Descriptors of Pain in the McGill Pain Questionnaire: Reduction and Reorganization," *The Journal of Pain*, Vol. 2, No. 6 (December, 2001): 318-325.

learning from the social environment about what pain is like and how people are expected to react.[49]

This small sampling of linguistic, structural, and operational inquiries into the MPQ proposed changes that did not alter its original structure. The proposed improvements showed how the MPQ stimulated research and crystallized debates over how to reconcile pain's dimensions in a clinically helpful instrument. The MPQ's goal of statistical validity and clinical value encouraged researchers to examine its methods and the implications of the scores it produced.

Other refashionings went further in devising new tools in order to address what they saw as significant shortcomings in the MPQ. In 1982 psychologists Bernard Tursky, Larry Jamner, and Richard Friedman introduced the Pain Perception Profile (PPP), which they described as a psychophysical approach to evaluating pain. The authors noted an ongoing shift to an understanding of pain as a complex phenomenon of many dimensions, few of which were well understood. They expressed surprise that this change had not led to a comparable evolution in how pain was assessed, noting that it was still measured along the single dimension of intensity.[50]

The Tursky study acknowledged the MPQ as an advance in the field and said that the PPP sought to address several methodological questions. One was the scores generated by a patient's choices from the 20 word groups. Each group lists words in a numbered sequence from least to most severe. When a patient picked a word, that choice was given the numerical score of its placement within the group, and totals within each of the three categories were calculated to yield a numerical score. This method raised several questions. Are the differences in severity between each word the same for all clusters? How much, or what kinds of, pain mark the differences in word choices? How

49. Weronika Kalwak, et al., " 'My Pain is more like a noun:' Linguistic issues concerning the usage of the McGill Pain Questionnaire," paper presented at 3rd Global Conference, "Pain: A Making Sense of Project," May 19-21, 2012, Prague, Czech Republic.
50. Bernard Tursky, Larry D. Jamner, and Richard Friedman, "The Pain Perception Profile: A Psychophysical Approach to the Assessment of Pain Report," *Behavior Therapy* 13 (1982): 376-394; McDowell, *Measuring Health*, 514-520.

do we know that patients mean the same things by the same words? Are the same numbered words in each group somehow comparable?[51]

The goal of the PPP was to deliver quantitative data on multiple dimensions of the pain experience, and it was positioned by its authors as an instrument designed for clinical use. It asks questions that measure sensory threshold and pain connotative judgments; it generates a laboratory measure of a person's ability to estimate the magnitude of controlled pain stimuli; it includes quantified pain descriptors derived in part from the lists developed by Melzack and Torgerson in the early 1970s; body diagrams; and a diary. The PPP applied scaling methods to assess qualitative and quantitative aspects of the reported pain experience. The pain diary asked for patients' self-evaluations of the chosen descriptors and ongoing recording of his or her experiences and emotions. The PPP generated measures of pain sensitivity, discomfort, threshold, and tolerance. The authors argued that these give clinicians better insight into how patients responded to pain.[52]

Another reinterpretation of the MPQ was published in 1982 as the Wisconsin Brief Pain Questionnaire, whose name was changed several years later to the Brief Pain Inventory (BPI). The authors of the BPI admired the MPQ for showing how broad the range of information relevant to the clinical assessment of pain could be. They expressed surprise at the dearth of methods for assessing cancer pain, which they attributed to the lack of a tool that was easier to use than the MPQ. The authors felt that the MPQ was too long and difficult. Beyond these operational hurdles, it ignored a patient's pain history and did not generate data on how pain was interfering with a person's daily activities. Like the MPQ and PPP, the BPI used a questionnaire and a human-figure diagram for the patient to mark. It asked the patient to pick words to describe his or her pain. While the BPI sought to address what its creators perceived as gaps in the MPQ, they noted that

51. Tursky, Jamner, and Friedman, "Pain Perception Profile," 380, 384.
52. Tursky, Jamner, and Friedman, "Pain Perception Profile," 379, 388.

their measurement tool did not address the emotional significance of the pain to the patient or the circumstances that might be causing pain. That the authors felt a need to acknowledge this dimension of pain suggests how fully questions of individual circumstances and meaning had permeated pain measurement by the early 1980s.[53]

The PPP and BPI are examples of how the MPQ was revamped based on research and deployment in clinical settings. They show how the MPQ stimulated research that sought to improve the questionnaire by making it more robust. Beyond their status as adaptations of the MPQ, the PPP and BPI are two of the dozens of scales, observational methods, and questionnaires for quantifying pain that have been developed since the mid-twentieth century. In 2014 historian Noemi Tousignant argued that innovation in the history of pain measurement innovation has occurred by building a steadily greater acknowledgment of pain as subjective into tools that have remained simple. Measurement methods developed after the mid-20th century track this growing understanding of pain as multidisciplinary, affected by psychological factors, and shaped by personal circumstances.[54]

Still, the question of whether the history of pain measurement has been a "history of failure" is open to question. If "success" is defined as the creation and widespread adoption of a single tool or method, then "failure" is an apt summary of this history, and there are substantial grounds for this evaluation. There are no stable, universal units of measure for pain. Research protocols and definitions of pain states have remained variable. Technologies that detect minute physical attributes and changes have been powerless to isolate pain. Compared with other ills, even other subjective conditions such as anxiety, pain's quantitative parameters have remained elusive. But if "success" is defined as knowledge gained from attempts to create a universal pain scale; as the

53. Tursky, Jamner, and Friedman, "Pain Perception Profile," 377-381.
54. Noemi Tousignant, "A Quantity of Suffering: Measuring Pain as Emotion in the Mid-Twentieth-Century USA," in *Pain and Emotion in Modern History*, ed. Rob Boddice (New York: Palgrave Macmillan, 2014), 112; Marcia L. Meldrum, personal communication, July 26, 2013.

development of body-part- or condition-specific assessment methods; and an increase in the ability of clinicians and patients to communicate effectively about pain, then the history of pain measurement can be seen as a failure comprising many successes. Attempts to quantify pain have advanced understanding of how nerve fibers, pain pathways, the spinal cord, and the brain work on their own and together to shape the experience of pain. This research has explored how external factors – personal history, social environment, and individual circumstances – can affect the response to, and perception of, pain through the electrochemical participation of brain regions that are involved in emotion and personal history.[55]

Anesthesiologist Thomas E. Rudy sketched the wider landscape of pain measurement that such research had forged by 1989:

> Over the past 20 years, pain measurement has gained considerably in both maturity and spheres of usefulness in a wide range of settings, from the laboratory to the clinic. During this time there has been a proliferation of measures, scales, questionnaires, inventories, observational techniques, and other assessment strategies designed to quantify pain and/or cognitive, behavioral, affective, and physiological consequences of the pain experience.[56]

Rudy here characterized a recent chapter in a history of pain measurement that stretches back to about 1800. Efforts to measure pain since then can be grouped into three broad activities – psychophysics, standardized questionnaires, and rating scales. Developed in the 19th century, psychophysics encompasses methods for quantifying the stimulus needed to create pain as well as the precise amount of added stimulus needed to produce increasingly intense pain. Psychophysics pioneer Gustav Fechner formulated a mathematical relationship between the intensity of a stimulus and the perception that results. He devised a way to scale sensation by a metric called the 'just

55. Marcia Meldrum personal communication July 26, 2013.
56. Thomas E. Rudy, "Innovations in Pain Psychometrics," in Chapman and Loeser, ed., *Advances in Pain Research*, 51.

noticeable difference.' Fechner sought to establish the objective magnitude of these differences as revealed by carefully graded levels of the stimulus. Seventy years after Fechner published *Elemente der Psychphysik* (1860), his ideas would shape mid-century experiments in pain measurement by the Cornell team of physiologist James D. Hardy, neurologist Harold G. Wolff, and research associate Helen Goodell. Fechner's ideas have been described as a conceptual starting point for debates over how to incorporate subjective factors in measuring illness and health. Psychophysics' focus was how people understand and evaluate physical properties such as the length of a line, the volume of a sound, or the intensity of pain. Psychophysics has been focused on humans' capacity to measure their world and to experience it as measurable.[57]

The second activity in pain measurement has been the standardized questionnaire. Here a patient describes his or her pain in terms of its intensity, location, character, duration, possible causes, and other dimensions. The MPQ is one of hundreds of questionnaires. The third category is the rating scale. There are visual, verbal, and numeric scales and some that combine the forms. Scales are widely used in assessing clinical pain and have played a major role in the development of pain relievers since the middle of the 20th century. Many people have been asked: "On a scale of one to ten, with one being no pain, and ten being the worst you can imagine, how would you rate your pain right now?" Examples include the Back Pain Classification Scale (1978), the Pain and Distress Scale (1983), and visual analogue rating scales (VAS) that began to appear in the 1970s.[58]

Several themes have emerged from this dense history of pain measurement after World War II. One is a focus on clinical utility. The tools described sought to help clinicians and patients. While theory has significantly informed pain measurement – and is crucial to understanding the MPQ -- the primary goal of most pain measurement studies was not to advance or contest a particular

57. Noble et al., "Measurement of Pain, 1945-2000," 14-18; James D. Hardy, Harold G. Woolf, and Helen Goodell, *Pain Sensations and Reaction* (Baltimore: The Williams & Wilkins Company, 1952); McDowell, *Measuring Health*, 16-17.
58. Noble et al., "Measurement of Pain," 14-18; McDowell, *Measuring Health*, 470-520.

theory. There was also a focus on trying to unify, in a practical way, dualities that have been persistent in the history of pain: physiology and psychology; the lab and the clinic; emotions and sensations. Finally, by the 1970s, a concept of the centrality of personal factors to the pain experience had grown substantially among clinicians and patients. The MPQ arrived at a moment when the notion of pain's crucial individuality had moved from the periphery of medical discourse to a position of growing strength. The premises, forms, and patient-centered approach of much pain measurement after 1945 show how personal factors had achieved new respectability in the assessment of pain. Tousignant's argument that pain measurement had advanced by increasingly incorporating notions of the subjective (defined as reportable only by the person experiencing it), rather than through the growing complexity of technologies and tools, captures this trend, and the MPQ is a leading example of Tousignant's idea.

Despite the proliferation of measurement tools after 1970, physicians continued to find clinical usefulness to be elusive. Looking back at the vogue between 1940 and 1950 for a device to measure pain called the dolorimeter, a physician wrote in 1967 that pain measuring tools were cumbersome, hard to use, not good at measuring, and basically unfit for clinical use. That was why they had been confined mostly to the lab. A 1990 report from Britain's surgeons and anesthetists stated that there simply were no current methods for the objective assessment of pain, even as it described the MPQ as having value as a research tool.[59]

The growth of conceptions of pain as multidimensional can be seen as a response to the forms and variations of pain that have made definitive measurement so difficult. Pain is associated with so many conditions, and in some cases with no apparent illness or injury, that measurement techniques have had to implement diverse experimental strategies, assumptions, and focus on a

59. Robert E. Peck, M.D., "A Precise Technique for the Measurement of Pain," *The Journal of Head and Face Pain*, Vol. 6, Issue 4 (January 1967): 189-194; Suzanne M. Skevington, "Pain control and mechanisms for the measurement of pain," *Journal of Psychopharmacology* 5 (1991): 360-370.

condition or population. If pain was as individual as Melzack and others believed, what did it mean to establish stable procedures for measuring it? Measurement methods have sought to isolate seemingly common attributes of pain – such as thresholds, tolerances, and the effects of pain relievers – from which researchers have sought to extract physiological patterns and laws.

These goals and methods embody beliefs about pain's mechanisms and what is important to measure. The MPQ articulated a theory of the underlying processes of pain as well as about its origins and nature. It had an especially close tie to pain theory since its creator was also co-developer of the highly influential gate control theory of pain (GCT, 1965). The MPQ sought to operationalize the GCT, and by the 1990s the intertwined careers of both had influenced development of the neuromatrix theory, Melzack's overarching statement of how pain worked. Understanding the GCT can help decode how the MPQ understood pain, what it was trying to measure, and why.

The importance of theory to pain measurement extends well beyond Melzack's role. Surgeon John Loeser noted in 1989 that pain measurement occurs at multiple levels – at the point of original stimulus, the electrochemical activities that follow, behavior that results, and self-reports from patients. In addition, knowledge of pain derives from animal and human studies in the laboratory and clinic. Theory seeks to connect ideas and results across all these domains. Theory is the bridge between empirical phenomena and how clinicians and researchers interpret them. Theory is where findings from different sectors of pain research converge and interact.[60]

60. Gary W. Donaldson, "The Determining Role of Theory in Measurement Practice," in Chapman and Loeser, ed., *Advances in Pain Research*, 32; W. Crawford Clark, Malvin N. Janal, and J. Douglas Carroll, "Multidimensional Pain Requires Multidimensional Scaling," in Chapman and Loeser, ed., *Advances in Pain Research*, 286.

**Gate Control Theory**

Although brisk debate is a staple among pain clinicians and researchers, few would dispute the claim that publication of the gate control theory in 1965 was the start of the contemporary era in pain's history. Its influence has been wide and enduring. It stimulated extensive research and debate on the physiology of pain and the psychological features that accompanied it, and the theory suggested numerous approaches to ideas and studies in both disciplines. Even more than the MPQ, gate control theory was crucial to how pain became subjective.[61]

When Melzack arrived at MIT in 1962, one of the first people he met was Patrick Wall (1925-2001), a neuroanatomist who Melzack had been advised to seek out in hopes of procuring lab space. Their meeting launched a collaboration between two scientific minds and personal styles in which vast differences were overcome by mutual respect and a shared abhorrence at the impact of pain on so many people. Their partnership resulted in significant contributions to the science and professionalization of pain. The collaboration was forged in sometimes heated debates. Melzack said that they had argued about nearly everything it was possible to disagree on. One of their first debates was about the idea that impulses that originate in the brain's centers for emotion and memory travel down the spine and can inhibit the transmission of pain signals and the perception of pain. Melzack said that Wall "sort of tolerated" this concept of descending inhibitory impulses, which Melzack believed in strongly.[62]

---

61. Fernando Cervero, "The Gate Theory, Then and Now," in Merskey, Loeser, and Dubner, ed., *Paths of Pain*, 33-49; Wailoo, *Pain: A Political History*, 77-87; Cervero, *Understanding Pain*, 33; Melzack and Katz, "The Gate Control Theory," in Hadjistavropoulos and Craig, ed., *Pain: Psychological Perspectives*,13-34.
62. *Oral History Interview with Ronald Melzack*, 16 October 1995 (Ms. Coll. No. _____), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise B. Darling Biomedical Library, University of California, Los Angeles, 51.

The gate theory offered a concept of pain whose conceivable forms were almost limitless. Melzack and Wall put forward the metaphor of a gate, located in the dorsal horns of the spinal column, that opened or closed to modulate the content, movement, and perceptual outcome of pain stimuli. The gate operated by balancing the excitation of two types of nerve cells: large-diameter fibers open the gate, whereas small ones close it. When an injury stimulates the fibers, impulses excite central transmission cells. These cells receive excitatory and inhibitory inputs from other types of nerve fibers. In their journey up the spinal cord to the brain, transmission cells are affected by nerve impulses traveling down from the brainstem and cerebral cortex. A person thus perceives pain that has been shaped by a complex interplay of electrochemically encoded signals originating and interacting in the brain and spine.[63]

The gate theory rejected a prevailing model of pain, summarized as specificity theory, which said that painful stimuli sent uniform and unmediated signals to a point in the brain that registered pain. Melzack and Wall believed that pain 's diversity was in part an outcome of dense patterns among nerve impulses. Melzack and Wall were not the first to propose a pattern theory of pain. They had influenced by earlier researchers, including Goldscheider, Livingston, and neurosurgeon Willem Noordenbos. The GCT emphasized the importance to these patterns of central neural mechanisms – brain processes that involved the cortex and limbic regions, "homes" to emotion, self-awareness, and memory, in opening and closing the gate. Gate theory proposed that signals traveling these pathways from the brain modulated input to the spinal cord from the periphery. The theory pushed medical and biological scientists to explore the brain as an active participant in modulating inputs that came from all parts of the body.[64]

63. McDowell, *Measuring Health*, 470-472; Cervero, *Understanding Pain*,135-136, 155; Melzack and Wall, *Challenge of Pain*, 149-195.
64. Cervero, *Understanding Pain*, 135-136; Hardy, Woolf, Goodell, *Pain Mechanisms*, 1-24; Melzack and Wall, *Challenge of Pain*,149-165.

The GCT had a significant impact on how specialists viewed the psychology of pain. It stimulated investigations into the mechanisms of how personal factors were implicated in the experience of pain. It moved the brain, and the central neural processes it managed, to "center stage" in the experience of pain. It offered a broad palette for the inclusion of psychological factors in assessing pain. It was a major stimulus to research on the role of emotion, cognition, and personal circumstances in pain. By linking physiology and psychology inseparably the GCT helped legitimize psychological dimensions for biomedical practitioners. It increased interest in treatment methods such as hypnosis, relaxation, and cognitive/behavioral therapies. Its ambition was to bring together the perspectives of neurophysiology, psychology, and clinical practitioners. Although subsequent research would overturn some of the theory's neurophysiology, the GCT provided a new model of pain for clinicians and researchers.[65]

In 2014 historian Keith Wailoo ascribed significance to the GCT that went beyond its influence in pain research. He saw the theory as culturally emblematic and productive. He argued that it had been in sync with the 1960s' political and cultural contests, legal battles, and changing pain management practices. This impact, for Wailoo, ranged well beyond doctors' offices and encounters with patients. Gate control theory implied a broader sociological challenge to a prevailing biomedical model of pain and to established medical practices and power relationships. Its impact on debates over who defined pain and society's obligations to those who suffered from it transformed the theory into a metaphor for diverse possibilities for treatment and the political reconfiguration of pain. The theory's unabashed lack of detail about how the body's pain gateways worked could be read to endorse a laissez faire or libertarian perspective on relief. Gate control theory pushed alternative pain management practices closer to the medical mainstream.[66]

---

65. Wailoo, *Pain: A Political History*, 77-79, 80-86, 87, 91, 95, 207; Bond, *Pain*, 22-25, 189; McDowell, *Measuring Health*, 470-472.
66. Wailoo, *Pain: A Political History*, 77, 79, 85.

Following three decades of research on the theory, Melzack proposed a neuromatrix model that sought to move attention from the dorsal horn of the spinal cord, which has been described as the main focus of forty years of studies on pain. Like the GCT, the neuromatrix theory sought to reconcile diverse actions of the spinal cord, brain, and periphery within a cohesive conceptual framework.[67]

The question that neuromatrix theory sought to answer was how the body experiences itself as a whole. What were the neurophysiological processes that underlie this experience, and how did they work? Melzack's theory proposed a complex set of intertwined neural networks that make up feedback loops among the cortex, thalamus, and limbic systems of the brain, which govern cognition, emotion, and memory. He argued that the patterns that these networks produce are coherent in ways we don't yet understand and that they produce pain when the mechanisms go awry. Melzack connected to traditional pain theories in his belief that pain could also result from the body's failed efforts at homeostasis and self-regulation by the nervous system.[68]

Melzack argued that multiple sectors of the brain were involved in processing inputs, generating patterns, and producing what a person experiences as his or her entire body. This neural network is grounded in genetics but can be modified by individual sensory experience. Just as the GCT's concept of descending impulses from the brain had the effect of marrying psychology and physiology, a concept of interplay between genetics and individual experience brings them together in the neuromatrix theory. For Melzack, diverse experiences were subserved by different portions of this dense network, each of which produces a distinct piece of what he called the total neurosignature. Behavior took place after diverse inputs have been analyzed and modulated to a

67. Cervero, *Understanding Pain*, 92; Ronald Melzack, "Evolution of the Neuromatrix Theory of Pain. The Prithvi Raj Lecture," *Pain Practice*, Volume 5, Issue 2 (2005) 85-94. Presented at the Third World Congress of World Institute of Pain, Barcelona, 2004; Ronald Melzack, "Phantom Limbs, the Self and the Brain," D. O. Hebb Memorial Lecture, *Canadian Psychology* 30:1 (1989): 1-16.
68. Melzack and Katz, "The Gate Control Theory," in Hadjistavropoulos and Craig, ed., *Pain: Psychological Perspectives*, 20-25, 31-35, 42.

degree sufficient to produce meaningful experience. Brain processes and outputs, as expressed in the GCT, generate the qualities of individual experience of the body and self.[69]

The multidisciplinary approach that Melzack and other have championed for the treatment of pain has been reflected in scholarly and scientific assessments of the MPQ. Diverse analyses of clinical, linguistic, historical, operational, and epistemological issues that the MPQ has raised has been a hallmark of its career. The MPQ has stimulated questions and theories about what it means to measure pain and how an individual experience can be captured, or some part of it captured, in numerical calculations.

In 2014 historian Joanna Bourke surveyed the MPQ's career. She said that the questionnaire had stimulated a massive research output and spirited debate that showed few signs of subsiding. For Bourke three broad issues were central. The first was translation. Researchers have studied how the MPQ's descriptors of pain are specific to the culture from which it emerged and thus might be differentially or less applicable outside that culture. She asked whether a specialized vocabulary in one language can be meaningfully translated. Bourke claimed that the MPQ assumed an unrealistic degree of linguistic homogeneity in Britain and America, citing the range of regional dialects and usages within both. Finally, Bourke asked what role the MPQ (and other questionnaires) played in shaping how patients describe what they are going through and thus creating what it purports to measure. Is the MPQ truly flexible enough to capture the diversity it attributes to pain? In contrast to those who have asserted that the MPQ assumes linguistic facility, she claimed that many people have a richer vocabulary for describing their pain than the MPQ. What are the implications of pain as fully describable, Bourke asked, by a small set of words? She suggested that the MPQ and other questionnaires repeated an error she attributed to Elaine Scarry, whose *The Body in Pain* (1985) has become a touchstone in the analysis of pain. Bourke argued that Scarry had been too literal in

69. Melzack, "Phantom Limbs," 1-16.

attributing agency to metaphors, as when pain is said to bite, stab, dominate, and subdue. In this way Scarry had given agency to pain, not a person. Bourke assessed this as an ontological fallacy.[70]

Linguistic and structural issues that the MPQ raised have also been examined. These include the makeup of the word groups; the suitability of choosing only one word from each category; the choice of summary scores; and whether the MPQ did reflect Melzack's theory of pain. On the construction of the word clusters, epidemiologist Ian McDowell noted studies that have validated Melzack's classification of pain descriptors and supported his emphasis on pain as multidimensional. The rule of just one word in each category helped make patients' descriptions more precise while it raised questions about potential distortions if words were missing, misunderstood, or did not fall neatly into one per cluster. The MPQ's summary scores offered numerical validity in reflecting the rank order of words in each group, but may not have had statistical validity that showed meaningful correlations between patients' responses and known pain conditions.[71]

In 2010 physician David Biro described clinical and operational factors that led to a decline in the questionnaire's use after the mid-1990s. Except for highly specialized pain clinics, use of the MPQ has become rare, in part because it was often difficult to explain and fill out. Biro said that, more fundamentally, the MPQ left clinicians and patients unsatisfied. He claimed that the MPQ's metaphorical language made doctors uncomfortable while patients wanted more of it. Biro's analysis reflected growing time constraints on physicians that increased in the 1990s as a managed care model became more prevalent in the United States. Biro's purported discomfort among doctors may be as attributable to long-standing de-emphasis of pain in medical education. Although Biro's comments on patients' interest in metaphorical language were drawn from his

70. Bourke, *Story of Pain*, 147-148, 151-154, 158; Elaine Scarry, *The Body in Pain: The Making and Unmaking of the World* (New York: Oxford University Press, 1985), 5, 32-33, 54-56. Scarry was among the earliest scholars to explore connections across the "mundane" experience of pain and rituals of torture and war.
71. McDowell, *Measuring Health*, 471, 488-9.

experience, it is not clear that patients really clamor to use metaphors in their interactions with doctors. Why isn't it as plausible that at least some patients appreciate the guidance given by the MPQ's word groups?[72]

In 2009 sociologist Cassandra S. Crawford raised epistemological questions in her analysis of the MPQ's role in the broader history of phantom limb pain. This form of pain had been noted by healers as early as the sixteenth century, and Melzack attributed particular significance to it in the history of pain. He believed phantom-limb raised defining issues for psychology – the nature of perception and awareness, the makeup of reality, and the links among body, mind, and individual history in the experience of pain. Crawford described what she believed was revisionist history. In 2005 Melzack said he had developed the list of descriptors from patients' input. However, the 1971 article with Torgerson on the language of pain said that the pain words had been drawn from sources in the clinical literature. These sources included a list of 44 words compiled by psychologist Karl Dallenbach in 1939.[73]

Crawford said her interest was not in nitpicking historical accounts but in what this apparent inconsistency signified. She argued that in 1971 patients' narratives about pain were deemed untrustworthy or insufficient so credibility for the MPQ required it to be rooted in clinical data. By 2005, the idea that words generated in direct communications with patients could be used to justify the validity of the instrument. Crawford has described an element of pain's subjectification as patient accounts of pain gained credibility that began approaching that of clinical data as sources of authority on pain. Growth in the clinical relevance of patient narratives was given form, impetus, and credibility by the MPQ's content and career.[74]

72. Biro, *Language of Pain*, 46, 196.
73. Cassandra Crawford, "From pleasure to pain: The role of the MPQ in the language of phantom limb pain," *Social Science and Medicine*, 69 (2009): 655-661; Melzack and Wall, *Challenge of Pain*, 61-70, 130-1, 158-9.
74. Crawford, "Pleasure to pain," 657-658.

The linguistic, clinical, operational, and historical issues that Bourke, McDowell, Biro, and Crawford raised had emerged from hundreds of research studies and substantial clinical deployment of the MPQ. They show how the questionnaire retained its relevance despite a decline in clinical use after the mid-1990s. Its clinical vogue between 1975 and 1995 furthered the subjectification of pain by promulgating widely a concept of pain as crucially shaped by individual factors and by the complex participation of the brain. Its vitality as a research platform and template lasted about a decade longer, as investigators homed in on examples of the issues.

## Conclusion

This chapter has described several ways in which the MPQ's depiction of pain played a critical role in pain's wider subjectification. The MPQ's clinical deployment and research history have made it the most widely used and studied measurement instrument in the last seventy-five years. Its word groups, three dimensions of pain, and numerical scores depicted pain as at once subjective and quantifiable for a wide audience of clinicians and patients. It privileged patients' descriptions as central to clinical assessment. It articulated a concept of pain as firmly tied to a person's circumstances, attitudes, and beliefs. In these ways the MPQ sought to reconcile pain's physiological elements with its psychological, social, and cultural dimensions. The MPQ is a rich case study in pain's subjectification because of its pioneering attempt to operationalize the measurement of pain in a way that would have concreteness and clinical relevance.

The MPQ, along with gate theory, posited psychological factors as co-equal with physiological elements of the pain experience. It was an ambitious attempt to unify findings in both disciplines and it regularly sought to incorporate growing knowledge of how the nervous system worked to shape pain. Its creator's influence in the understanding and professionalization of pain helped create interest in the MPQ among researchers in diverse fields. It spawned proposals for improvement, such as the PPP and BPI, that took its marriage of psychology and physiology in new

directions. It attempted to show a physiological basis for the role of personal factors in pain perception via the influence of nerve impulses that descended from regions of the brain involved with emotion, cognition, and memory.

The MPQ thus sought to operationalize an understanding of pain as both subjective and measurable. In its ambition, its success, and its ability to provoke further inquiry, the MPQ promulgated an understanding of pain that would linger long after the scores it generated had been left behind.

**Chapter 3 – Pain Management -- A Lucrative Ambiguity**

Between 1945 and 1978 changes in the clinical status of pain management contributed to a wider transformation in pain's status within medicine that *A Disease Itself* investigates. While developments in the treatment of pain took several forms, this chapter focuses on the growth of pharmacological remedies as a key driver of changes in how pain was treated. This expansion featured the growth of therapeutic options within treatment categories. Overall, pain treatment became more diverse, personalized, and variable, with the outcome of pain management increasingly defined by success against pain's chronicity. Changes in treatment both reflected and promoted evolution of the understanding of pain as a diverse and distinct clinical identity. The enhancement of treatment options reflected the splintering of a monolithic concept of pain in which the word itself increasingly referred to a clinical syndrome that encompassed many forms and varieties. An expansion of the treatment arsenal helped rework a prevailing concept of pain from a simple, predictable accompaniment of conditions and events to a complex and elusive disease in its own right.[1]

This chapter examines these changes in pain treatment and focuses on history of Darvon, a pain reliever introduced in the United States in 1957. Darvon's five-decade career was marked by strong market presence and enduring controversies over its safety, effectiveness, and the reasons for its commercial success. The chapter contends that Darvon's career both expressed and helped promote an inclusive, personalized, and ultimately ambiguous and contingent concept of pain. Its

1. The chapter uses pain "treatment," "medicine," and "management" as synonyms while recognizing the potential for analytical differences among them. Other areas of pain management that grew significantly after World War II included the growth of alternative and complementary treatments, such as acupuncture, and the expansion of multidisciplinary pain management clinics and practices. See Adriana Petryna et al., editors *Global Pharmaceuticals: Ethics, Markets, Practices* (Durham, NC and London: Duke University Press, 2006); Joseph Kotarba, *Chronic Pain: Its Social Dimensions* (Beverly Hills: Sage, 1983); Mitchell J. M. Cohen and James Campbell, ed., *Progress in Pain Research and Management, Volume 7: Pain Treatment Centers at a Crossroads: A Practical and Conceptual Reappraisal* (Seattle: IASP Press, 1996).

career has suggested a wider uncertainty of pain's etiology and forms as well as its patterns of arrival and decline. Focusing on pharmaceutical therapies, this chapter argues that after 1945 the expansion of treatment options critically reshaped pain management in ways that advanced a change in pain's clinical status. A growing treatment arsenal helped legitimize the clinical importance of individual factors in the pain experience. In addition, evolving treatments aligned well with, and benefited from, wider social currents. Between 1945 and 1980 America's political and social upheavals could hardly leave pain and its treatment untouched. Overall growth in the cultural authority of personal experience affected how clinicians and patients dealt with pain.

This chapter's case study contends that Darvon was a compelling technology of pain's transformation. It was one of many drugs that supported a view of pain as diverse, but Darvon's long-running commercial success and clinical uncertainty created a market and social niche of powerful ambiguity. Darvon was an ingenious platform. From pre-market testing until its removal from the US market as agreed to in late 2010, Darvon helped patients, clinicians, and scientists grow more comfortable with an inclusive notion of pain. Darvon was a technology of change as well as its emblem, ally, and mirror. Its genial ambiguity was made taut by strong marketing and cultural tailwinds. These enabled Darvon to forge and maintain a position of lucrative uncertainty.

The controversy over Darvon encapsulated the growing ambiguity of pain's origins, forms, and treatment after 1945. Darvon's rich career arc exemplified both the transformation of pain management and a more fundamental shift in the clinical status of pain. It was a mainstay of clinical pain treatment despite enduring uncertainty about its effectiveness and safety. Its ability to alleviate mild to moderate pain showed both the diversity contained in that category and the variability of responses to the "same" therapy. Darvon was far from the only post-1945 pain reliever to embody this fluidity; but its long-running commercial success and clinical uncertainty created a market and social niche of powerful ambiguity. Thanks to an astute blend of biochemistry

and branding, supported by an uninterrupted record of commercial success, Darvon was able to forge and maintain a position of lucrative uncertainty that expressed a fundamental ambiguity about pain and how to treat it.

The wider post-war setting in which Darvon became a prominent pain reliever was characterized by growth in both the scale of clinical medicine and the array of pain therapies available to clinicians. After 1945 there were substantial changes in American medicine produced by the introduction of new classes of drugs, wider regulatory and legislative scrutiny, and steady growth in the scale of business done outside the United States. New treatment modalities and options abounded. There were new synthetic and semi-synthetic opiates, such as methadone and propoxyphene, the chemical heart of Darvon. In addition, antidepressants, anti-anxiety drugs, and nonsteroidal anti-inflammatory drugs were increasingly deployed against pain. Behavioral and cognitive treatments, including biofeedback, hypnosis, meditation, and homeopathy, took their places alongside acupuncture and physical medicine as multidisciplinary approaches to pain won favor. There were novel nerve-block and neurosurgical techniques. This expansion of treatment options pointed toward the clinical realities of pain's many individual presentations; it also enabled clinicians and patients to personalize treatment and helped legitimize the diversity of forms and treatments.[2]

2. Jonathan Liebenau, *Medical Science and Medical Industry: The Formation of the American Pharmaceutical Industry* (Baltimore: The Johns Hopkins University Press, 1987), 9; Carol A. Warfield and Zahid H. Bajwa, *Principles and Practices of Pain Medicine, Second Edition* (New York: McGraw-Hill Medical Publishing Division, 2004), 581-811; Norman Gevitz, editor, *Other Healers: Unorthodox Medicine in America* (Baltimore: The Johns Hopkins University Press, 1988); Thernstom, *The Pain Chronicles,* 49-50*,* 102-103, 129, 146-155, 159-166; Mark S. Wallace and Peter S. Staats, ed., *Pain Medicine and Management: Just the Facts* (New York: McGraw-Hill, 2005). Physician Steven F. Brena has noted that between the 1920s and the 1960s, "hope was high that chronic pain might be controlled by surgical or chemical interruption of the nervous system's pain-pathways." This hope was gradually dashed by discoveries, described in Chapter 1, of the neurophysiological complexities of the transmission and modulation of pain within the nervous system. See Steven F. Brena, ed., *Chronic Pain: America's Hidden Epidemic* (New York: Atheneum/SMI, 1978); James C. White and William H. Sweet, *Pain and the Neurosurgeon: A Forty-Year Experience* (Springfield, IL: Charles C. Thomas, 1969), 3-8.

Within this expanded pharmacopeia, synthetic and semi-synthetic opiates such as propoxyphene achieved notable growth. These were often based on petroleum by-products and were laboratory-concocted hybrids of pharmacologically refined morphine. They began to appear in the US during World War II. Meperidine, known by its brand names as Demerol, Dolantin, or Pethidine, was launched as a non-addictive pain killer and did not require a prescription for five years after its introduction. It was a powerful analgesic that quickly proved to be addictive and potentially lethal. Methadone, created by a German army researcher in 1942, has had a rich career as an analgesic and treatment alternative to heroin addiction. Fifteen years after the war ended, more than 60 such therapies were available. They carried very little of opium's taint, because they had been marketed as unrelated to it for their entire careers.[3]

In their numbers and capabilities, the new agents had a dual and contradictory impact on the clinical status of pain management. Progress against acute pain both hindered and supported the emergence of chronic pain as a distinct clinical entity. In bringing acute pain under better control, the new class of opiate-based treatments hindered the emergence of chronic pain as a clinical entity by creating a perception that pain, in the acute forms in which most clinicians understood it, was widely predictable and increasingly manageable. At the same time, new treatments supported the emergence of chronic pain as a clinical entity by exposing the inadequacies of those therapies in cases where pain persisted in the apparent absence of organic causes. Over time, the proliferation of synthetic opiates brought the differences between acute and chronic into sharper relief and

3. Dormandy, *Worst of Evils*, 417; Bond, *Pain*, 152-166; Spanswick and Main, *Pain Management*, 269-285. Authors have categorized pain treatments along different dimensions. Bond described how opium-based pain relievers act centrally, and, based on molecular structure, he identified six subgroups: alkaloids of opium such as morphine; semisynthetic alkaloids, such as heroin; thebaine derivatives, such as buprenorphine, structurally related to morphine but far more potent; synthetics with morphine-like properties, such as fentanyl and oxycodone; benzomorphan derivatives, such as pentazocine; and the methadone group, which includes propoxyphene. Categories based on drugs' targets include the antipyretics and anti-inflammatories; NSAIDs, such as aspirin and ibuprofen; tranquillizers, antidepressants, and anticonvulsants. Steven Brena noted four groups of pharmacological treatments that were known to have some utility in addressing pain: 1) salicylates 2) opiates 3) barbiturates, and 4) tranquilizers. See Brena, editor, *Chronic Pain*, 38, 72.

suggested limits even for opiate-based therapies that set the "gold standard" for the treatment of many kinds of pain.[4]

Shifts in the boundaries and perceptions of acute and chronic pain were concurrent with the unfolding of social and demographic events that were making chronic pain more prominent after 1945. Longer life spans; the armies of chronically injured, physically and psychologically, from two world wars; and steady growth in vehicular and industrial accidents made chronic pain more visible in clinicians' offices and helped to refashion the challenge those clinicians faced. Progress against acute and transient pain masked, for many clinicians, the inroads chronic pain was making across the population. After 1945, pain joined the list of conditions for which the basic strategy became long-term management and mitigation, often measured by improvements in functional capabilities and a decline in the ability of pain to interfere with normal activities.

If changes in the treatment of pain advanced a concept of pain as complex and chronic, Darvon was a rich example of how this could work. Darvon was the brand name for a family of products based on propoxyphene, a synthetic morphine derivative that was a chemical first cousin to methadone. Darvon arrived on the US market in 1957 after scientists at Eli Lilly and Company

4. Robert A. Johnson et al., *Trends in the Incidence of Drug Use in the United States, 1919-1992*, (Rockville, MD: U.S. Department of Health and Human Services Substance Abuse and Mental Health Service Administration Office of Applied Studies, March 1996), 36-42. David Courtwright's studies of the history of opiates are essential background to this story. See also Jill Jonnes, *Hep-Cats, Narcs, and Pipe Dreams: A History of America's Romance with Illegal Drugs* (New York: Scribner, 1996), 25, 114-115, 238-239; Caroline Acker, *Creating the American Junkie: Addiction Research in the Classic Era of Narcotic Control* (Baltimore: Johns Hopkins University Press, 2002); Martin Torgoff, *Can't Find My Way Home: America in the Great Stoned Age 1945-2000* (New York: Simon and Schuster, 2004); Musto, *The American Disease*, 5, 6, 13, 151-182. Two enduring debates that have stemmed from shifting parameters of acute and chronic pain have been the role of opioids in addressing chronic pain and what can be termed the under-treatment of pain/epidemic misuse dynamic. Between 1980 and 1995, physicians' deployment of opioids in chronic pain grew with the encouragement of studies that purported to show extremely low addiction risk from new therapies. After 1995, growing reports of addiction were forming a backlash against this approach as experience with the compounds piled up. Under-treatment of pain, especially in cancer patients, became a mantra among clusters of clinicians and an article of faith among pain "dissenters" and a wider circle of drug-policy reformers. By the mid-1990s, growing fear of inducing addiction, and later, of legal liability inhibited use of opiates among clinicians followed revelations of the darker potentialities of synthetic opiates. These events showed the enduring variability of pain's forms and people's reactions to treatment as well as the mercurial personalities of the "same" therapeutic molecules.

formulated and began to test it in 1953. Propoxyphene was also studied at the Addiction Research Center (ARC), the research wing of the federal narcotics prison at Lexington, Kentucky, which had opened in 1935. Positioned from the start as a treatment for mild to moderate pain, Lilly marketed Darvon aggressively as a low-risk, modest-reward therapy that patients tolerated well and that helped with numerous painful conditions. Sales rose rapidly after its introduction despite questions about propoxyphene's stand-alone effectiveness and safety that would endure across Darvon's history. It was not clear how much analgesic power propoxyphene delivered on its own. Beyond this there were danger signs. As an opiate Darvon could nurture dependence; an ongoing question was the extent of this ability. Darvon also looked able to disrupt the heart's electrical systems.[5]

While this chapter asserts that changes in treatment advanced a change in pain's clinical status as decisively as did changes in measurement, there have been significant divergences between their histories. Measurement has had a more steady accretion of questionnaires, observational methods, and physiological testing, with acceleration after 1800 and again after 1965. By contrast, the history of treatment features more defined continuities and milestones. Opium, aspirin, ether, or some version of their active components have been deployed against pain since Biblical times. Important inflection points in treatment have included the isolation of morphine from opium (1805); the arrival of surgical anesthesia (1846); and the introduction of aspirin as a consumer product (1899). Differences in the historical arcs of measurement and treatment contrast with an important convergence between them after 1945. In an intense contest to capture a growing market, manufacturers needed to assess the analgesic effects, variations with dosage and condition,

5. Campbell, *Discovering Addiction*, 81, 91, 94; W. T. Beaver, "Are Synthetic Narcotics Adequate Substitutes for Opium-Derived Alkaloids?" *Advances in Neurology* 4 (1974): 519-525; I.F. Bennett, "Misuse of Propoxyphene," *JAMA* 235 16 (1976): 1686; Y. H. Caplan, et al., "Propoxyphene Fatalities: Blood and Tissue Concentrations of Propoxyphene and Norpropoxyphene and a Study of 115 Medical Examiner Cases," *Journal of Analytical Toxicology*, 1 (1977): 27-35.

and the side effects of potential pain relievers. This brought measurement and management into closer interdependence as the assessment of treatments required reliable measurements.[6]

**Technologies of Pain Relief, 1800-1945**

During the 19th century significant advances in the technology of pain relief included the isolation of opium derivatives including morphine, cocaine, and heroin; invention of the hypodermic syringe, and the discovery of inhalation anesthesia. In 1805, Friedrich Serturner, a 21-year-old pharmacist's assistant in Westphalia, isolated an alkaloidal base of opium. He tried the substance in dogs and showed that its effects were similar to those of opium. What Serturner had isolated was morphine. Serturner's discovery was followed by the identification of other alkaloids of opium, including strychnine (1817), caffeine (1820), and nicotine (1828). These developments provided a neurophysiological foundation for a concept of pain as complex. At the same time, they advanced the treatment of acute pain and stimulated the growth of technologies and practices that would lead to a clinical refashioning of pain after 1945.[7]

In 1898 the Bayer company of Germany introduced a new pain reliever based on an opium alkaloid that had been isolated 24 years earlier. Heroin's arrival in clinical medicine trailed by two weeks the synthesis of what would become commercial aspirin in the same laboratory. Heroin was first marketed as effective against pain without the respiratory depression and addictive capacity of earlier opiates. Between 1898 and the mid-1920s, additional variations on morphine, codeine, and other pain-relieving alkaloids of opium were identified. Heroin and other derivatives helped drive

6. Barbara Hodgson, *Opium: A Portrait of the Heavenly Demon* (Vancouver: Greystone Books, 1999), 15-17; Dormandy, *Worst of Evils*, 254-258; Bourke, *Story of Pain* 272, 277; Marcia L. Meldrum, "A Capsule History of Pain Management," *JAMA* 290 No. 18 (2003): 2470-2475.
7. Dormandy, *Worst of Evils*, 257; Eddy and May, "Search for a Better Analgesic," 407-414; Eddy and May encapsulated almost two centuries of work after Serturner as "the search for a better morphine."

significant expansion of the analgesic arsenal, personalize pain relief, blur the boundaries between approved and illicit use, and individualize drug-taking.[8]

Along with a growing base of knowledge in and contests over the neurophysiology of the nervous system, an economic structure for pain relief as a market was developing. The first contemporary pharmaceutical companies were founded in the first half of the 1800s, mostly in Germany, France, and Switzerland. American companies soon followed. Many were "ethical" pharmaceutical firms that developed alongside a less structured world of patent medicines, whose contents and purveyors were often mysterious.[9]

German companies also led research collaborations between businesses and campuses, and here too the US responded. American graduate students went to German universities and industrial laboratories in growing numbers between 1870 and 1900. One estimate placed at 3000 the number of Americans who studied in Germany during the 1880s. American universities followed the lead of their German counterparts and began to emphasize basic research as the key to drug development and discovery. As the companies we know today as Squibb, Merck, Lilly, and others grew during the inter-war years, they brought on scientists trained in Europe. These companies provided stipends for university researchers, the budgets for which steadily increased in rare defiance of dire economic conditions in the US of the 1930s.[10]

---

8. The introduction and marketing of heroin as safe and non-addictive is an example of the arc that many synthetic opiates, including propoxyphene, have traversed; introduced as safer and more effective than what already existed to a redefined status as useful and potentially dangerous. See Carnwath and Smith, *Heroin Century*, 17-18; Dormandy, *Worst of Evils*, 23-25, 127-131, 363, 435, 486; Musto, *American Disease*, 5, 60-61, 101-104, 198-199, 200-202.

9. Sykes with Bunker, ed., *Anaesthesia and the Practice of Medicine*, 97; Jonathan Liebenau, *Medical Science and Medical Industry: The Formation of the American Pharmaceutical Industry* (Baltimore: The Johns Hopkins University Press, 1987).

10. Liebenau, *Medical Science and Medical Industry*, 3, 8, 36, 37, 51, 72. Liebenau's estimate of how many Americans studied in Germany is from Thomas N. Bonner. *American Doctors and German Universities: A Chapter in International Intellectual Relations, 1870-1914*. (Lincoln, NE: University of Nebraska Press, 1963), 30-40; Bourke, *Story of Pain*, 275.

Further impetus to pursue directions first pursued by scientists in pre-war and wartime Germany was provided in 1946, when the US Department of Commerce issued a report on what post-war investigation had found regarding work to develop synthetic opiates in support of battlefield efforts. The report helped provide direction to development of the synthetic opiates. Along with Darvon, Demerol (introduced in 1949) and Percodan (1950) were in this category.[11]

Between 1900 and 1945, increasing success against acute pain, thanks mostly to a steadily expanding set of pharmacological therapies, helped reinforce a prevailing notion of pain as largely predictable, manageable, and symptomatic. New pharmaceuticals were coming on line and a commercial apparatus for marketing them to clinicians was coming into place. At the same time, increasing control over acute pain highlighted shortcomings in addressing chronic pain as it became more prominent clinically. Pain was fragmenting into many forms in newly articulated ways.

**Darvon -- A Case Study in Lucrative Ambiguity**

In 1948 Eli Lilly & Company, based in Indianapolis and founded in 1876, launched a systematic search for a non-addictive pain reliever. After testing more than 400 compounds, scientists Albert Pohland and Hugh R. Sullivan found that proproxyphene hydrochloride, one of four different arrangements of the compound's molecules, showed promise in pain relief. Lilly sent samples to the University of Michigan lab and to the ARC in Lexington. In 1956 a committee of the National Research Council reviewed the work led by H. Franklin Fraser and Harris Isbell between 1953 and 1955 on propoxyphene at the ARC. The researchers had concluded that propoxyphene carried addiction liability, with key attributes listed as (a) creation of opiate-like symptoms when large doses were given to former opiate addicts, (b) ability partially to suppress signs of abstinence from

11. *United States Department of Commerce Report #981*, 1946; Campbell, *Discovering Addiction*, 81, 91, 94; Noemi Tousignant, "The Rise and Fall of the Dolorimeter: Pain, Analgesics, and the Management of Subjectivity in Mid-Twentieth-Century United States," *Journal of the History of Medicine* 66:2 (2011): 145-79.

morphine, (c) production of consistent, if mild, signs of abstinence when the drug was abruptly discontinued after 7-8 weeks of regular use in five subjects. Isbell and Fraser estimated that propoxyphene's addiction potential was not greater than, and was probably not less than, that of codeine.[12]

A later review by the Department of Health, Education and Welfare (HEW) credited these pre-market evaluations of what would become Darvon with influencing recommendations to control propoxyphene under emerging international protocols. The World Health Organization's (WHO) Expert Committee on Addiction-Producing Drugs evaluated propoxyphene and in 1956 and 1958 recommended control of the drug under existing international drug conventions. The Committee noted that propoxyphene had been shown to have some ability to produce or sustain addiction. As a result, 32 nations placed propoxyphene under controls, but this group did not include the United States.[13]

On August 16, 1957 the FDA approved Lilly's New Drug Applications (NDA) for 32- and 65-milligram propoxyphene capsules with the brand name Darvon. Three months later, approval of a second NDA brought three Darvon combinations to market: 32 milligrams of propoxyphene hydrochloride, 389 milligrams aspirin, and 32.4 milligrams of caffeine; the same amounts of aspirin and caffeine with 65 milligrams of propoxyphene; and a blend of 65 milligrams propoxyphene and 325 milligrams of aspirin. Lilly reported sales of 84 million capsules and tablets, or between three and four million prescriptions, in its short first year. In 1958 sales rose to 202 million capsules and tablets, or about seven million prescriptions, including new customers and refills. Domestic sales

12. J. E. Bauerie, "New Non-Narcotic Analgesics," *Journal of the San Antonio District Dental Society* 13:6 (1958); Beaver, "Are Synthetic Narcotics Adequate Substitutes?" 519-525.
13. Theodore Cooper, "Scheduling Recommendations for Dextropropoxyphene," letter and memorandum to Peter Bensinger of the Drug Enforcement Administration, August 12, 1976.

of capsules and tablets hit 470 million in 1961, 846 million in 1965, and 1.34 billion in 1969. The peak year for capsules and tablets was 1974 at 1.57 billion.[14]

From the start, the promotion of Darvon to physicians established themes that would persist. Early ads focused on its effectiveness and on the fact that Darvon did not require a narcotic prescription. Darvon's debut ad in the 1958 Physician's Desk Reference (PDR) described it as "a new, non-narcotic, chemically different analgesic … potency equal to codeine, yet much better tolerated. Chemically useful doses do not produce euphoria, tolerance, or physical dependence." A 1958 Annals of Surgery ad focused on its versatility; doctors "will find 'Darvon' helpful in any condition associated with pain … useful in relieving pain associated with recurrent or chronic disease, such as neuralgia, neuritis, or arthritis, as well as acute pain of traumatic origin." The *American Journal of Medicine*'s September 1959 ad touted Darvon Compound as "potent – safe – well tolerated." Its non-addictive property was the first distinguishing attribute mentioned in a Darvon ad in September 1960. Two years later, in the Annals of Surgery, Lilly said, "Nausea and constipation are much less frequent than with codeine (… and Darvon Compound 65 does not require a narcotic prescription.") The latter had been true of Darvon at all times and remained so until 1977. In 1979, Peter H. Rheinstein of the FDA noted that this early, aggressive marketing had established Darvon as safe and potent for a wide range of complaints.[15]

While these ads were running, ongoing research on propoxyphene led to an unusual reversal. Scientists at the ARC and others conducted tests that spelled out the opiate-like attributes of propoxyphene and that supported Isbell and Fraser's earlier finding of addiction potential. But in 1962 the NAS/NRC Committee on Drug Addiction and Narcotics looked at this evidence, as well as at five years of market experience, and, while acknowledging some potential for abuse, concluded

14. Peter H. Rheinstein, M.D., "The Popularity of Darvon – Promotion of Darvon as a Non-Narcotic," Memorandum from FDA to Office of Legislative Services, January 30, 1979.
15. *Pharmaceutical Specialties and Biologicals* (New York: Medical Economics, Inc., 1958) ___; Rheinstein, "The Popularity of Darvon," January 30, 1979. The FDA view throughout the 1970s was that, from its introduction until the FDA ordered it to stop, Darvon was promoted aggressively and unambiguously as non-narcotic.

that propoxyphene did not need to be controlled as a narcotic, given the low number of abuse cases seen. In 1962 the WHO also took this market experience into account in reversing its view of propoxyphene. Its committee agreed that "there was now no need for narcotics control of propoxyphene or dextropropoxyphene or their preparations."[16]

While U.S. researchers and the WHO were taking a more favorable view of propoxyphene and Americans consumed it in rapidly growing numbers, ongoing research was telling a more complicated story. The 1960s produced a range of studies that appeared to affirm propoxyphene's ability to produce dependence and addiction, albeit not as powerfully as other opiates. A February 1963 Journal of the American Medical Association (JAMA) study reported that psychological craving, euphoria, tolerance and dependence had been observed among users of propoxyphene. Studies published between 1966 and 1969 supported these findings. A 1964 review described propoxyphene as a mild analgesic that appeared to be less effective than aspirin and codeine. Its status as a narcotic was "muddled" and the enormous popularity of the chemical was puzzling. The review attributed this appeal to the superior pain relievers, such as aspirin, with which propoxyphene was almost always combined. The fact that doctors did not need to complete a narcotic prescriptions added to propoxyphene's popularity.[17]

In 1962, passage of the Kefauver-Harris amendments to the 1938 Food, Drug and Cosmetic Act required new and previously approved drugs to show effectiveness as well as safety prior to approval for market. The FDA's Drug Efficacy Study Group (DESI) looked at Darvon by itself in 32-

16. "Propoxyphene Evaluations by Medical and Governmental Groups Regarding Its Drug Abuse Potential and Dependence Including 1976 FDA Scheduling Recommendation," submitted by Eli Lilly and Company to United States Department of Health, Education and Welfare, February 1977; *World Health Organization Expert Committee on Addiction-Producing Drugs, 13th Report, No. 273* (Geneva: WHO Technical Reporting Services, 1964), 5, 8.
17. A. Elson and E.F. Domino, "Dextro Propoxyphene Addiction: Observations of a Case," *Journal of the American Medical Association* 183 (1963): 482; Carl D. Chambers, Arthur D. Moffett, and Walter R. Cuskey, "Five Patterns of Darvon Abuse," *The International Journal of the Addictions* 6(1) (1971): 173-189; Louis Lasagna, "The Clinical Evaluation of Morphine and Its Substitutes as Analgesics," *Pharmacology Review* 16 (1964): 73-75.

and 65-milligram doses; and in combination with several times as much aspirin, phenacetin (need generic descriptor), and an equal amount of caffeine. On April 8, 1969 the Federal Register published the FDA's conclusion that adequate doses of these products did provide relief of mild to moderate pain. However, the 32-milligram dose, by itself, did not seem to offer any real relief. The FDA listed sedation, somnolence, paradoxical excitement, stomach discomfort, and euphoria among potential reactions. The FDA's decision noted that incidents of accidental or intentional overdose with propoxyphene were comparable to narcotic overdose; one difference was a higher likelihood of convulsions from propoxyphene than with other narcotics. Other manifestations, such as coma, respiratory depression, and circulatory collapse, had been observed with propoxyphene and other narcotics.[18]

The cumulative effect of these studies was to establish propoxyphene as a synthetic opiate with moderate addictive potential and other risks. On May 28, 1969 J. K. Kirk of the FDA sent a letter to Eugene N. Beesley, President of Lilly. After 12 years on the market, the FDA acknowledged for the first time in this letter that propoxyphene carried genuine risk. Kirk notified Beesley that the FDA no longer accepted Lilly's consistent promotion of Darvon as a non-narcotic, and it ordered the company to stop making such unqualified references to Darvon.[19]

By 1970, Lilly's description of Darvon in the PDR used almost verbatim the FDA's statement in its letter that "Tolerance, psychological dependence and physical dependence have been reported; the abuse liability of propoxyphene hydrochloride is qualitatively similar to that of codeine although quantitatively less." The PDR noted that 'a narcotic prescription is not required.'" On September 9, 1971 the FDA approved four new combinations: Darvon-N tablets, Darvon-N oral suspension,

18. *Federal Register*, Volume 34, Number 6264, "Drugs for Human Use: Drug Efficacy Study Implementation," April 8, 1969.
19. Letter from J. K. Kirk of the FDA to Eugene N. Beesley of Lilly, May 23, 1969. Kirk's tone conveys thinly veiled anger: "It has come to our attention that your promotion of Darvon . . . characterizes the drug as 'non-narcotic.' . . . We regard any unqualified reference to Darvon as 'non-narcotic' in advertisements and promotional labeling as lacking in fair balance and misleading."

Darvon-N/aspirin tablets, and Darvon-N/aspirin capsules, while Darvocet-N capsules were approved on December 19, 1972, containing 32.5 mg of propoxyphene and 325 mg. of aspirin. For 1971, Lilly's domestic sales were just under 1.5 billion capsules and tablets; the next year they were just over 1.5 billion.[20]

While sales growth continued, new questions emerged. In April 1972 scientists at the Mayo Clinic looked at why Darvon was more widely used than Zactane, a competing product from Wyeth. They worked with 57 patients who were in mild to moderate pain from a variety of cancers. The products may have differed in market status, but the study indicated they were comparably inept as pain relievers -- both were markedly inferior to aspirin. The oral 65-milligram Darvon dose showed virtually no therapeutic capacity. Neither Zactane nor Darvon demonstrated a significant superiority to placebo. In addition to propoxyphene and Zactane, the study found aspirin to be superior to five other marketed pain relievers, including codeine and acetaminophen, brand name Tylenol.[21]

Lilly's response was quick but careful. It sent a "Dear Doctor" letter that conceded that the pain-relief capabilities of propoxyphene were "very equivocal." Lilly's goal in the letter was to ensure that the Moertel study would not be read as an authoritative condemnation of Darvon. Lilly's rebuttal acknowledged that aspirin was a fine pain reliever but noted that many patients could not tolerate it. Lilly reminded doctors that, in its view, Darvon's effectiveness in relieving pain was "well established." Lilly noted that the National Research Council panel that had reviewed Darvon in 1969 found it to be effective. The company pointed out that the Moertel study did not look at propoxyphene combinations and ended by saying that in 15 years Darvon had won wide

20. *Physician's Desk Reference to Pharmaceutical Specialties and Biologicals* (North Olmsted, OH: Medical Economics, Inc., 1970), _____.
21. C. G. Moertel et al., "A Comparative Evaluation of Marketed Analgesic Drugs," *New England Journal of Medicine* 286(15) (1972): 813-815.

acceptance in the marketplace, been vetted in research and found effective and safe, and delivered real value in combination with other analgesics.[22]

The FDA cried foul. It ordered Lilly to revise what the agency considered an "unbalanced" presentation of Darvon in replying to the Mayo Clinic study. Lilly sent a follow-up letter in which it noted the FDA's objection to the idea that Darvon was a more effective pain reliever than aspirin and at least as strong as codeine but with fewer side-effects. Lilly wrote that the FDA considered none of these claims to be valid and that the agency had asked the company to remind physicians that there was no evidence to show that 65 milligrams of Darvon was more effective than two aspirin (650 milligrams) and that most evidence indicates it was somewhat less effective.[23]

The 1972 controversy reinforced Darvon's ambiguous status at a time when its market status was going through significant change. Lilly's patent expired in 1972, and while the company would continue to derive substantial revenue from it, the early peak was evolving. After 15 years on the market and almost 20 of research, Darvon was entrenched in medical practice in the US, and Lilly felt little need to tamper with the arguments that had served it well. Darvon was effective for many kinds of moderate pain and was safe. This had been shown independently by numerous Federal agencies, researchers, and clinicians in their practices. Safety issues arose almost entirely from misuse. The 1972 dialogue was a skirmish that previewed a "wider war" that would begin in 1978. In that battle Lilly would continue to adapt its core arguments to changing conditions.

Soon after Lilly had addressed fallout from the Mayo Clinic study, the Bureau of Narcotics and Dangerous Drugs (BNDD), soon to be reorganized and rechristened as the Drug Enforcement

22. Letter from Eli Lilly and Company, April 17, 1972 and submitted May 5, 1972 to the Assistant to the Director for Medical Communications, FDA Bureau of Drugs.
23. Cooper, "Scheduling Recommendation," August 12, 1976; Statement of Mr. Kenneth A. Durrin, Director, Office of Compliance and Regulatory Affairs, Drug Enforcement Administration, Before the U.S. Senate Monopoly and Anticompetitive Activities Subcommittee, Select Committee on Small Business, Hearings on Propoxyphene, January 31, 1979.

Administration (DEA), sent a memo to the FDA in which it proposed placing propoxyphene in Schedule IV of the Controlled Substances Act (CSA) of 1970. The CSA established five schedules of prescription and street drugs with criteria for inclusion and corresponding policy and administrative requirements. The Bureau said Lilly had resisted the idea of putting propoxyphene into any CSA schedule and had offered extensive data to the FDA to make its case. The BNDD recommendation began a new Federal review of the science and market experience.[24]

As the FDA considered the BNDD proposal, the Federal government was expanding its ability to understand what was happening on the ground. In 1973 the DEA established the Drug Abuse Warning Network (DAWN) to monitor drug use patterns and impacts in a handful of metropolitan areas and to supply data to policy-makers. DAWN worked with emergency room personnel, medical examiners, and coroners to track individual drugs' mentions in fatality reports. A DAWN report could include up to six substances per episode.[25]

The DAWN program would start to formalize field reporting on medical incidents and boost understanding of different drugs' roles in fatalities. In 1975, the North Carolina state toxicologist wrote in a JAMA letter that deaths associated with propoxyphene were increasing in his state. Lilly looked into the North Carolina reports and reviewed what it learned with the FDA and DEA. Lilly also commissioned a study that it said showed the number of deaths associated with propoxyphene was declining. Still, in 1976 Lilly strengthened the risk warnings on Darvon's labels, sent a brochure to doctors and pharmacists, and provided its May 1972 JAMA letter "personally to 114,000 physicians." Lilly would reprise this outreach effort in 1979-1980 as part of its response to the 1978 HRG petition.[26]

24. Cooper, "Scheduling Recommendation," August 12, 1976; Durrin statement, January 31, 1979.
25. Cooper, "Scheduling Recommendation," August 12, 1976; Durrin statement, January 31, 1979.
26. Lilly submission to FDA, "A Brief History of Major Developments Relating to Propoxyphene Products," April 22, 1976.

In February 1977 the DOJ announced it would place propoxyphene in Schedule IV of the CSA. After aggressively positioning propoxyphene as a non-narcotic since 1957, Lilly accepted the demands, largely administrative, of this placement. Schedule IV requirements covered registration, initial inventory, record-keeping, and limitations on prescription refills, and they became effective for propoxyphene in March 1977. Six months before its 20th anniversary on the U.S. market, the unauthorized production, sale, or possession of propoxyphene became a crime. Prior to the March date, Lilly distributed information to pharmacists that included forms for inventory tracking and other control procedures.[27]

Darvon's life as a controlled substance began less than two years before the HRG filed its petition. The intervening months, along with the growth of DAWN, brought more structured scrutiny to Darvon. By 1977, propoxyphene ranked second only to the barbiturates as the leading prescription drug implicated in overdose deaths in the United States. Between 1,000 and 2,000 such deaths, accidental and intentional, were linked to propoxyphene in that year. In early 1978, the FDA notified physicians for the first time of the possibility of accidental death associated with propoxyphene. Eleven months later the FDA issued another statement on the increase in accidental death associated with propoxyphene. The statement spelled out several major hazards, including death due to suicide attempts with propoxyphene alone or combined with other drugs as well as accidental deaths in which people took large amounts of propoxyphene with alcohol or other drugs. Later in 1979 the FDA added a major new risk warning to the Darvon package as well as a voluntary patient information sheet with warnings about drug combinations and the risk of exceeding the maximum recommended daily dose.[28]

27. *Federal Registe*r, Volume 42, Number 19, 8636, "Placement of Dextropropoxyphene in Schedule IV," February 11, 1977; Lilly submission, "A Brief History," April 22, 1976; Durrin statement, January 31, 1979.
28. Dave Mace, R. Ph., "Re: Safety of 130 mg of propoxyphene Hydrochloride," in Perspective from an IDIS Subscriber, Iowa Drug Information Service, n.d.

The activities at the FDA, Lilly, and in the medical community in the second half of the 1970s reset Darvon's legal and regulatory status. At the same time those activities legitimized the uncertainties over the effectiveness and safety of propoxyphene, as agency reviews for scheduling Darvon rolled forward. On a wider scale, Darvon's changes took place as behavior, perceptions, and discourses on prescription drugs careened in many directions across the decade. To understand how the Darvon controversy would evolve after 1978, it is helpful to sketch this setting briefly.

The backdrop to the 1978-1980 challenge to Darvon's market niche by HRG comprised two main elements. The first was growing public concern, after 1960, over reports of prescription drugs' capacities for harm. The thalidomide episode in the early 1960's had produced a new FDA mandate to evaluate the effectiveness of existing and proposed drugs. It also led to increased scientific and public scrutiny of the pharmaceutical industry's methods and products. Research published between 1965 and 1975 described risks associated with Percodan (pain reliever), Tuinal (sedative), Seconal (sedative), Librium (tranquillizer), Miltown (tranquillizer), and others. DAWN data, which covered about 30 percent of the US population, linked 200 deaths between April 1976 and April 1977 (in 9,300 emergency room visits) to Librium, a chemical predecessor of Valium, and another 100 deaths to Dalmane (more than 11,000 visits), a drug with a comparable chemical structure.[29]

29. The secondary literature on the products of, and historical issues within, America's post-World War II pharmaceutical industry is vast. One thread within this history is how commerce, science, politics, and shifting cultural patterns converged amidst unprecedented levels of drug consumption and pressing issues of medical authority and personal autonomy. Starting points include Jerry Avorn, *Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs* (New York: Vintage Books, 2005); W. Duncan Reekie and Michael H. Weber, *Profits, Politics and Drugs* (New York: Holmes & Meier Publishers, Inc., 1979); Andrea Tone, *The Age of Anxiety: A History of America's Turbulent Affair with Tranquilizers* (New York: Basic Books, 2009); David Healy, *Pharmageddon* (Berkeley: University of California Press, 2012); Joseph Dumit, *Drugs for Life: How Pharmaceutical Companies Define Our Health* (Durham: Duke University Press, 2012); Richard Hughes and Robert Brewin, *The Tranquilizing of America: Pill Popping and the American Way of Life* (New York: Warner Books, 1979); David Herzberg, *Happy Pills in America: From Miltown to Prozac* (Baltimore: The Johns Hopkins University Press, 2009). The mainstream news media covered drug issues extensively in the 1970s; examples include "Boom in Illegal Pills," *Newsweek*, August 14, 1978, 41-42; Al Coombes et al., "Drugs and the Stars: Hollywood's Own Horror Story," *Ladies Home Journal*, March 1979, 34, 157-160; and Myra MacPherson, "Betty Ford: The Untold Story," *McCall's*, July 1978, 18-24, 144.

An example of shifting cultural currents was the "Valium panic" of the late 1970s. Introduced in 1963, Valium was by the early 1970s the most widely prescribed drug in the country. At the 1975 peak, Americans received 120 million prescriptions for it. About 20 percent of regular users said they had used the drug every day for more than a year. In 1975, data from the DAWN network showed Valium to be the most frequently discovered drug in the systems of overdose victims. In 1979 Senator Edward Kennedy chaired Congressional hearings on Valium and Librium. Reports of celebrities' struggles with Valium included singer Tony Orlando and comedian Jerry Lewis, who named Valium as a culprit in their drug torments.[30]

A second element of the setting for the Darvon debate was unrest at the FDA. By the late 1970's the agency faced resource constraints and broad disfavor with the public, Congress, and industry. With a charter to oversee not just pharmaceuticals but food (then about 13 times the size of the drug industry), cosmetics, and medical devices, the FDA had approximately 1,000 inspectors to monitor some 50,000 food processing plants and about 2,500 drug companies. The legislative branch showed an enduring interest in the FDA. Between 1973 and 1976 Congress held an average of 35 hearings per year on FDA-related topics before more than 20 subcommittees, and the General Accounting Office issued 45 FDA reports. Controversies over a proposed ban on saccharin in March 1977, and its stance on laetrile, which supporters championed as a cancer treatment that the FDA was keeping from patients, led 10 states to legalize the compound. The pharmaceutical industry condemned what it called the agency's cumbersome and costly process for new-drug approval. Articles on America's "drug lag" – time lost to more nimble competitors – focused on the FDA. In 1978 a government panel, the Commission on the Federal Drug Approval Process, was created to explore industry complaints about the FDA and to make recommendations.[31]

---

30. Herzberg, *Happy Pills*, 138-139; Hughes and Brewin, *Tranquilizing of America*, 19, 62.
31. Scott Lucas, *The FDA* (Millbrae, CA: Celestial Arts, 1978); Daniel Carpenter, *Reputation and Power: Organizational Image and Pharmaceutical Regulation at the FDA* (Princeton: Princeton University Press, 2010); Philip J. Hilts, *Protecting America's Health: The FDA, Business, and One Hundred Years of Regulation*

Even with its broad charter, small staff, and list of issues, the FDA devoted significant attention to prescription and over-the-counter (OTC) pain relievers in the late 1970s. Americans were spending about $10 billion every year on pain medicines, surgery, and time lost from work due to pain. The OTC pain market alone was about $830 million annually. In 1978 John Bonica estimated that more than 86 million Americans, more than one-third of the population, suffered from pain, chiefly recurrent headaches and musculoskeletal problems.[32]

Shifting perceptions of prescription drugs and turmoil at the FDA were key elements of the backdrop to the Darvon controversy that began when the HRG submitted its petition in November 1978. Between then and May 1980, an intense exchange among federal agencies, Lilly, Congress, and the research community sought to determine whether Darvon was a narcotic, whether it was safe and effective, and what role it played in fatalities. The dialogue drew on more than 800 published papers; the records of dozens of Congressional and regulatory hearings and reviews by the FDA, Department of Justice (DOJ), and the DEA; and 21 years in which doctors had prescribed more than 20 billion Darvon doses. Beginning in 1973, the DEA's DAWN program collected data on Darvon (and many other drugs) from coroners and medical examiners in two dozen metropolitan areas.

The episode began when the HRG launched a two-part effort to alter Darvon's market status. First, HRG petitioned the Department of Justice and the DEA to move propoxyphene from Schedule IV to Schedule II of the CSA. Schedule II included amphetamine, barbiturates, and other substances deemed to have "currently accepted medical use; high abuse potential with severe psychic or physical dependence liability." Schedule IV included Valium, Librium, and (since March 1977) Darvon – drugs that were classified as significantly lower-risk. HRG's second action was to submit a

---

(Chapel Hill: The University of North Carolina Press, 2003); Peter Temin, *Taking Your Medicine: Drug Regulation in the United States* (Cambridge: Harvard University Press, 1980).
32. Matt Clark et al., "Bitter Pills for the FDA," *Newsweek*, July 18, 1977, 93-95; Lynn Langway, with Jane Whitmore, "The Painkiller War," *Newsweek*, April 25, 1977, 46.

memo to the FDA asking it to suspend any Darvon New Drug Applications (NDA) then under way, to support HRG's petition to put Darvon in Schedule II, and to remove it from the market immediately as an imminent hazard to public health.[33]

HRG's petition and memo of November 1978 drew on propoxyphene's full history while using DAWN field reports to convey the immediacy of the problem. HRG argued that Darvon was clearly a narcotic with proven potential for abuse, high risk of accidental harm, and culpability in a growing number of deaths. The HRG claimed that Darvon posed a much greater threat than doctors or patients understood -- a legacy of Lilly's aggressive promotion of it as a non-narcotic since 1957. HRG asserted that propoxyphene posed a particular threat to cardiac health because a metabolite, norpropoxyphene, could disrupt electrical conduction within the heart. As a narcotic, propoxyphene could cause respiratory depression, especially when used with alcohol or barbiturates.[34]

HRG claimed these attributes had been clear from the start. Pre-market research had shown that propoxyphene, like other synthetic opiates, could slow breathing, produce euphoria, engender tolerance, and create dependence. The petition cited a 1963 study that showed that such dependence could be "strong," with a sudden end of use provoking "mild to moderate" withdrawal symptoms such as sweating, nausea, and shaking. The petition also mentioned a 1976 DOJ study that said that propoxyphene was a narcotic. While the HRG conceded that physical dependence on Darvon was usually moderate, psychological dependence could be severe. HRG strenuously disputed propoxyphene's stand-alone effectiveness. It claimed that no acceptably rigorous study had yet shown that propoxyphene by itself offered much relief. The petition cited 1970 and 1977

33. "Petition Requesting Transfer of the Narcotic Dextrpropoxyphene (Darvon) and its Salts From Controlled Substances Schedule IV to Schedule II," Sidney M. Wolfe, M.D. and Public Citizen Health Research Group, November 21, 1978, to Griffin Bell, Attorney General, and Peter Bensinger, DOJ, hereafter referred to as the HRG petition; "Memo to Secretary Califano," from Sidney M. Wolfe, M.D. and the HRG, November 22, 1978; hereafter referred to as the HRG memo; Senate Hearings, Durrin statement, January 31, 1979, 8.
34. HRG petition, 3; HRG memo, 4.

literature reviews in which the authors evaluated all available double-blind studies. Those reviews showed that propoxyphene's superiority over a placebo was marginal at best.[35]

The HRG homed in on recent field reports that painted an alarming picture. Medical examiners in North Carolina and Oregon had reported that Darvon-related deaths were increasing sharply. In about two-thirds of the deaths that implicated Darvon, the drug was named as "cause of death." DAWN data from 14 metropolitan areas showed that propoxyphene abuse deaths were more frequent than those attributed to heroin and morphine combined. The petition cited a recent update to a 1975 study (partially funded by Lilly and led by University of Utah pharmacologist Bryan Finkle) that found that Darvon-related deaths were increasing more rapidly than overall drug deaths.[36]

While Lilly would argue that Darvon's placement in Schedule IV was showing good results, to HRG, Schedule IV had proven inadequate, in part because the total number of prescriptions had barely been affected. In the year after their placements in Schedule IV, prescriptions for Valium and Darvon had declined by 7 and 10 percent, respectively. But in Schedule II, prescriptions for amphetamines had gone down by 50 percent, Quaaludes (a sedative) were down 52 percent, and Seconal (a sleep aid) were lower by 48 percent. The HRG further claimed that Darvon was being abused more than other Schedule II drugs.[37]

Five weeks after the HRG submitted its petition and memo, Lilly sent a response. The company began by making an argument that would remain central to its case throughout the controversy: that Darvon had proven itself safe when used properly; by implication, the company should not be liable for irresponsible overuse or pre-existing individual circumstances that might make Darvon more risky. Lilly said Darvon was useful in treating many forms of mild to moderate pain and that

35. HRG petition 3-4; HRG memo 4.
36. HRG petition 4; HRG memo 5-6.
37. HRG petition 5-6; HRG memo 5-8.

it had displayed safety and effectiveness in more than 20 years of research, new drug applications, agency reviews, and use by millions of patients. Lilly said that when used as intended, there was no valid evidence that propoxyphene caused death or serious injury and that its margin of safety was actually substantial. The company said HRG had misread the data on fatalities and that deaths had been declining since Darvon had been placed in Schedule IV.[38]

Lilly defended its promotion of Darvon to physicians and the public since 1957 as consistently forthright and accurate. The company cited numerous updates to labeling; a steady stream of information provided by mail and in person to physicians, pharmacists, and dentists; and its ongoing cooperation with the FDA and other agencies on Darvon. For Lilly, problems arose only, and rarely, when people took too much or in combination with alcohol and other drugs – a point Lilly said it had been making clear on the labeling since the late 1960s.[39]

On the issue of Darvon-related deaths, Lilly asserted that the limitations of the DAWN data precluded their suitability as the basis for regulatory action. Even so, the company believed the HRG had misread these data. Deaths associated with propoxyphene were not increasing but had been declining since the first quarter of 1977, when the DOJ had assigned Darvon to Schedule IV. Lilly said Finkle's studies showed a decline in such deaths in some locations. Just as important, both Finkle studies had shown that most deaths associated with Darvon involved outsized amounts and frequent use with alcohol and other central nervous system depressants. In addition, many people who had died had a history of suicidal tendencies or the abuse of other drugs and alcohol. Lilly said that DAWN data showed that about two-thirds of the deaths associated with propoxyphene involved multiple drugs.[40]

38. "Preliminary Submission of Eli Lilly & Company Concerning the Health Research Group's Letter of November 21, 1978 to Secretary Califano," submitted December 28, 1978; hereafter referred to as Lilly preliminary response.
39. Lilly preliminary response 3, 4.
40. Lilly preliminary response 2-3.

Lilly contested HRG's claim that propoxyphene was associated with more deaths than heroin and morphine combined. The manufacturer said that when the annual number of new prescriptions was taken into account, total deaths from propoxyphene were a tiny percentage of those attributed to heroin and morphine and were far fewer than those linked to other prescription drugs. Lilly disputed the dangers HRG ascribed to norpropoxyphene, citing animal studies that showed the metabolite did not have significant opioid capability and was unlikely to contribute to CNS-depressant effects.[41]

In closing its argument, Lilly said that more than 21 years on the market and a vast body of research had consistently shown Darvon to be safe and effective when used properly. For Lilly, issues arose almost entirely from improper use or abuse. The company contended that placement in Schedule IV was a sufficient response and that rescheduling was not warranted or reasonable.[42]

The HRG petition and memo, along with Lilly's preliminary response, encapsulated 21 years of Darvon debate and set a template for future policy deliberations. A US Senate subcommittee held hearings on Darvon between January 31 and February 5, 1979, which brought together key researchers; medical examiners from Oregon and North Carolina; Donald Kennedy, Director of the FDA; Robert Furman, a Lilly senior executive; and Sidney Wolfe, HRG's lead petitioner. Overall, the testimony focused on Darvon's status as a narcotic, its effectiveness, its role in causing deaths, and its placement in the CSA schedules. But the Senate witnesses also gave their views on what they saw as a paradox of Darvon's popularity in light of persistent questions about its effectiveness and safety.

Leadoff witness Kenneth Durrin of the DEA sketched Darvon's standing in early 1979. In the U.S. 59 companies were making about 150 propoxyphene products, mostly in combinations. In 1978, more than 31 million prescriptions containing propoxyphene had been written out of a U.S. total of

41. Lilly preliminary response, 4.
42. Lilly preliminary response, 6.

nearly 1.5 billion. Durrin noted that the debate over proper controls for Darvon had started in 1956 with the pre-market research and had continued until 1977 with the decision to place it in Schedule IV of the CSA. For Durrin, the critical issue was propoxyphene's potential for abuse and addiction.[43]

Charles Moertel of the Mayo Clinic had been the lead researcher in the 1972 study that found that Darvon had not been shown to be much better than a placebo in a majority of clinical studies. Moertel believed Darvon to have some analgesic "activity" but said it did not appear to have significant pain-relieving effects on its own. It was clearly inferior to less expensive drugs such as aspirin. When asked to give a medical rationale for using Darvon, he said he could find none, adding that prescribing Darvon for severe pain, even in combination, bordered on inhumane medical practice. In explaining Darvon's popularity, Moertel noted that doctors, like the general public, were heavily influenced by advertising in their decisions about what to prescribe.[44]

For William Beaver, a pharmacology professor at Georgetown University who had studied Darvon extensively, Lilly's aggressive promotion was a factor in its popularity but not the only one. He described the positive psychological effects on many patients of getting a prescription at the end of a doctor visit. Since Darvon had not been scheduled under the CSA until 1977, patients and doctors believed it must be safe. For Beaver, the best reason to use Darvon was the increment of pain relief, with little increase in side effects when combined with fever-reducing pain relievers such as aspirin and Tylenol (acetaminophen). In his testimony Beaver foreshadowed Califano's assertion of the wide variability in pain as a rationale for using Darvon.[45]

The Senate committee heard from medical examiners and pathologists as well. Page Hudson, Chief Medical Examiner in North Carolina, described how it had slowly become apparent to him and

43. Durrin testimony, Senate hearings, 1.
44. Moertel testimony, Senate hearings 3, 6, 8.
45. Beaver testimony, Senate hearings, 6, 12, 14, 17.

his colleagues that they were seeing something unprecedented: A pain reliever that was very popular, mostly ineffective, and implicated in more fatalities than any other drug. In a September 1975 letter to JAMA, Hudson and his colleague Arthur McBay had described the increase in Darvon-related deaths in their state as "alarming." They said Darvon had been overtaking barbiturates as the most lethal drug in North Carolina since the mid-1970s. In his testimony McBay noted that, in the past five years, 183 deaths in the state had been attributed to propoxyphene, compared with 26 to aspirin, three to codeine, and none to Tylenol. If that rate applied to the entire American population, there would be about 1,200 Darvon deaths annually, a higher number, according to McBay, than the number of deaths attributed to heroin. Like Beaver, McBay credited improved capabilities in forensic analysis with providing greater clarity about propoxyphene's role in fatalities.[46]

Hudson was asked to describe the medical justification for Darvon. He cited habit and overall nonchalance by physicians and patients as key factors, even though there were less expensive, safer, and more effective pain relievers than propoxyphene available, even over the counter. He claimed that doctors overall were largely unaware of Darvon's risks. Individual doctors had told him that "I think it's a good drug, my patients ask for it," and "I don't know why I use it; it isn't worth a damn without aspirin in it." Hudson noted that OTC drugs lack the "psychic authority" of prescription drugs. Another factor in Darvon's popularity with physicians was that insurance companies reimbursed for Darvon but not for aspirin or Tylenol. Hudson supported putting Darvon into Schedule II. [47]

Testimony from the FDA and Lilly followed these field reports. Together, the statements of FDA Director Donald Kennedy and Furman, a Lilly vice president, spelled out many of the points the

46. Hudson testimony, Senate hearings, 11; "Propoxyphene Overdose Deaths," letter to the *Journal of the American Medical Association* 233:12 (September 22, 1975): 1257; McBay testimony, Senate hearings, 4.
47. Hudson testimony, Senate hearings, 5.

company had made for more than two decades and that Califano would make in his mid-February decision. In particular, Kennedy and Furman described as pivotal the question of whether Darvon was safe and effective when used as intended. In announcing his rejection of the HRG petition 10 days later, Califano would cite this as the decisive issue.

Kennedy started by acknowledging that the committee and his agency were facing a complex regulatory challenge. He inferred benefit and safety from Darvon's wide popularity and attributed analgesic effect to propoxyphene when he said that its contribution to pain relief when combined with aspirin and Tylenol may be "relatively small." Kennedy's reading of the data showed that most fatalities associated with propoxyphene happened due to intentional overdose or abuse, suggesting that when people took Darvon as directed, and didn't mix it with alcohol and depressants, it was safe. Kennedy did acknowledge concerns about Darvon's effect on electrical conduction in the heart, but he did not accept HRG's claim that the DAWN system missed a significant number of accidental deaths traceable to heart issues.[48]

Robert Furman summarized Lilly's case for maintaining the status quo. Furman said Darvon had consistently proven its safety and value as a pain medication when used as directed. In 21 years on the market, the company was not aware of a single death or serious injury caused when Darvon products were used as the label instructed. This track record made propoxyphene a proven resource for the physician who was helping patients manage pain. Since the beginning, Furman said, Lilly had marketed the drug responsibly. All earlier reviews had confirmed the company's position, including NDAs, the 1962-1969 DESI review, and the decision to put Darvon in Schedule IV, while wide clinical experience corroborated these findings. Furman said propoxyphene's spotty record in research studies was comparable to that of codeine. He disputed McBay's and Hudson's interpretation of the North Carolina data, since most of those deaths involved amounts of

48. Kennedy testimony, Senate hearings, 3, 5, 9.

propoxyphene that were far beyond therapeutic dosage, and he contested HRG's assertion of health risks associated with propoxyphene's metabolite, saying that many drugs shared this property and that studies on humans did not support the petition's claim.[49]

Ten days after the Senate hearings ended, Secretary Califano issued the government's response to HRG's petition and memo in a press release and supporting document. In the case he made for keeping Darvon on the market, Califano nonetheless breathed new and, as it turned out, close-to-eternal life into the questions that animated the HRG petition. He did this by validating as in need of further study virtually the whole set of unresolved issues that HRG had raised. Califano crafted the template from which future defenses and critiques of Darvon, including in a revived HRG petition in 2006, would flow. Scanning hundreds of studies, broad clinical experience, numerous NDAs, and several agency reviews, Califano nonetheless characterized the evidence on Darvon as limited and said the issues were difficult. Califano's HEW team kept Darvon on the market, left scheduling under the CSA up to the Department of Justice, and requested more work to address the issues HRG raised. In emphasizing those issues, Califano was in greater agreement with Lilly than with the HRG, but his caveats and next steps fully legitimized the arguments of the petition and launched new activities on its content. His decision reflected agreement with Lilly's view that Darvon was safe and effective when used as directed. He said there was no evidence that "therapeutic use" (as intended by the manufacturer) of propoxyphene, with no alcohol or tranquilizers, had led to accidental death.[50]

But the caveats that Califano added, and the actions he ordered, were crucial in legitimizing Darvon's uncertainties and in establishing that these issues remained unresolved. Califano deftly

49. Furman testimony, Senate hearings, 3, 5, 7, 9.
50. "Statement by Joseph A. Califano, Jr., Secretary of Health, Education and Welfare," February 15, 1979; hereafter referred to as the Califano press release; "United States Department of Health, Education and Welfare, Office of the Secretary, In re: Petition to Suspend New Drug Applications for Propoxyphene, Order of the Secretary Denying Petition," February 15, 1979, hereafter referred to as the Califano supporting document.

depicted 21 years of propoxyphene's clinical ambiguity. He said propoxyphene was a narcotic and could create physical dependence. He acknowledged its role in fatalities, putting propoxyphene at number 12 out of 27 drugs in its ratio of drug-associated deaths to prescriptions. He validated the questions raised by the HRG when he asked the FDA to review the research and conduct further study. He also asked Lilly to inform doctors, pharmacists, and patients about the latest understanding of risks through an information campaign and new label warnings; this request would spark a pointed dispute between Lilly and the FDA over the subsequent 15 months. Califano urged doctors and pharmacists to deploy Darvon with care and to keep it from people who were suicidal, accident-prone, drinking a lot, or taking tranquilizers. Healthcare providers should look for signs of abuse and remind people that mixing Darvon with alcohol and/or tranquilizers was dangerous.[51]

Califano ordered the distribution of a special *FDA Drug Bulletin* dedicated to the risks of propoxyphene to a million doctors, dentists, pharmacists, and other health professionals. He encouraged these people to talk to patients about it. He asked to have an article on propoxyphene published in the FDA consumer magazine and requested print and broadcast public service announcements. He scheduled a public hearing, and he ordered a review of the literature and evidence that had been presented at the recent Senate hearings. Califano further asked that an FDA Advisory Committee meet and prepare a recommendation to the Justice Department on whether propoxyphene should be moved from Schedule IV into Schedule II, as HRG had proposed.[52]

Califano's statement posed several questions about deaths attributed to Darvon. He asked the FDA to look into the "actual extent" of harm caused by propoxyphene. He said that in 1977 the DAWN data showed just more than 600 deaths from propoxyphene-related products. But the DAWN system recorded how many times coroners' and medical examiners' reports mentioned

51. Califano supporting document, 18.
52. Califano press release and supporting document, 11.

different drugs. It did not attribute causality to the substances. He asked the FDA to clarify specifically 1) the amount of propoxyphene that by itself could cause death and how this amount compared with the recommended dosage; 2) the proportion of deaths attributable to accidents, suicides, or abuse; 3) the ways in which propoxyphene might cause death – by disrupting the heart's electrical system, suppressing breathing, or others; and 4) the possible role propoxyphene played in making aspirin or other products more effective as pain relievers. Califano acknowledged that it was not clear that propoxyphene by itself offered much relief. But he linked its market success in part to the wide variability in people's pain and to the possibility that propoxyphene was somehow synergistic with other pain relievers.[53]

In addition, the FDA's February 1979 rejection of the HRG's petition legitimized a connection between Darvon's commercial and scientific status. In keeping Darvon available, Califano cited its market success as useful if not conclusive evidence of safety and therapeutic value. Lilly had consistently made the same point. It cited years on the market in which billions of doses had been consumed with, in the company's view, no deaths or serious injuries when used as intended. For Califano and others, Darvon's commercial success, along with the frequent appearance of other drugs in propoxyphene fatalities, conferred a common-sense scientific legitimacy. With so many people taking it, and with relatively few suffering ill effects, Darvon's overall track record could be read reasonably to support the claim that it was safe when used properly.

The FDA's early-1979 rejection of HRG's Darvon petition launched activities that unfolded over the next 15 months. The review of existing research, new studies, and the distribution of information to clinicians would maintain the status quo for Darvon on the market while solidifying the ambivalence of the risks HRG alleged. When hearings on propoxyphene by a House of Representatives committee ended in late May 1980, the scientific ambiguity that had surrounded

53. Califano press release and supporting document, 13.

Darvon, and the question of how to regulate it, had been certified as worthy of ongoing inquiry and advocacy. Between early 1979 and mid-1980, the debate stamped Darvon's ambiguity as acceptable in terms of its market presence and its ongoing status as a focus of inquiry at the FDA, the Department of Justice, the DEA, and the HRG. There may have been disagreements about Darvon's ultimate nature, but consensus that the issues were unresolved prevailed. Lilly portrayed itself as glad to participate as long as Darvon stayed available.

In the first half of 1979, as Califano had ordered, the FDA oversaw a multi-agency review of research on propoxyphene. Through the second half of 1979, the agency worked with Lilly on a new effort to inform doctors, pharmacists, dentists, and consumers on the latest findings on risks. In the first half of 1980 the FDA studied the impact of this campaign, and soon after issued two recommendations. The first encouraged doctors to add "do not refill" when they wrote Darvon prescriptions. The other suggestion was that doctors put all such prescriptions in writing rather than submitting them by phone. In making these recommendations, the FDA proposed that physicians voluntarily start to treat Darvon much as they would have to if it was in Schedule II of the CSA.[54]

On January 24, 1980, Dr. H.A. Barnett of Lilly's Regulatory Affairs division sent a letter to Judith K. Jones, Director in the Division of Drug Experience in the FDA's Office of Biometrics and Epidemiology. The letter was the company's second report to the FDA on the Darvon informational campaign that had started in August 1979. After identifying about 125,000 physicians classified as significant prescribers of Darvon, the company sent them revised labeling, a booklet on managing overdoses, patient information sheets, warning stickers to be put on prescription vials, and business reply cards. By December 1979 Lilly salespeople had met with about 75,000 of these doctors; the rest received the information by mail. Exactly what transpired in the in-person

54. Soumerai, Stephen B. et al., "Effect of Government and Commercial Warnings on Reducing Prescription Misuse: The Case of Propoxyphene," *American Journal of Public Health* Vol. 77, No. 12 (1987): 1518-1523.

sessions would become a matter of dispute between Lilly and the FDA. Lilly distributed the same printed materials to an additional 145,000 physicians and about 25,000 psychiatrists. In the first part of August 1979, the company sent new Darvon information to about 50,000 community pharmacies and 10,000 hospital pharmacies.[55]

Lilly's letter to the FDA did not mention that the start of its informational campaign had coincided with the end of Califano's tenure as Secretary of HEW. On August 3, 1979, his last day on the job, Califano issued a statement in which he described recently approved label revisions for Darvon as insufficient. He said Darvon was dangerous and should be avoided, and that the materials Lilly had prepared for the campaign, which the FDA had seen a few weeks earlier, did not tell patients what amounts of Darvon could be dangerous and what doctors and others should look for as signs of dependence.[56]

Barnett's letter reported that between August 1 and December 21, 1979 Lilly estimated 4.1 million new prescriptions for Darvon and Darvon-N products had been filled, or an average of about 820,000 per month, based on its reading of National Prescription Audit (NPA) data. For the same period 2.9 million prescriptions were re-filled, or about 580,000 per month. Lilly used these numbers to show that in five months it had provided enough patient information sheets for just under 10 months' worth of prescriptions. The FDA would challenge Lilly's estimates of new prescriptions and refills in the agency's response to the company's letter.[57]

Lilly had been tracking more than the scope of the campaign. The company hired a research firm to conduct phone surveys to learn how well doctors understood the latest information on Darvon. To Lilly, the survey showed that the campaign had been highly effective, especially given the extensive promotional activity on pain relievers in August and September 1979, when doctors and

55. Letter from H. A. Barnett to Judith K. Jones, Director, Division of Drug Experience, January 24, 1980.
56. "Califano Busy Up to the End," *New York Times*, August 4, 1979, 6; "Half Way on the Darvon Warning," *New York Times,* August 14, 1979, A16.
57. Barnett letter, 6-7.

pharmacists were learning about new uses and dosages for Upjohn's Motrin and a new version of Emperin with codeine from Burroughs Wellcome. Lilly characterized recall by doctors about Darvon as "remarkable" and said that the informational campaign had produced this result. According to Lilly, more than 97 percent of the physicians said they knew that people should not take Darvon with alcohol. More than 93 percent understood that caution was indicated when using Darvon in combination with drugs that depress the central nervous system. Ninety-one percent said that emotionally disturbed or depressed patients were not good candidates for Darvon. Additionally, the doctors indicated that the primary source of information on these precautions had been contact with Lilly's representatives or mailings from the company. Medical journals, newspapers, magazines, and television lagged considerably in their impact on physicians' awareness.[58]

For Lilly, another positive effect of the campaign was reflected in progress in reducing the number of times propoxyphene was mentioned in coroners' and medical examiners' reports. The first quarter of 1977 had been the peak with 150 mentions; there had been 58 in the second quarter of 1979. Part of the decline was attributable to fewer total prescriptions, which Lilly said were down by about 20 percent from 1978. Lilly highlighted new 1979 data from Wisconsin, where in nearly 6,000 drug samples analyzed in two police labs, only 20 contained propoxyphene. There had been 30 in 1978 and 50 in 1977 from the same labs. More recently, the company had begun a study in Los Angeles County to investigate the roles of propoxyphene and codeine in a year's worth of fatalities in that county.[59]

Overall, Lilly's January 1980 letter was bullish on the informational campaign. The letter shrewdly integrated new data into Lilly's established defense of Darvon: propoxyphene was very safe when used properly, it delivered relief to many people, and its involvement in fatalities was

58. Barnett letter, 8, 9, 11.
59. Barnett letter, 6, 7.

mostly due to its use in ill-advised combinations by people with problematic histories. Lilly believed the campaign had proven itself to be the best way to achieve the goals it said it shared with the FDA. The company expressed respect for the autonomy of doctors and their ability to know individual patients' needs and risk factors.[60]

At the FDA, Jones circulated Lilly's letter to colleagues for their review. The staffers raised questions about what they considered Lilly's vague terminology, a lack of definitions of the factors the company used to adjust its estimates of prescriptions, and the consistent use of new prescription estimates rather than total prescriptions. The FDA reviewers cited NPA data for August-December 1979 that showed 4.8 million new prescriptions for Lilly propoxyphene products and another 3.7 million refills -- both much higher than the company's estimates. While the FDA agreed that prescriptions were down in 1979 from 1978, the agency challenged the methods Lilly used to get to 4.1 million new prescriptions and 2.9 million refills.[61]

On February 5, 1980, Louis Morris, a psychologist in Jones's department, sent her a brief report on Lilly's phone survey of three hundred physicians. Morris was far less sanguine than the company in assessing the results. He said that 62 percent of the doctors said they knew about new information on oral pain relievers, with in-person visits deemed somewhat more effective than mailings in informing doctors. The results showed that about two-thirds of the doctors remembered being contacted but that their recall of the content was weak. Only about a quarter of the doctors recalled, without help, that they had received information on Darvon. When helped, 55 percent remembered that Darvon was the topic. Among those who recalled that they had received information on Darvon, just under half could not spontaneously remember the message. Among those who could, 61 percent remembered that the message was about cautions, while 26 percent recollected that the message promoted the effectiveness or the safety of the drug. Morris calculated

60. Barnett letter, 15.
61. "Comments on Lilly's Second Quarterly Darvon Report Submitted to FDA January 24, 1980," Louis Morris.

that just 20 of the 300 physicians surveyed, or 7 percent, remembered the actual content regarding potential dangers of using Darvon with alcohol.[62]

Morris concluded that physicians did not in fact have a very good understanding of precautions that should be taken when prescribing Darvon. The educational campaign had not had much impact on doctors' decisions about Darvon, Morris said. Doctors' recall was fairly good when the survey-taker specifically mentioned Darvon. But unaided recall was low, which for Morris meant that the update on risks and precautions did not often factor into what doctors decided to prescribe.[63]

On March 17, 1980 Dr. J. Richard Crout, who led the department at the FDA where Jones and Morris worked, wrote to Richard Wood, Lilly's president and CEO. Crout's letter fused professional frustration with bureaucratic restraint into a stern challenge to Lilly's results and intent. For Crout, Lilly had not come close to meeting the commitment to update doctors that it had made in early 1979 to the FDA. "The character of this 'informational campaign' is so different from what we expected that I am obliged to bring this matter to your attention," he wrote.[64]

When Lilly had committed to the Darvon campaign, the FDA had told the company that the agency would use National Detailing Audit meeting write-ups from doctors who summarized what they had talked about with pharmaceutical company sales people. To the FDA, these transcripts, known as "verbatims," revealed several disturbing trends. At the campaign's start, only about 60 percent of the visits had included an appropriate message about new information on Darvon precautions. The September verbatims put this figure at 45 percent, and in October and November, fewer than one in ten visits included this message. To the FDA's dismay, the reverse was happening in another aspect of the visits. In August just under half the doctors visited had received Darvon

62. "Lilly Quarterly Report on Darvon," memo from Louis Morris (Psychologist/HFD-107) to Jones, February 5, 1980.
63. Morris memo to Jones, 2.
64. Letter from J. Richard Crout, M.D. to Richard D. Wood, March 17, 1980.

samples. This rate rose to 60 percent in September and more than 75 percent in October and November.[65]

Crout said the FDA had expected Lilly's sales people to focus only on the new warnings about Darvon. The verbatims showed that in more than half the visits, Darvon was not the first drug talked about. When it did come up, it did not take up much time. In August, less than half of each visit was devoted to Darvon; after that, less than a third of the typical visit was on this topic. Doctors were asked about specific messages they had heard. The responses appalled the FDA: "Darvon and Lilly won FDA battle;" "Analgesic – few if any side effects;" "OK by Drug Commission." Crout said the FDA believed Lilly had essentially implemented a standard promotional campaign for Darvon in which salespeople occasionally included mentions of the new warnings. He spelled out what Lilly needed to do. First, every visit had to focus on the precautions doctors should apply in prescribing Darvon. It should be the first, if not always the only, drug discussed. Samples were not to be left behind. Lilly should consider excluding Darvon sales when determining commissions or other compensation to salespeople who had implemented the informational campaign.[66]

The proximate backdrop for this exchange was a recent United Nations (UN) decision on Darvon. In February 1980, the UN's Commission on Narcotic Drugs had voted unanimously, with U.S. backing, to put propoxyphene into Schedule II of its international drug- control framework. Under the 1961 Single International Convention for Narcotic Drugs, this meant that the U.S. and more than 100 other countries were required to place tighter controls on the drug's production. The DEA said it was working to comply with the UN requirement and would look to the FDA to address how best to control the manufacture of tablets and capsules purchased by consumers; the DEA would focus on determining the level of bulk materials and medical inventories that were appropriate. An

65. Crout letter, 3.
66. Crout letter, 3.

intriguing question is why the U.S. acceded to tighter international regulation of Darvon while deciding that this was not needed for its domestic market.[67]

Along with Lilly and the DEA, members of the U.S. Congress were aware of this U.N. decision and its prospective impact. In May 1980 Lilly sent three senior managers to testify before a House committee chaired by Henry Waxman of California. Robert Furman opened Lilly's testimony by saying that the company was pleased to report a substantial decrease in Darvon abuse and that he would describe how the 1979 educational program had contributed to this progress.[68]

Furman's comments reprised the Darvon defense that the company had honed since the 1950s. Furman asserted Darvon's long-proven effectiveness and safety when used as intended. He acknowledged Darvon's appearance in reports of accidental deaths and suicides while ascribing this largely to overuse, often with other drugs, by a small number of people whose histories and inclinations made them poor candidates for Darvon.[69]

After disavowing Darvon's direct role in fatalities, Furman described what Lilly believed was an encouraging decline in propoxyphene abuse. He began with two points that Lilly had been making since DAWN data had become available starting in 1973. The first was that improper use of Darvon correlated highly with the use of multiple drugs, often including alcohol. The company also pointed to the frequency of suicidal intent as an element in misuse. Furman said the company had reviewed recent DAWN reports as well as data collected by pharmacologist Bryan Finkle for an update of his 1975 study. These new data covered 1976 through the third quarter of 1979. Since the campaign rollout propoxyphene mentions by medical examiners were down by 30 percent, and there had been a 55 percent decline from the peak in the first quarter of 1977. For Lilly, propoxyphene's rate of involvement in fatalities was declining more rapidly than the rate of new prescriptions was

67. "U.N. Move Spurs Drug Agency Curb on Darvon Output," *New York Times*, April 25, 1980, A7.
68. Statement of Robert Furman Before House Committee, May 21, 1980.
69. Furman statement, May 21, 1980.

growing. The news from emergency rooms was just as encouraging. Propoxyphene mentions from DAWN sites were down 36 percent since the first quarter of 1977, with a 27-point decline in 1979 alone.[70]

Furman turned next to the Crout letter of March 1980 to Lilly CEO Richard Wood. After receiving the letter, Lilly executives had met with Crout and his staff to reassure the FDA that the informational effort was not a promotional campaign. Lilly noted that it had sent out tens of thousands of brochures, information sheets, redone labels, letters, and booklets. Lilly representatives had spoken with thousands of doctors and felt confident that physicians understood the risks and precautions on Darvon. Furman cited the physician survey whose results had been submitted to the FDA and analyzed by Louis Morris. That survey showed that 88 percent of the doctors indicated awareness of the cautions needed when prescribing Darvon. Regarding Crout's objections to leaving Darvon samples with doctors, Furman said that the only doctors to receive such samples were those who had sent in a signed request for them. This practice conformed with Lilly's rules and federal regulations on the distribution of controlled substances, Furman noted. Lilly's records showed that the actual level of such sampling was about half of that reported.[71]

Furman concluded by describing the 1979 informational campaign as far-reaching and productive. He stated flatly that doctors were aware of precautions they needed to take with propoxyphene. All the data showed that propoxyphene's "involvement" in fatalities had declined substantially and was continuing to decrease. Overall, Furman's testimony repeated the case Lilly had made through the 1970s challenge to Darvon while drawing on what it saw as encouraging

70. Furman statement, 6.
71. Furman statement, 9.

trends from the field. For Lilly, Darvon's involvement in fatalities was largely guilt by association with alcohol, other drugs, and the wrong people.[72]

Congressman Waxman asked Furman about the guidelines that the FDA's Crout had suggested for salespeople's visits with doctors. When asked if Lilly's campaign had met this standard, Furman termed the suggestions "highly idealized" and added that "upon reflection Dr. Crout might agree." Lilly believed that any doctor who believed him- or herself to be aware of Darvon's risks would not allow a salesperson to rehash this topic. Nor would doctors be inclined to let the Lilly person focus exclusively on Darvon if the doctor had other topics on his or her mind. Waxman asked if Furman felt that a reason many physicians seemed unaware of the risks of Darvon was Lilly's long-standing marketing approach. Furman did not see the problem as a deficiency of "merchandising techniques" but rather as a result of Darvon's success, contending, as Secretary Califano had, that the widespread popularity of Darvon was sound evidence of the drug's safety and usefulness. Since 1957, patients had taken billions of doses. Furman said its classification as a non-narcotic was based on the World Health Organization's 1962 ruling. A main reason many physicians were now aware of the precautions, Furman claimed, was broad media coverage and the work of the FDA to publicize the latest findings.[73]

The dialogue between Lilly's Furman and Rep. Waxman emphasized Darvon's safety record and risks more than whether it helped with pain. In May 1980 Lilly believed that current knowledge of Darvon's risks was pervasive among doctors and that their data showed it. Congress, some medical professionals, and consumer advocates sought to square this with the lived experience behind

72. Furman statement, 11.
73. Furman statement, 26.

North Carolina Medical Examiner Page Hudson's 1979 comment that "doctors could not have been less aware of the risks."[74]

Seven years after the May 1980 hearings ended, a study of the impact of Lilly's 1979-1980 informational campaign examined whether the program had produced changes in how Darvon was prescribed or implicated in deaths. A time-series analysis of data on U.S. propoxyphene use between 1974 and 1983 was applied to drug overdose death rates among slightly more than 80 million people. The findings supported the FDA's concerns that the campaign had delivered many positive messages about Darvon and had made little to no impact on Darvon behavior among doctors or patients. Nationwide use of Darvon products during the campaign declined by about the same 8 percent that it had been declining for several quarters before the campaign began. After the campaign, this decline ended. The early 1980 FDA recommendation to encourage doctors to write "do not refill" on Darvon prescriptions had no discernible effect. In 1987 the rate of overdose death per Darvon prescription had been roughly constant since 1979.[75]

**Interpreting Darvon's meaning in pain management**

Darvon's lucrative ambiguity enabled it to carve a distinct niche in an increasingly crowded universe of pain-relief therapies. It was pervasive in hospitals and was included on six missions of the Apollo space program between (dates here). Attempts to put Darvon's capabilities and effects on a more sure grounding ultimately enhanced its ambiguous status. At the 1979 and 1980 Congressional hearings, Lilly executives, scientists, and elected officials debated research results and DAWN data. By shedding light on use patterns by geography and with other drugs, these studies helped raise propoxyphene's visibility within federal agencies and established Darvon as an unresolved topic that called for government study and decision-making. Lilly had nurtured this

74. Page Hudson, M.D., testimony at hearings of United States Senate, Monopoly and Anticompetitive Activities Subcommittee, Senate Select Committee on Small Business, January 31, 1979.
75. Soumerai et al., "Effect of Warnings," 1518, 1521.

ambiguity from the start in its marketing and work with regulators. In 1975 the FDA said Lilly had resisted attempts to place Darvon on international and federal drug regulation schedules, having argued that Darvon's chemical make-up and track record did not warrant such statutory controls. Between 1957 and 1969, when the FDA ordered Lilly to change its messaging about the product's potential to create dependence, Lilly had aggressively promoted Darvon to clinicians as a non-narcotic. The company fought what it saw as needlessly restrictive legal and regulatory classifications. Lilly engaged in a nearly continuous dialogue with regulators, legislators, clinicians, researchers, and its staff in an attempt to sustain this pillar of its commercial success.[76]

In Darvon's early years, these concerns had been muted by unregulated market success. By 1978, when the first attempt to remove Darvon from the US market began, more than 20 billion doses containing propoxyphene had been dispensed by pharmacists, in hospitals, and in pain management clinics. As a new drug, strong market response had helped Darvon evade inclusion in US laws and international conventions on drug control. In the late 1950s the World Health Organization (WHO) had recommended adding it to existing international conventions for the control of drugs. In 1962 the WHO reversed this position, citing commercial acceptance and what it deemed an acceptably small number of problems. Propoxyphene initially avoided inclusion in the US's main federal drug control legislation, the 1970 Controlled Substances Act (CSA), but here a change in policy went in the other direction. Darvon was added to the schedules of the CSA in 1977, following a recommendation by the Drug Enforcement Administration (DEA) to the Department of Justice (DOJ). By the second half of the 1970s, Federal regulators had been influenced by growing reports of fatalities in which Darvon was implicated.[77]

---

76. Cooper, "Scheduling Recommendations," 4. Cooper noted that "Eli Lilly and Company opposed any control of propoxyphene under the CSA [Controlled Substances Act, passed in 1970 as the guiding framework for federal drug control efforts] and provided extensive data and opinions to the FDA supporting this opposition to control under the CSA."
77. Cooper, "Scheduling Recommendations," 1.

The contrasting reversals made by the WHO and the US Department of Justice between 1962 and 1977 showed how readily the evidence on Darvon could be interpreted in different ways. This was a steady driver of Darvon's ambiguity but not the only one. In the US Darvon required a prescription, which suggested more therapeutic impact than an over-the-counter (OTC) product. But, despite its chemical structure, it didn't require one for a narcotic, which made life easier for physicians and patients. In addition, Darvon was often eligible for compensation under workplace health insurance plans, where aspirin and others were not. Finally, Darvon was indicated for mild to moderate pain, a condition that welcomed diverse interpretations and treatments based on the personal experiences of patients and the perspectives of clinicians. In its first two decades Darvon became what American physician Michael Newman had termed in 1979 a "celebrity drug," one that was more popular than its clinical prowess might warrant.[78]

Darvon was a synthetic opioid, a crafted variation on the morphine molecule that was one of several dozen such compounds introduced after 1945. But these were not the only class of drugs to promote an increasingly expansive concept of pain. Another contributor to treatment's role in the clinical transformation of pain was the use of drugs designed to affect outlook, mood, and coping skills for alleviating pain. Starting in the 1950s, antidepressants, so-called "minor" tranquillizers, and anti-anxiety medications, including Valium, began to be used in conjunction with analgesics. By the mid-1980s these drugs had been accorded recognition as valid adjuncts to treatment. After about 1970, evidence that pain and mood dimensions shared pathways and destinations in the spinal cord and brain began to give neurophysiological support for the practice. While the full history of mood-modifying drugs in treating pain has yet to be written, their role shaped how

78. Michael A. Newman, M.D., testimony to Senate Select Committee on Small Business, February 1, 1979, 1.

treatment furthered the transformation of pain in clinical medicine. Their use signaled growing clinical acceptance of the importance of psychological and emotional states in the pain experience.[79]

**Epilogue**

In November 2010, two days before the 32nd anniversary of the Health Research Group's (HRG) first petition to remove Darvon from the market, the FDA and Xanodyne Pharmaceuticals, a private company based in Newport, Kentucky, announced that the firm had agreed to remove Darvon and Darvocet (a combination of propoxyphene, acetaminophen, and caffeine) from the U.S. market. Since by 2010 the vast majority of these were combinations sold as generics, the FDA called on their manufacturers to do the same. HRG's executive director in 2010, Sidney Wolfe, had been lead petitioner in the organization's 1978 and 2006 lawsuits. In his response to the 2010 announcement, Wolfe excoriated the agency for what he considered its costly delay in following the decisions of the United Kingdom in 2005 and the European Union in 2009 to begin phased removals of propoxyphene products from their markets. Wolfe estimated that between one thousand and two thousand people in the U.S. had died from taking Darvon since the U.K.'s action.[80]

The FDA's 2010 decision was an ironic close to a decades-long Darvon controversy. The issues and arguments that shaped the 2010 decision were updates of long-standing controversies. In announcing its actions, the FDA cited one study that showed propoxyphene could disrupt the heart's electrical activity with potentially fatal consequences. Dr. Gerald Dal Pan, director of the FDA's office of surveillance and epidemiology, described these investigations as the last, missing

79. Bond, *Pain*, 166-175; Gary J. McCleane, *Pain Management: Expanding the Pharmacological Options* (Oxford, UK: Wiley-Blackwell, 2008), 7, 33-39; Spanswick and Main, *Pain Management*, 274-275.
80. "FDA Urged to Ditch Darvon," January 31, 2009, at http://www.zimbio.com/ConsumerAffairs.com/articles/489/FDA+Urged+to+Ditch+Darvon; Duff Wilson, "Darvon Pulled From Market by FDA," *New York Times*, November 19, 2010, at http://prescriptions.blogs.nytimes.com/2010/11/19/darvon-pulled-from-market-by-FDA; "FDA's Darvon Decision Too Late, Critics Say," in *Product Liability*, The Bell Law Firm PLLC, November 22, 2010, at http://www.charlestonpersonalinjuryblog.com/2010/11/fdas-darvon-decision-too-late-critics-say.

piece of the Darvon puzzle. But Wolfe and others had contended for decades that evidence of propoxyphene's risk to the heart's electrical functions was substantial.[81]

The 2010 similarities to earlier debates contrasted with recent changes in the global regulation of propoxyphene that had reverberated in the U.S. In January 2005 the United Kingdom's Committee on Safety of Medicines announced the withdrawal of propoxyphene from its market. Its statement noted that a combination of Darvon's questionable efficacy and a genuine risk of toxicity in overdoses, both accidental and deliberate, was unacceptable. In June 2009 the European Medicines Agency announced its ban on propoxyphene, allowing 15 months for removal from European Union markets. The agency claimed that a phased withdrawal in Scotland between 2005 and 2007 had resulted in a substantial reduction in the number of deaths associated with propoxyphene.[82]

The momentum for a Darvon ban in the U.S. had been growing as well. In January 2009, as the Department of Health and Human Services prepared to turn down the HRG's 2006 petition, an FDA Advisory Panel joint meeting an FDA Advisory Panel, comprising the Anesthetic and Life Support Drugs and Drug Safety Committee and the Risk Management Advisory Committee -- took place on January 30, 2009. The committees voted 14-12 in favor of removing propoxyphene products from the market. Comments on the vote reprised much of what clinicians and scientists had debated about propoxyphene throughout its career. Sharon Hertz, deputy director of the FDA's pain drugs division, described the Darvon landscape as murky and unclear and said it was anything but straightforward as to whether Darvon should remain available. Ruth Day of Duke University characterized Darvon as "little 'b,' big 'r'," meaning little benefit, big risk. Dr. Ajay Wasan of Brigham and Women's Hospital in Boston believed Darvon should remain available. He cited the

81. Matthew Perrone, "FDA Pulls Darvon Painkiller Due to Safety Risks," at SFGate, http://www.sfgate.com/cgi-bin/article.cgi?, November 19, 2010.
82. Perrone, "FDA Pulls Darvon," November 19, 2010; Todd Zwillich, "FDA Panel Urges Ban of Pain Drug," WebMD Health News, at http://www.medicinenet.com/script/main/art.asp?articlekey=97355, January 30, 2009.

vast range of people's pain experiences and their reactions to different pain relievers. Wasan noted that there were some patients who were helped by propoxyphene without adverse consequences. He expressed a belief that many doctors and patients saw Darvon as a gentle opioid, a lower-risk, lower-reward compound.[83]

In its 2009 presentation to the FDA, Wolfe and the HRG had sketched their far less sanguine view of the Darvon landscape. More than 20 million prescriptions containing propoxyphene had been written in 2007. HRG presented data that showed 503 deaths in 2007 in which propoxyphene was given as a contributing factor. In its 2006 petition, Public Citizen had included data from the Drug Abuse Warning Network (DAWN) data system that "implicated" propoxyphene in 5.6 percent of drug-related deaths from 1981 to 1999. The HRG said that DAWN showed 2,110 accidental deaths related to propoxyphene in the same period. In Florida in 2007 there had been 85 deaths listed in which propoxyphene was the cause, including 25 where it was the only drug found in the deceased. The HRG attributed these accidental deaths to adverse cardiac events, a lowered ability of the heart to contract properly, and the interruption of electrical impulses transmitted in the heart.[84]

More than three decades after the HRG had first sought to remove Darvon from the market, fundamental issues of safety and effectiveness could plausibly be described as still subjects of dispute. This chapter has argued that debates that fueled the Darvon controversy starting in 1978 had legitimized and sustained established debates within medical and policy communities. The 1978-1980 petition and response validated this controversy by acknowledging the merit of the HRG's contentions and scientific uncertainty of arguments over Darvon while deciding to keep it on the market, updating product labels, and reaching out to clinicians via an informational campaign to be launched by Lilly and the federal department of Health, Education and Welfare (HEW). The

83. John Gever, "FDA Panel Calls for Propoxyphene Withdrawal," at *MedPage Today*, at http://www.medpagetoday.com/PainManagement/PainManagement/12692, February 2, 2009; Zwillich, "FDA Panel Urges Ban," January 30, 2009.
84. Jennifer Corbett Dooren and Alicia Mundy, "Panel Urges Darvon Ban," *The Wall Street Journal*, at http://online.wsj.com/article/SB123326421629330211.html, January 31, 2009.

1978-1980 dialogue and decisions foreshadowed three decades of controversy by enhancing Darvon's status as permanently and acceptably ambiguous. After 1978, Darvon deepened its niche as an opiate that did not produce dire dependence or wrenching withdrawal. Evidence of recreational use was scant. The alarm that Wolfe and HRG felt about Darvon never caught on with consumers or with many clinicians, in part because so many had had unremarkable experiences with Darvon.

Chapter 2, which focused on the McGill Pain Questionnaire, showed how changes in the measurement and assessment of pain had advanced an understanding of pain as complex and individual -- put another way, subjective. This chapter examined how changes in pain treatment had an analogous effect and asserted that, after 1945, a proliferation of treatment options promoted a concept of pain as highly variable, circumstantial, and clinically elusive. As with changes in pain measurement, post-WWII developments in treatment implemented a concept of pain as multidimensional and decisively tied to a person's history and attitudes. In addition, by 1978, compelling evidence of the involvement of multiple brain regions and CNS processes in the experience of pain had accumulated. Pain's complexity was proving to be grounded in the vast complexities of the body's neuro-chemical operations.

The ambiguity that marked Darvon's history can be seen as a thread across the post-war history of pain management. By 1945, the pain treatment landscape could be divided into five main sectors. All would be enlisted in the expanding post-1945 fight against chronic pain. These modalities were 1) medication, centrally or peripherally acting, including opiate-based and non-opiate products as well as antidepressants, anti-migraine, and antiepileptic treatments 2) physical methods such as therapy and rehabilitation, transcutaneous neurostimulation, and the use of heat and cold 3) cognitive-behavioral techniques, including relaxation, biofeedback, hypnosis, and stress

reduction 4) anesthetic methods such as nerve blocks, in which the strategic injection of local anesthetics impeded passage of nerve impulses and 5) neurosurgery.[85]

One form that this ambiguity took was in the shifting clinical status of acute and chronic pain. After 1945, increasing success against acute pain, thanks largely to the proliferation of pharmacological remedies, helped obscure the scope and diversity of chronic pain, impeded development of medical training in pain medicine, kept pain in organizational limbo, and forestalled but did not prevent the emergence of chronic pain as a central clinical challenge. Darvon's history embodied this ambiguity across the more than 50 years that separated pre-market testing from the 2010 FDA decision to oversee its departure from the U.S. market. As always, there was more about pain that was ambiguous and variable than the shifting boundaries between acute and chronic pain: the origins and courses of painful conditions, the ability of different treatments to help, the responses of people to the same treatments, the diverse risk-benefit profiles that a molecule could create within groups, and the reasons for the persistence of pain beyond the cure of an illness or healing of an injury. For its part, Darvon was consistently unclear as to its stand-alone analgesic capabilities; its ability to engender dependence; the risks it posed, or didn't, to cardiac and liver functioning; and its potential for lethality when combined with other drugs.

Darvon's career thus encapsulated a transformation of pain management from straightforward to contingent. As something akin to a blank slate on which physicians and patients could inscribe their pain experiences, Darvon matched the ambiguities of pain itself. It was an opiate that seemed to come without much of what had tainted opiates for decades among many clinicians and patients. Darvon basked in the reflected glow of pharmaceutical science while it was for many people an

85. Margo McCaffery and Chris Pasero, *Pain: Clinical Manual, Second Edition* (St. Louis: Mosby, Inc., 1999); McCleane, Pain Management, 1-14; Bond, *Pain*, 149-192; Debra S. Cole, *Pain Management Solutions: Managing Pain in Stages* (Bloomington, IN: iUniverse, Inc., 2012)

agreeable and serviceable ally against pain. Its chemistry and market positioning seemed artfully constructed to achieve the niche that it did.

## Chapter 4 – Reformulating Pain: Model and Practice in Formative Tension

After 1945, clinical, professional, and epistemological transformations profoundly altered pain's standing within the medical profession. With publication of the gate control theory (GCT) in 1965 and the first board certification of pain medicine specialists in 1993 as markers, this chapter describes how new institutional forms helped refashion a fundamental understanding of pain among clinicians and patients. Pain slowly became a distinct medical entity defined by complexity, chronicity, and decisive subjectivity as organizational efforts brought ideas and people into increasingly structured interactions through publications, meetings, and research collaborations. These produced debates between an established and insurgent models of pain as efforts to implement a new model moved through clinical practice, research, and teaching. Between 1965 and 1993 this insurgent paradigm and groups that sought to implement it were in productive tension with a deeply entrenched perception of pain as a known clinical entity. Two significant drivers of this refashioning were the launch of the International Association for the Study of Pain (IASP) and the establishment of pain medicine as a recognized sub-specialty by the American Medical Association (AMA). Within these and other groups, pain was reformulated from symptomatic, simple, and largely understood to diverse in its origins and forms, clinically elusive, and deeply personal. This shift unseated a prevailing clinical understanding in ways that affected pain's assessment, treatment, and standing within the medical profession; patient-clinician dynamics; and the fortunes of dozens of pharmaceutical and medical services companies.

Contests over the nature of pain also were contests over the meaning and scope of professional authority and personal autonomy as they applied to pain's assessment and treatment. A more inclusive model of pain's dimensions challenged more than a set of clinical ideas. It was a claim on the authority of professionals to define the nature, scope, and responses to pain in new ways. A new model of pain brought the assumptions, practices, and results of pain's clinical history into increasingly sharp dispute. Existing patterns of medical authority came under attack as some clinicians sought new kinds of authority and autonomy based on their belief that clinical medicine had mostly gotten pain disastrously wrong. If pain was a distinct condition and critically at epistemological remove from clinicians, how could a biomedical model of disease, geared for universal causes and full cures, offer useful guidance? What were the differences between acute and chronic pain, and why did they matter? What qualified a clinician to treat chronic pain? What standards of practice should exist for managing of pain, who should set them, and what did it mean to "manage pain?"[1]

1. The work of Elliot Freidson, Everett Hughes, and Paul Starr pertains to issues of authority and autonomy in medicine and the understanding of pain after 1945. See Eliot Freidson, *Profession of Medicine: A Study of the Sociology of Applied Knowledge* (New York: Dodd, Mead & Company, 1970), 279-283, 304, 312, 368-370. According to Freidson, autonomy is central to the analysis of professions because "it bears on who may determine what the problem is, how the problem is to be dealt with, and what price is to be paid for dealing with it." A potential downside of a profession's autonomy was a "self-deceiving view of the objectivity and reliability of its knowledge and the virtue of its members. … it encourages the profession to see itself as the sole possessor of knowledge and virtue." What Freidson termed control of the work was crucial; the ability to determine what the work consisted of, who was qualified to perform it, and what processes would implement that authority. Hughes described similar issues in terms of license and mandate. License included formalized exchange relationships of activities for money, goods, or services, while members of an occupation claimed a mandate to define proper conduct, the technical content of work, approved styles of delivery, and "most critically, the patterns of public demand and response." Hughes saw professions as a "prime illustration … of the scope of a mandate" crucially by the ability to set the "very terms of thinking about problems which fall in their domain." Another dimension of their authority is their trafficking in dangerous tasks – health, salvation, conflicts of rights and obligations – that involve "guilty knowledge" of sin, disease, and crime. Paul Starr asserted that the establishment of legitimate professional authority involved three claims: the ability of a group of practitioners to "regulate itself through systematic, required training and collegial discipline; a base in technical, specialized knowledge; and a service rather than profit orientation, enshrined in its code of ethics." He described the rise of the medical and other professions as the result of a "struggle for cultural authority as well as social mobility." Robert Dingwall, *Essays on Professions* (Burlington, VT: Ashgate Publishing Company, 2008), 1, 3-5; Everett Hughes, *Men and Their Work* (New York: The Free Press of Glencoe, 1958); Paul Starr, *The Social Transformation of American Medicine* (New York: Basic Books, 1982), 4, 5, 7, 9, 13, 15, 17.

Two critical projects in the transformation of pain's status were launch of the IASP (1973) and the work to define, and achieve AMA recognition for, pain medicine as a specialty. Together, these activities articulated, operationalized, and ratified an inclusive model of pain that had found initial expression in the GCT and had been developed in hundreds of studies divided quite evenly between those that sought to support and those attempting to debunk the theory. Work to establish the IASP and a pain specialty included significant knowledge-formation projects that articulated groups' claims to clinical and social authority in addressing pain. The IASP's pain taxonomy (1979), classification of chronic pain syndromes (1986), and the development of standardized exams in pain by 1992 operationalized a new pain paradigm and, by 1993, ratified that model within medicine.[2]

Three themes unified the refashioning of pain's professional standing. First was pain's complexity, long known by clinicians and increasingly grounded in findings on the involvement of numerous brain processes in pain. Discoveries in neurophysiology after 1900 had slowly revealed that diverse electrochemical activities in the nervous system that were involved in pain were also involved, neuro-chemically, in emotions, beliefs, attitudes, self-perception, and other affective dimensions of mental life. Pain's complexity comprised increasing awareness of how personal history, circumstances, beliefs, and experiences were encoded in brain and spine processes.[3]

Another dimension of pain's refashioning was the rise of chronic pain as a defining clinical challenge. A large group of physically and psychologically wounded from two world wars; an aging population; growth in vehicular and industrial accidents; and medical advances against infectious

2. The IASP's history has been described in numerous studies; a full history has yet to be compiled. Michael R. Bond, Ronald Dubner, Louisa E. Jones, and Marcia L. Meldrum, "The History of the IASP: Progress in Pain Since 1975," in Harold Merskey, Loeser, and Dubner, ed., *Paths of Pain,* 23-33*; Oral History Interview with Louisa E. Jones*, 11 July 1993 (Ms. Coll. No. 127.18), John C. Liebeskind History of Pain Collection, History & Special Collections for the Sciences, UCLA Library Special Collections; Jones, *First Steps*. Jones had worked closely with IASP founder John Bonica at the University of Washington since 1961. She was widely recognized as a significant contributor to the group's strong growth in its first decade.
3. Keele, *Anatomies*, 102-122; Rey, *History of Pain*, 132-230.

disease all helped drive chronic disease, conceived broadly, to the forefront of clinical attention. The IASP saw chronic pain in post-1945 America as an urgent clinical problem that required a fundamental shift in the teaching and practice of medicine.[4]

The third pillar of this reformulation was a belief that pain had long been marginalized within clinical medicine. Pain's familiarity in many specialties meant that no one discipline had taken clinical or organizational leadership in the profession's engagement with pain. Formal education and training on the topic were scant. As a result, doctors had frequently felt unprepared to help patients whose pain hadn't gone away after an illness had ended or an injury had healed.[5]

These principles were implemented in a long list of activities between 1973 and 1993. Among them were regional, national, and global meetings; scientific publications; the development of curricula, training, and testing procedures for certification; partnerships with industry and existing groups in the medical profession; media outreach; political advocacy; the establishment of venues of care; and a growing number of board-certified pain practitioners. Another arena in which an insurgent model of pain was operationalized was in multidisciplinary pain clinics, whose number grew rapidly in the United States after 1960. Diverse in treatment modalities, clinical focus, staff makeup, and, sometimes, medical legitimacy, pain clinics were nonetheless important implementations of the IASP's dissenting concept of pain. [6]

---

4. Zimmermann, "The History of Pain Concepts," Merskey et al., *Paths of Pain*, 330-337; Baszanger, *Inventing Pain Medicine,*72-79, 88-96, 131.
5. In 2014, journalist Judith Foreman found only four medical schools in the United States that required students to take a course on pain. See Foreman, *A Nation in Pain*, 5.
6. The secondary literature on pain clinics expansively depicts this diversity. See Gerald M. Aronoff, *Pain Centers: A Revolution in Health Care* (New York: Raven Press, 1988); J. C. D. Wells, "The place of the pain clinic," *Bailliere's Clinical Rheumatology*, Vol. 1, No. 1 (April 1987); Chris L. Kleinke, "Patients' Preferences for Pain Treatment Modalities in a Multidisciplinary Pain Clinic," *Rehabilitation Psychology*, Vol. 32, No. 2 (1987): 113-120; Akiko Okifuil, "Interdisciplinary Pain Management with Pain Patients: Evidence for Its Effectiveness," *Seminars in Pain Medicine*, Vol. 1, No. 2 (2003): 110-119; Herta Flor, Thomas Fydrich, and Dennis C. Turk, "Efficacy of multidisciplinary pain treatment centers: a meta-analytic review," *Pain*, 49(1992): 221-230; J. Eugene Ruben, "Experience with a Pain Clinic," publication TK, Vol. 12 (September 1951): 601-603; Gerald M. Aronoff, Wayne O. Evans, and Pamela L. Enders, "A Review of Follow-Up Studies of Multidisciplinary Pain Units," *Pain,* 16(1983): 1-11; H. U. Gerbershagen, R. Frey, F. Magin, W. Scholl and N.

After 1973, no group was more central to the refashioning of pain than the IASP. The next section sketches its role in the reformulation of clinical pain.

**IASP – Organizing the Challenge**

Starting in 1973 the IASP provided direction and structure to a coordinated, global, trans-specialty effort to improve the understanding and treatment of pain. The IASP articulated and coordinated a global challenge to a dominant model of pain by operationalizing an alternative model in organizational forms and activities that defined an ancient problem in new ways. The IASP functioned as a trans-specialty hub in its publications, meetings, and organizational development. It sought clinical and epistemological acceptance of a model of pain constituted by complexity and fundamental subjectivity. Through its committees and task forces, dozens of national chapters, and partnerships with government, the United Nations, and industry, the IASP brought intellectual and organizational rigor to a growing global cohort of clinicians and researchers who had largely been isolated across geographic and disciplinary borders. The IASP's work to create a trans-specialty society sought to end pain's marginality by refashioning the core clinical challenge into chronic pain. Without the IASP, a renegade concept of chronic pain as central might have remained in a handful of scattered laboratories and offices whose inhabitants had long been mostly unaware of their shared perspectives.[7]

Between 1973 and 1982 the IASP achieved consistent growth in membership, the size and readership of its journal, and its global reach. This growth signaled its ability to demarcate an emerging field by bringing together diverse talents, temperaments, and beliefs around an inclusive and insurgent pain model; the IASP brought together a scattered but growing group of clinicians

---

Muller-Suur, "The Pain Clinic: An Interdisciplinary Team Approach to the Problem of Pain," *British Journal of Anaesthesia* (1975): 47, 526.

7. Bond et al., "The History of Pain Concepts," in *Paths of Pain*, Merskey, Loeser, and Dubner, ed., 23-33; Oral History Interview with John C. Liebeskind, 17-19 July 1995 (Ms. Coll. No. 127.21), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise M. Darling Biomedical Library, University of California, Los Angeles.

into self-awareness and a scientific society. A steady output of work products articulated the model and were central to the formation of distinct identities for the organization. The journal *Pain* (launched in 1975); the taxonomy of pain terms (1979, revised 1986); a classification of chronic pain syndromes (1986, revised 1989 and 1994); and global meetings every three years starting in 1975 implemented the IASP model as well as claims on authority in the assessment and treatment of pain. In 1982 the Committee on Education published a pain bibliography, and one year later the IASP ethics committee published guidelines for research with conscious animals. The IASP produced in 2004 a Curriculum for Professional Education in Pain Management that proposed guidelines for practitioners. Taken together, these projects of definition and taxonomy mutually shaped a concept of pain and the organizational structures of practitioners. These projects also made claims to authority by delineating concepts, meanings, and expressions for a wide selection of highly complex words, concepts, and clinical conditions. The creation of a pain taxonomy, where none had previously existed, sought a new form of clinical authority by changing the definition of the problem and encouraging new forms of collaboration across specialty and geographical boundaries.[8]

Founded eight years after publication of Ronald Melzack and Patrick Wall's game-changing GCT, the IASP benefited from and helped coordinate a surge in research that sought to affirm or refute the theory. The GCT had sparked an outpouring in research in the physiology and psychology of pain by proposing a model that elevated psychological dimensions to a rough parity with neurophysiology. The GCT was as controversial as it was influential; even with the many questions it left unanswered, it unambiguously rejected a mechanistic model of pain processes that largely

8. Liebeskind Oral History Interview, UCLA History of Pain Collection, 55, 65-68, 81-86; Bond et al., "The History of the IASP," in Merskey, Loeser, and Dubner, ed., *Paths of Pain*, 23-33; Nikolai Bogduk, "Taxonomy," in *Encyclopedia of Pain, Volume 3,* Robert F. Schmidt and William D. Willis, ed., (Berlin: Springer-Verlag, 2007): 2396-2398; John Bonica, Editorial, "The Need of a Taxonomy," *Pain*, 6 (1979): 247-252, and "Pain Terms: A List With Definitions and Notes on Usage, as Recommended by the IASP Subcommittee on Taxonomy.); Bruce Nicholson, M.D., "Taxonomy of Pain," *The Clinical Journal of Pain* (16:2000): S114-S117.

excluded individual factors from the neurophysiology in the experience and management of pain. To some, like Ed Perl, whose team had identified nerve fibers with heightened sensitivity to pain, the GCT appeared to diminish the significance of what happened at the periphery of the body too radically. Founding of the IASP also coincided with the first publications on the existence of endogenous opioids and a complex network of opioid receptors in the spine and brain. The discovery of the body's own pain management system energized research and debate and captured wide public interest.[9]

IASP's four-decade journey started at a former convent outside Seattle between May 21st and 25th in 1973. Thirty-seven years after she had done two years' of day-to-day work that brought the meeting to Issaquah, Louisa Jones recalled:

> It seemed to me that the meeting got going smoothly once people had adjusted to the somewhat austere living conditions – a university dormitory for the most part. There was a positive attitude even through the scientific arguments. This setting, with its quirks and surprises, seemed to work as Dr. Bonica had intended: good science, good presentations, and good discussions. It was obvious at the end of the meeting that fertile seeds had been sown and that there was good will. One attendee said that, for people interested in pain, it "was like being at a party in Hollywood where all the biggest movie stars were present."[10]

Bonica's goals for Issaquah were both broad and targeted. The overarching goal was to bring together clinicians and basic researchers to explore issues of interest across disciplines that had previously not communicated either frequently or well. Organizers counted 339 clinicians, researchers, and scientists, representing 13 countries and 57 medical and scientific disciplines, at the International Symposium on Pain. The short-term plan was to obtain approval to proceed

9. Perl, "Ideas about pain," 71-80; Cervero, *Understanding Pain*, 138-140; Baszanger, *Inventing Pain Medicine*, 3, 65-66, 69.
10. Jones, *First Steps*, 2; *Liebeskind Oral History Interview*, UCLA History of Pain Collection, 70-73; *Wall Oral History Interview*, UCLA History of Pain Collection, 33-38.

formally with establishing a society, launching a journal, and organizing a global meeting two years later. Supported by funding from the National Institutes of Health, the University of Washington School of Medicine, and several pharmaceutical and medical equipment companies, Issaquah attendees heard 102 papers, all in plenary session, on findings on processes of the spine and brain in modulating pain "signals," the structure and functioning of neurochemicals, and new pain-management methods such as electrical stimulation. In the months prior to Issaquah Bonica and Jones had organized and scheduled for the event small-group meetings, between talks or at off-hours, to discuss organizational topics, solicit ideas for a society and journal, and deepen people's awareness of work that others were doing.[11]

Among the 339 registrants at Issaquah was a group that would provide leadership across the IASP in its founding years. Patrick Wall had worked closely with Bonica in the two-year run-up to Issaquah and had his own strong views on what a pain society might look like, even considering that Wall, and others, weren't sure whether such a society was a sound idea or even possible. Ron Melzack, Wall's collaborator on the GCT; John Loeser, a neurosurgeon, disciple of Bonica, and eventual back-pain expert; physiologists Kenneth Casey and Perl, whose views on peripheral mechanisms of pain often clashed with those of Bonica; psychiatrist Harold Merskey, who would play a key role in IASP's taxonomy and classification systems; neurologist Raymond Houde, who had worked with Ada Rogers in New York in the 1950s and 1960s testing new pain relievers against morphine and other existing medications; neurosurgeon Benjamin Crue, founder of an early pain clinic in Los Angeles in 1960 and another who disagreed, sometimes strenuously, with Bonica; neurophysiologist Howard Fields; and neurosurgeons Willem Noordenbos and William Sweet. Even with allowances for their diverse backgrounds and perspectives, these people converged on

11. Jones, *First Steps*, 3-6, 42-47; Bond et al., "The History of the IASP," in Merskey, Loeser, and Dubner, ed., *Paths of Pain*, 23-33; Liebeskind UCLA interview, 1995; Oral History Interview with Patrick Wall, 10 August 1993 (Ms. Coll. No 127.2), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise M. Darling Biomedical Library, University of California, Los Angeles.

an inclusive concept of pain and on the gross inadequacies of the then-current model for helping with what clinicians were seeing. These and others would provide significant, long-lasting leadership on the IASP's launch and beyond.[12]

Jones's mention of arguments at Issaquah hints at sharp debates from the IASP's earliest days. The status quo on pain in 1973 can be summarized broadly as "most pain is acute (and treatable) and the rest is likely in the patient's head." For the IASP's early leaders, this prejudice had been promulgated in medical training and was a significant "blind spot" and moral shortfall in medicine. Many scientific controversies had been reanimated by the GCT, which by 1973 had attracted vocal supporters and skeptics as it stimulated inquiry. Findings in the 1970s bolstered such critiques by showing that some mechanisms predicted by the GCT were inaccurate. Enduring questions abounded: how to reconcile physiology and psychology in the experience of pain; the roles and significance of the peripheral and central nervous systems; the basis and mechanisms of action for acupuncture, about which Wall angrily and publicly expressed skepticism; the usefulness of electrical stimulation and other alternative therapies; and how the body's internal analgesic system worked.[13]

Beyond these scientific controversies, organizational issues shaped the IASP. Even someone as committed as Wall to overturning what he felt was a woefully inadequate model of pain asked whether it was clinically valid to set pain up as a distinct entity. There were disagreements about what credentials should be required and sufficient for membership. How should a group that sought to bring together diverse specialties be organized in a profession that largely structured

12. *Crue Oral History Interview*, UCLA History of Pain Collection, 13-16, 46-49, 58-60, 106; Lewis, *Medicine and Care of the Dying*, 176.
13. Karl M. Dallenbach, "Pain: History and Present Status," *American Journal of Psychology* 52 (1939): 331-347; Daniel De Moulin, "A Historical-Phenomenological Study of Bodily Pain in Western Man," *Bulletin of the History of Medicine*, 48:4 (1974:Winter): 540; John D. Loeser, "Pain History Musings," *Pain Forum* 4(2) (1995): 134-140; Merskey, "Some Features," 3-8.

itself by discrete specialties? Bonica was sensitive to how the appearance or reality of undue American influence could be avoided.[14]

The centrality of psychology to the IASP's long-term model was foreshadowed in the number and diversity of psychologists at Issaquah. Among the 13 who identified themselves as psychologists or psychiatrists were Melzack, who had been trained by Donald Hebb in experimental psychology; John Liebeskind, a physiological psychologist whose laboratory produced early studies on the role of the brain in modulating pain; and Merskey, a psychiatrist who would lead the IASP's taxonomy subcommittee. The inclusion of psychological dimensions and the ability to ground these dimensions in the neurophysiology of the nervous system were key to the IASP's model of pain. Cognitive-behavioral pain treatments were joining biofeedback and electrical stimulation as emerging treatments for chronic pain; the IASP was pivotal in conceptualizing and promoting legitimacy for these approaches.[15]

On Issaquah's final day the attendees voted to approve publication of the meeting's proceedings and to form committees on establishing a professional society, publishing a journal, and organizing a global conference every three years. Bonica led a small team that wrote the organization's bylaws, and the IASP incorporated in May 1974. Three goals would drive the organization in the 28 months between Issaquah and the First World Congress in 1975: growing membership, establishing the journal Pain, and organizing a global meeting scheduled 30 months later.[16]

Issaquah set a clear path for the IASP as global, committed to multidisciplinary treatments, rooted in scientific research, and implacable in its challenge to the biomedical status quo. The IASP had 652 members in 42 countries by the end of 1974, compared with 339 in 13 nations 18 months

14. *Liebeskind Oral History Interview*, UCLA History of Pain Collection, 67-69, 72; *Crue Oral History Interview*, UCLA History of Pain Collection, 16, 56-58, 106-107.
15. Melzack and Wall, *Challenge of Pain*, 281-282; Hadjistavropoulos and Craig, ed., *Pain: Psychological Perspectives*, 333-338; Jones, *First Steps*, 42-47.
16. Baszanger, *Inventing Pain Medicine*, 80; Jones, *First Steps*, 1-12; Bond et al., "The History of the IASP," in *Paths of Pain*, Merskey, Loeser, and Dubner, ed., 23-25.

earlier. When the First World Congress convened in 1975, membership was about 1300. The last founding member was listed at end of February 1975; 35 years later there were 113 people with founder's designations. By 1976 the IASP had close to 1,600 members. By the Edinburgh Congress in 1981 membership was just under 1,800 and reached 2,000 in 1982.[17]

The journal *Pain* was central to the IASP's steady growth in membership and global reach. Its first issue in March 1975 began six years that averaged 400 published pages annually. Between March 1975 and September 1981 the first 10 volumes comprised 32 issues with an average of 13 articles per issue. There were contributions from journals in neurology, physiology, and psychology, book reviews, occasional letters, and editorials. The journal's content embodied the IASP's inclusive model by incorporating the perspectives of many medical disciplines and in its openness to studies of diverse treatment modalities. These helped the journal to legitimize diversity among clinicians and researchers. The publication's emphasis on chronic pain's origins; an openness to studies on acupuncture, electrical stimulation, and cognitive-behavioral therapies; and the consistent prominence of animal studies as essential in the neurophysiology of pain embodied core concepts.[18]

The makeup of the journal's editorial board in its first six years showed how the IASP focused on global perspectives and a perceived need to avoid any appearance or reality of undue American influence. The initial board listing in March 1976 had 14 topic-based editorial panels; each with a director and one or two members. The 14 directors and total of 36 members, exactly half of whom had been at Issaquah, suggest the development of a core leadership group in the IASP. Panels included dentistry, physical medicine, psychology, psychological therapy, and psychiatry. Leaders

17. Jones, *First Steps*, 1, 6, 7, 9, 10.
18. *Pain*, Volumes 1-10, 1975-1981.

of the editorial panels numbered five from the US, three from Western Europe, two from the United Kingdom, and one each from Canada, Eastern Europe, Asia, and Israel.[19]

The allocation of editorial space to different topics in the journal's first six years reflected these themes. There were more than 40 topic headings, although the possibilities for placement of the same article in two or more headings were numerous. Between 1975 and 1981, articles in neurophysiology (128) edged out animal studies (121) as the most frequent topics. The IASP's emphasis on psychology and psychiatry was shown in 56 articles, including an examination of responses to a sugar pill; personality correlates of chronic pain; psychosocial factors in osteoarthritis of the hip; the relationship of memory and pain; the detection of psychological disturbance in low-back pain; and the role of behavior modification in treating chronic pain. Closely related were 24 articles on patient report and experience, with articles on the perception of dental pain; diurnal variations in chronic pain; the effects of naloxone, an opiate antagonist, and epidural narcotics on perception of pain; and pain thresholds.[20]

The clinical urgency of chronic pain was a consistent theme of the journal's first years, with 40 articles. Here too the topics showed a range of psychosocial analyses to which the IASP was open. Examples included articles on the potential roles of spousal behavior, marital adjustments, family dynamics, and bed design on chronic pain; the formative influences of genetic factors and social context; and the utility of acupuncture and transcutaneous electrical stimulation in treating chronic pain. Wall's personal skepticism about acupuncture had been loudly expressed in sessions at Issaquah and the first global meeting; this did not prevent him from publishing articles that explored its mechanisms and effects. Pain management was the keyword for 24 articles, including studies of pain relief from relaxation and neurological management, cognitive modification, vibratory stimulation, guided group experiences, biofeedback for chronic headache, nerve block,

19. Jones, *First Steps*, 11; *Pain*, Volumes 1-3, 1975-1977.
20. *Pain,* Volumes 1-10, 1975-1981.

hypnosis, and the omnipresent electrical stimulation. Pain measurement was the focus of 18 articles in the first six years. The September 1975 issue introduced the McGill Pain Questionnaire (MPQ), and while there were two articles on the MPQ to assess cancer and dental pain, there was greater interest in measuring the comparative efficacy of morphine, propoxyphene, fentanyl, and other analgesics for different conditions.[21]

An example of the journal's interest in the complexities of chronic pain, and of the conceptual distances from which such pain could be linked to non-physiological factors, was published in 1979. Three psychiatrists reported on work to correlate marital and family dynamics with the occurrence and characteristics of chronic pain. They studied 13 patients in each of two groups: one with depression and persistent pain (DP group), and the other with depression and no pain (D group). The DP group showed more evidence of prior pain problems, spouses with pain problems, pain issues in their families, and similar issues in spouses' families. The authors concluded that depressed patients whose main complaint was pain made up a useful subgroup of the depressed population. The article posed a difficult question. If family and marital factors could play a role in causing a person's pain, were there any such personal or social factors that could be excluded from shaping the individuality and variability of pain?[22]

The journal's embodiment of the IASP model and principles was matched by the significance and impact of the IASP's global meetings every three years starting in 1975. The congresses stimulated intense exchanges, strengthened personal and organizational networks, and brought diverse clinicians into contact with other disciplines' perspectives and issues in pain. While Bonica's ideas and personality were prominent in the early years, the proceedings and personal accounts reveal a contentious ferment in the group. IASP members brought diverse scientific views, professional experiences, and personal beliefs to the organization's early years. The meetings also showed how

21. *Pain*, Volumes 1-10, 1975-1981.
22. Patrick D. Wall, "25 Volumes of Pain," *Pain*, 25 (1986): 1-4.

steadily the IASP grew. The 1978 Montreal Congress included more than 375 papers, an increase of nearly 25 percent over 1975, while new features included breakfast sessions, a poster format, and an expanded press room and activities. In 1981 at Edinburgh 220 of the 350 "free communications" were in poster form; slides were declining. Almost 1,670 people from 41 nations attended in Edinburgh. By 1980 IASP chapters were forming in France, Japan, Great Britain, Korea, Spain, Israel, Brazil, and Ireland; the Eastern Canada chapter became the Canadian Chapter.[23]

Louisa Jones recalled "an aura of excitement, camaraderie, and purpose" as nearly 1,100 people gathered for the IASP's First World Congress (FWC) in early September 1975. The meeting brought clinicians, nurses, and researchers to Florence from 35 countries and 75 scientific and medical disciplines. It covered three-and-a-half days and included 18 special lectures intended as overviews and 252 10-minute presentations followed by 5-minute discussions. Attendees saw six motion pictures on pain and could choose among four related workshops. National and regional chapters were approved for Argentina, German-speaking, Netherlands, Northeastern USA, and Western USA. After 1975 the US's two regional chapters would compete for the right to manage a merger and become the United States' IASP chapter. Jones recalled hearing from several excited attendees who "had met someone from New Zealand or elsewhere who was doing the same research and neither knew it."[24]

Bonica stepped to the podium in Florence to open the first Congress with an overview of the history, origins, status, and future objectives of the IASP. His speech was a useful snapshot of the organization and of how a medical field in formation understood itself, its mission, and the issues it faced. The Florence meeting, less heralded in IASP accounts than Issaquah, was a rich signpost of the transformation of pain, an event that helped propel the shift while chronicling it at the same

23. John J. Bonica, "Introduction to the First World Congress on Pain: Goals of the IASP and the World Congress," in *Advances in Pain Research and Therapy, Volume 1: Proceedings of the First World Congress on Pain*, ed. John J. Bonica et al. (New York: Raven Press, 1976), xxvii-xxxix. Jones, *First Steps*, 4-6.
24. Jones, *First Steps*, 9-11; Bonica, "Introduction," in *Advances in Pain Research and Therapy*, xxvii-xxix.

time. The Florence meeting anticipated later effort to create an integrative, synthetic specialty by facilitating exchanges across disciplinary and geographical boundaries. Florence and its successor events were critical in operationalizing the IASP model.

Bonica began with a sketch of the current state of pain as marginal, urgent, and replete with clinical opportunity. Bonica saw his profession's tepid engagement with chronic pain as a disaster and a moral failure. Others in Florence shared this frustration with pain that was untreated or mistreated and with what they perceived as pervasive ignorance about chronic pain in their profession. For Bonica and other early leaders of the IASP, relief of pain was inseparable from medicine's most basic mission and indivisible from the identity of all medical practitioners. He reminded his listeners that genuinely chronic pain was a force for great suffering in the world -- emotional, physical, economic, and cultural stress and trauma for patients, families and society were vast and relentless. He believed that medicine needed to be on the front line in addressing this reality but wasn't currently doing a good job at it.[25]

Bonica acknowledged progress in elevating pain's status within medicine over the prior 20 years. Thanks largely to gate control theory, there had been a substantial spike of interest among basic researchers in the mechanisms of chronic pain and in collaborating with clinical investigators and practitioners. The two years since Issaquah had included encouraging growth in the IASP and a good start for the journal. Recent discoveries of endogenous opioid systems had excited medical professionals and the public imagination, bringing pain and its relief wider attention. He praised current work in neurosurgery and psychology, with the latter singled out for helping define the differences between acute and chronic pain in cultural, psychological, and environmental terms. Over the last two years the National Institutes of Health (NIH), the federal agency responsible for

25. Bonica, "Introduction," in *Advances in Pain Research and Therapy,* xxix-xxxi. He said that pain, "in its chronic persistent pathologic form, is a malefic force that often imposes severe emotional, physical, economic, and sociologic stresses on the patient and his family as well as on society."

biomedical research, had shown more support for pain studies. In the 15 months since IASP had been incorporated there had been progress on many of the objectives in the Articles of Incorporation.[26]

Bonica's account of positive developments contrasted with his assessment of pain's ongoing marginality and of what needed to change. There were three reasons for medicine's consistent shortfalls in treating pain: gaps in knowledge, inadequate application of existing knowledge, and issues in communications between the bench and the bedside. There were no pain taxonomies, real epidemiological data, or national data banks. Communication between clinicians and researchers ranged from poor to non-existent.[27]

He noted the continued importance of research, built on the work of physiologist Charles Bell and anatomist Francois Magendie, on structures and mechanisms of the nervous system. But most of what had been learned did not yet help patients. In 1975, the medical profession remained slow to grasp the differences between acute and chronic pain or the scope of the latter. Basic scientists were not much concerned with clinical pain, and the data and hypotheses they produced were mostly irrelevant. Until the GCT in 1965, pain research and therapy had been intellectually stagnant for decades. The inability to measure pain in a useful way was an additional impediment to clinicians.[28]

For Bonica, wider forms of neglect amplified these weaknesses. Medicine faced a shortfall of trained workers in the pain field. Research funding from government agencies was paltry. In 1975 the NIH had spent about US$2.2 billion, with US$34 million, or 1.5 percent, going to pain-related studies, with most of this for research on anesthesia, pharmacology, and cardiology in order to keep pain from worsening and to avoid pain-related complications. Research spending on pain as a

26. Bonica, "Introduction," in *Advances in Pain Research and Therapy*, xxxi-xxxiii.
27. Bonica, "Introduction," in *Advances in Pain Research and Therapy*, xxxiv-xxxv.
28. Bonica, "Introduction," in *Advances in Pain Research and Therapy*, xxxv.

disease in its own right was less than US$3 million. An example of pain's neglect was at the National Cancer Institute, which spent about US$500 million per year on research while paying what Bonica assessed as very little attention to cancer pain, which was a major focus of patients.[29]

Bonica cited several reasons for what he considered the poor application of his profession's limited knowledge of pain. Teaching about pain, both in medical school and afterward, was sporadic and unorganized. Powerful trends toward specialization meant that pain was familiar in many disciplines but "owned" by none. Many clinicians were disinclined to develop pain knowledge and skills. The IASP sought to help the entire biomedical scientific community, health professions, and societies to work together on a much greater research effort, more effective teaching, and better patient care.[30]

American neuro-oncologist Kathleen Foley was in Florence as Bonica opened the 1975 Congress. She was a recently minted clinician who had started a job in the neurology section at Memorial Sloan-Kettering (MSK) Cancer Center in New York. MSK had been seeking someone to study pain. At her job interview she said to Dr. Jerry Posner, the department chairman, that she didn't know anything about pain. "Don't worry about that," Posner replied. "No one else does either." Foley would eventually lead the first pain service at a cancer center in the United States. She was an early contributor to defining the epidemiology and classifying pain syndromes in cancer patients. In 1975, the work of John Liebeskind's laboratory on the role of the brain in modulating pain had energized practitioners across medicine, including people in Foley's field, and had nudged the investigation of pain toward greater respectability among clinicians.[31]

In Florence Foley led a one-day meeting on the epidemiology of cancer pain that Bonica had asked her to organize and that 150 people attended. She had hastily put together, along with MSK

29. Bonica, "Introduction," in *Advances in Pain Research and Therapy*, xxxi.
30. Bonica, "Introduction," in *Advances in Pain Research and Therapy*, xxxii.
31. *Oral History Interview with Kathleen Foley*, UCLA History of Pain Collection, 3.

researcher Ada Rogers, a study of the prevalence of pain in MSK's patients. In Florence she met Bonica, anesthesiologist Robert Twycross, and neurologist Venito Ventafridda, with whom she became part of a group in IASP that focused on cancer pain and brought this extremely difficult issue in pain management squarely within the IASP's purview.[32]

Foley's experience in Florence highlighted a brisk debate across the IASP's full history. Pain management issues that Foley and her colleagues faced at MSK barely resembled pre- and post-operative pain management that anesthesiologists such as Bonica and surgeons such as Benjamin Crue and William Livingston were familiar with. At MSK Foley and her colleagues' patients had manifest illness, and among these clinicians concerns over tolerance and addiction were virtually non-existent. The Bonica group would long argue that opiates were strongly contraindicated for chronic-pain, in part because of what some in the IASP perceived as excessive restraint on the basis of misinformation, or a lack of information, about the use and dangers of opiates with different patient populations. A debate over opiates in chronic pain took shape in the 1970s and has persisted to the present.[33]

In his address to the Florence congress Bonica mentioned the importance the IASP attached to its work on taxonomy and classification. Bonica and other early IASP leaders attributed some of pain's marginality to a lack of agreement on definitions. One Florence attendee had noted that "one person's pain is another's suffering and still a third's nociception." Proposing definitions of elusive and fundamental terms, and coordinating their refinement, were fundamental to the IASP's claim to

32. *Oral History Interview with Kathleen Foley*, UCLA History of Pain Collection, 10-12, 26. Rogers became a research nurse at Memorial Sloan-Kettering in 1951 and remained there until 1993. In the 1950s through the 1970s she worked with anesthesiologist Raymond Houde in studying the efficacy and side-effects of a wide array of pain medications. See *Oral History Interview with Ada Rogers*, 12 September 1995 (Ms. Coll. No. 127.31), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise M. Darling Biomedical Library, University of California, Los Angeles.
33. *Oral History Interview with Kathleen Foley*, UCLA History of Pain Collection, 5, 8, 10, 19, 26, 33; Russell K. Portenoy, "Opioid Therapy for Chronic Nonmalignant Pain: Clinicians' Perspective," *Journal of Law, Medicine & Ethics*, 24, no. 4 (1996): 296-309; Staffan Arner, "Opioids and long-lasting pain conditions: 25-year perspective on mechanism-based treatment strategies," *Pain Reviews 7* (2000): 81-96.

clinical authority and a critical project of pain's refashioning. Bonica and many others at Florence knew that efforts to establish definitions across a diffuse medical landscape would generate contention. They also grasped that the act itself was an attempt to establish clinical and epistemological authority. By taking the lead in work that could fall far short of perfection but still succeed, the IASP made an attainable claim on legitimacy for its model. It did not have to, and never could, forge unanimity. But genuine progress would be a step forward for the IASP and for its model of pain.[34]

Many people in Florence believed a definition of pain, a uniform list of terms, and a useful classification of pain syndromes to be impossible. Bonica appreciated the difficulty but did not accept the impossibility. He thought a well-run effort would advance the field by promoting ongoing refinement and improvement of definitions through interchanges that the IASP could facilitate. There were precedents in the development of classifications in heart disease, diabetes, and psychiatric disorders.[35]

With some urging from Bonica, physiologist Denise Albe-Fessard, first president of the IASP, sought out psychiatrist Harold Merskey to lead the taxonomy committee. Merskey was surprised since as a psychiatrist he felt he had less to offer than colleagues who dealt with somatic conditions. But Bonica liked Merskey for the job since he was a non-American native English speaker; Merskey was British, and, beyond his belief that Merskey was well suited to the task, Bonica was fearful of any appearance or actuality of American domination of the IASP. The makeup of the taxonomy group showed this concern as well as a commitment to global perspectives. Members of the taxonomy subcommittee were Albe-Fessard; Bonica; Merskey; Israeli (physiologist) Amiram

34. Bogduk, "Taxonomy," in *Encyclopedia of Pain*, 2397; John D. Loeser and Richard G. Black, "A Taxonomy of Pain," *Pain*, 1 (1975): 81; Harold Merskey, "Terms and Taxonomy: Paper Tools at the Cutting Edge of Study," in Merskey et al., *Paths of Pain*, 329-337.
35. John Bonica, Editorial, "The Need of a Taxonomy," in *Pain*, 6 (1979): C2, 247-248; "Pain Terms: A List With Definitions and Notes on Usage, as Recommended by the IASP Subcommittee on Taxonomy," *Pain*, 6 (1979): C2, 249-252.

Carmon, American neurologist Ronald Dubner, American neurophysiologist Howard Fields, American surgeon Frederick Kerr, Swedish neurologist Ulf Lindblom, British oral surgeon James Mumford, Dutch neurosurgeon William Noordenbos, Italian neurosurgeon Carlo Pagni, Belgian _____ Marcel Renaer, American psychologist Richard Sternbach, and Austrlian anesthesiologist Sir Sydney Sunderland. Ten of the 13 members had attended the Issaquah meeting, and seven had presented papers at the First World Congress in 1975.[36]

Some Florence attendees knew about a recent effort by the National Institute of Dental Research in the United States to classify orofacial pain. This work did not succeed. If specialists could not agree on terminology for a much smaller set of clinical issues, how could agreement be reached across a wide spectrum of disciplines and clinical diversity? Lindblom, Mumford, Belgian surgeon Willem Noordenbos, and Peter Nathan, a neurologist and consultant to the IASP, were the working group that prepared a series of definitions. These, after considerable discussion and some modifications, were adopted by the taxonomy subcommittee and were published in 1979.[37]

The IASP taxonomy covered 19 words, with commentary on 14 terms ranging from a brief sentence to two critical paragraphs for "pain," the first word defined. Among the others were pain threshold, nociceptor (described as "preferable to terms like pain receptor, pain pathway"), central pain (pain associated with a lesion of the nervous system), and allodynia, or pain due to a non-noxious stimulus to normal skin.[38]

The simultaneous breadth and precision of the IASP's definition, and its widespread use as a starting point for hundreds of studies, have helped drive the IASP's growth. The definition's reach has strengthened the influence of pain as defined by subjectivity. More than 25 years after it was published, psychologist David Bowsher commented that virtually the entire health professional

36. Bond et al. in *Paths of Pain*, Merskey, Loeser, and Dubner, ed., 330.
37. Bond et al. in *Paths of Pain*, Merskey, Loeser, and Dubner, ed., 331.
38. "Pain Terms," IASP Subcommittee, 250.

community of health professionals was likely familiar with it. The IASP defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage," This astutely distilled the IASP model down to a robust and flexible meaning with several key attributes. First, the definition gave equal weight to sensory and emotional dimensions of pain. By saying pain is "associated with" genuine or "potential" damage, the IASP definition asserted the reality of pain due to organic illness and pain whose tie to such illness or injury may not be as clear. The commentary started with a simple declaration: "Pain is always subjective." By defining pain as having an emotional component in all instances, the IASP made its insurgent concept the centerpiece of its model and its efforts to promote it. The definition was suggestive and left room for application in diverse clinical settings.[39]

The act of defining basic terms made an epistemological claim on authority and clinical utility. By defining pain as anything described in terms of tissue damage, the IASP encouraged full equality of psychological and personal factors in descriptions of neurophysiological mechanisms and clinical assessment of pain. The definition sought to level the epistemological status between signs of organic damage or illness and the description of the condition provided by the person enduring pain. The scope of the 1979 taxonomy and 1986 classification of chronic pain syndromes made them unprecedented claims on this authority. Physiologist Sir Thomas Lewis, in the first decades of the 20th century, had publicly despaired of devising a satisfactory definition of pain. The IASP definition has been a critical contribution to the ascent of a concept of pain defined by subjectivity.[40]

In his introduction to the 1979 taxonomy, Bonica called for its refinement by clinicians and researchers after acknowledging that what was presented was far from flawless or complete. This assessment solidified the document's credibility in acknowledging the complexities that many in

39. Bonica, "The Need of a Taxonomy," 247; David Bowsher, Letter to the editor, *Pain* 113 (2005): 430.
40. Lewis, *Pain*, 3.

the IASP had confronted for decades. Merskey's introduction noted that the definitions were intended to serve as a "minimum standard vocabulary." Except for the definition of pain, words are "defined primarily in relation to the skin and the special senses are excluded." Soon after publication in 1979 the IASP taxonomy was translated into Portuguese and adopted by the Brazilian Association of Anesthetists. It had been "favorably noticed" in JAMA in 1980, and publishers of Webster's Dictionary had inquired about using the definition in future editions.[41]

Two years after the taxonomy appeared, Merskey spoke at the 1981 Edinburgh meeting to report on the committee's then-current work on the classification of pain syndromes. The group's plan was to publish this in 1986 along with an update of the 1979 taxonomy. The classification of chronic pain syndromes expanded the IASP's claims to authority for its model and ideas. Beyond defining words and phrases, it sought to convey defining attributes, markers, co-conditions and physical effects of conditions that it also believed were highly variable, individual, and often poorly understood. Like the MPQ, it sought clinical usefulness. Four principles shaped the work that led to the classification scheme. Its goal was to describe syndromes in which pain is a prominent feature. It strived to craft descriptions that were current and sound given current knowledge. The committee would not provide textbook-ready descriptions. It delivered useful information for the syndromes but did not offer guidelines for practice or diagnostic rules.[42]

Merskey used low-back pain to describe some of the dilemmas the taxonomy group was sorting through. Low-back pain was diverse and its origins often obscure. The committee's challenge was to identify and isolate syndromes amidst a clinical universe where symptoms or presentations of different conditions were similar; the conditions themselves varied widely; and available ways of examining patients either didn't exist or weren't effective. The committee was struggling with what

41. Bonica, "Need of a Taxonomy," 247; "Pain Terms," IASP Subcommittee, 249.
42. Harold Merskey, "The Work of the Taxonomy Committee," in *Advances in Pain Research and Therapy: Volume 5: Proceedings of the Third World Congress on Pain* (New York: Raven Press, 1983): 33-54.

should be considered basic data and information on newer syndromes such as painful legs, moving toes, and cluster headache. Earlier approaches to medical classification had been by causal agent, systems of the body, patterns and types of symptoms, or time of occurrence. Overlaps and variations among these schemes were the rule. Some systems, such as that in Diagnostic and Statistical Manual (DSM)-3, a comprehensive and pervasive classification system of behavioral and psychiatric conditions, used axes along which categories of conditions were classified, including clinical syndromes, personality disorders, physical disorders, severity of psychosocial stressors, and highest level of adaptive functioning in past years.[43]

The goal of the IASP classification of chronic pain syndromes was to engage the clinical community in crafting operational definitions and then to encourage tracking and revision in order to attain the usefulness needed in clinical practice. The IASP defined a few general syndromes and then arranged others first by region and then by the bodily system involved, the pattern of pain, its duration and severity, and last by its origins. Its authors granted that this approach raised valid issues, but felt that putting etiology at the top of the hierarchy would have led to far more. The choice of bodily location at the top of the scheme affirmed the centrality of neurophysiological processes in conceptualizing pain. The hierarchy was an epistemological statement that sought to ground the influence of psychological and social factors in the neurophysiology of chronic pain.[44]

The subcommittee on classification included British psychiatrist Michael Bond, neurophysiologist Howard Fields, and Merskey. They decided on an axis system, and they approached 64 IASP colleagues to work on the descriptions of syndromes. The group started with head, neck, shoulder, and upper limb syndromes, and their hope was that several people steeped in each condition would exchange descriptions with appropriate colleagues. The taxonomy group had

43. Merskey, "Taxonomy Committee," 40; Harold Merskey, "Development of a Universal Language of Pain Syndromes," in *Advances in Pain Research and Therapy, Vol. 5, Proceedings of the Third World Congress on Pain*, John J. Bonica, Ulf Lindblom, and Ainsley Iggo, ed., (New York: Raven Press, 1983): 62-84.
44. Merskey, Taxonomy Committee," 46-48.

decided to cover all syndromes that lasted more than three months and to include one or two acute episodes that displayed patterns that frequently became chronic, such as post-herpetic neuralgia.[45]

In 1986 the IASP published the *Classification of Chronic Pain Syndromes*. The introduction reprised Merskey's collaborate-to-revise theme from 1979 and described the document as provisional, with gaps, inaccuracies, and inconsistencies sometimes knowingly included. The system reflected the IASP's contention that research in pain's epidemiology, aetiology, prognosis, and treatment required the ability to group clinical events into agreed-upon patterns. The group's work sought to supplement, not replace, the current International Classification of Diseases-9 categories published by the World Health Organization. Noting that pain syndromes were often distinguished on the basis of duration, site, and pattern, the IASP started with descriptions of general conditions that could take many forms, such as stump pain and peripheral neuropathy. After this group, the second basic category was by location. Each syndrome was described in terms of its definition, site, the systems involved, main features of pain including prevalence, age of onset, sex ratio if known, duration, severity, and quality; associated features; what provided relief; characteristic signs; usual course; complications; social and physical disabilities; specific lab findings; pathology; treatment when it was 'special' to the case; diagnostic criteria's differential diagnoses; and, lastly, the alpha-numeric code that was derived from placement of the syndrome along the axes listed. It used five axes to delineate these syndromes and to generate the alphanumeric code assigned to each condition: regions (thoracic, abdominal), systems (musculoskeletal, nervous, respiratory), temporal characteristics or pattern of occurrence (single episode, recurring regularly or irregularly), patient's statement of intensity or time since onset (mild, medium, severe), aetiology (trauma, infection, degenerative). In an effort to systematize the enormous variety of low-back pain the system kept some traditional categories as well as conditions that occur without pain but are often part of the "total picture." They divided low-back

45. Merskey, "Taxonomy Committee," 46-48.

pain along acute, recurrent, and chronic strain or sprain axes. The IASP classification and descriptions were both "popular and neglected."[46]

A 1994 update of the 1986 document included revised definitions and descriptions; additions; and deletions. The most extensive update was on spinal pain, where 96 new entries replaced all previous entries on neck, back, and other spinal pain. The new items covered spinal pain attributable to tumor, infection, metabolic disease, and arthritis. Perhaps the most comprehensive change was the introduction of the rubric "spinal pain of unknown origin." The 1994 version comprised an introductory section in which the terms used to describe pain were defined and its forms and associated clinical features were listed. The longer section listed possible diagnoses, with criteria for the diagnosis stipulated. The entries were listed according to bodily region.[47]

The IASP's pain taxonomy and chronic pain classification system were critical to the clinical and epistemological claims that the organization made. The IASP sought to strengthen its legitimacy through an inclusive development and revision process. The IASP offered a working set of definitions and a system that encouraged input from an expanding pain network. Wide acceptance of the IASP definition of pain has furthered a notion of an elemental inseparability of personal and psychological dimensions in the pain experience. The taxonomy projects demarcated the field, coordinated feedback, incorporated clinical and research findings, and established the IASP as a definitive source of fundamental articulations of a new concept of pain.

Looked at more broadly, the organization's growth between 1973 and 1981 showed the strength of its concept, the good fortune of its timing, and the impact of strong leadership. In publications, meetings, working groups, task forces, standing committees, national chapters, and liaison with other medical groups, government agencies, regulators, and industry, the IASP operationalized a

46. *Pain*, Volume 24, Supplement 1 (1986): S4, S6; Harold Merskey, "Terms and Taxonomy: Paper Tools at the Cutting Edge of Study," in *Paths of Pain*, Merskey, Loeser, and Dubner, ed., 329-337.
47. *Pain*, Volume 32, Supplement 1 (1994): _____.

concept of chronic pain as an urgent and complex clinical challenge. By stressing critical differences between acute and chronic pain, the IASP led a refashioning of the understanding of pain across medical and scientific disciplines.

**Pain as a Specialty -- Ratifying the Challenge**

An important driver and reflection of pain's organizational refashioning was the establishment of a recognized sub-specialty in pain medicine by the AMA. After 1983, pain medicine became a specialty organized around a concept of pain as the primary illness, a multifaceted, discrete condition that encompassed bodily, affective, spiritual, and socioeconomic dimensions. The specialty has emphasized ongoing management of chronic pain that is viewed as a complex human experience.[48]

The creation of a specialty in pain medicine has ratified the model that the IASP articulated in several ways. It operationalized that model in establishing standards of training as well as measures of knowledge and skill. It achieved recognition of pain as a distinct entity within three specialties. The IASP paradigm favored multidisciplinary approaches to assessment and treatment, and worked to carve out a specialty analogously aspired to integrate the perspectives of numerous disciplines into a cohesive set of clinical tools, practices, and insights in order to tailor treatments to individuals. Efforts to create a specialty were also claims on autonomy for practitioners to make clinical judgments, devise treatment regimens, and work with other specialists. If the launch of the IASP can be seen as an effort to establish professional authority to define and characterize pain, the work to create a specialty was its counterpart in asserting claims of autonomy for diverse clinicians based on the IASP model. In its attempt to synthesize diverse viewpoints into a coherent discipline,

48. Rollin M. Gallagher and Scott M. Fishman, "Pain Medicine: History, Emergence as a Medical Specialty, and Evolution of the Multidisciplinary Approach," in *Neural Blocks in Clinical Anesthesia and Pain Medicine, Fourth Edition*, ed. Michael Cousins et al. (Philadelphia: Wolters Kluwer/Lippincott William & Wilkins, 2009): 633-639; Michel Y. Dubois and Kenneth A. Follett, "Pain Medicine: The Case for an Independent Medical Specialty and Training Programs," *Academic Medicine*, Vol. 89, No. 6 (June 2014): 863-868.

pain medicine's evolution has been broadly comparable to how emergency medicine as well as physical medicine and rehabilitation developed. In 2016 the knowledge base and skill set for pain medicine are established by the American Board of Pain Medicine and the US Accreditation Council for Graduate Medical Education's Committee on Fellowships.[49]

Since 1988 there have been two paths to, and versions of, accreditation in pain medicine in the United States – via the AMA or the American Academy of Pain Management. Establishment of a specialty over these two paths ratified claims on authority that the IASP made by demonstrating to the AMA's and other groups' standards that pain was a distinct clinical entity, a condition in its own right with recognizable patterns and attributes. The involvement of multiple specialty boards and paths to certification can be seen as agreement with a multidisciplinary model; a legacy of pain's familiarity in all medical disciplines but home in none; and recognition of pain's underlying clinical complexities.

The American Academy of Pain Management was launched in 1988 as an educational, credentialing, and advocacy group for diverse clinicians who practice pain management. The Academy has advanced what it terms an "integrative, patient-centered model" of care. In 1990 the group launched the General Credentialed Pain Practitioner (GCPP) program; by 2012 some 6,500 practitioners "from nearly all clinical disciplines" have become GCPPs. In 2012 the Academy introduced an Advanced Credential Pain Practitioner (ACPP) program to help meet a growing need for physicians to show regulators and patients that they were responsible and law-abiding dispensers of pain medicines. The ACPP requires passing a 200-question exam and a clinical evaluation or skills assessment using standardized patients. The Academy takes care to remind people that none of their offerings should be considered board certification. The Academy has

49. Gallagher and Fishman, "Pain Medicine," 633; Philip Lippe, "Conceptual Construct of the Specialty of Pain Medicine," *The Clinical Journal of Pain*, Volume 13(3) (September 1997): 183-185; Steven Feinberg, "The Pain Medicine Specialist as a Physician-Healer," *The Clinical Journal of Pain*, Vol. 12(1) (March 1996): 3-5.

more than 6,000 members with 57 percent of these physicians. There are three levels of certification: diplomates have Ph.D. and at least two years clinical work; master's and same clinical experience are fellows; and bachelor's plus five years clinical experience are associates.[50]

While the American Academy of Pain Management's certification programs have engaged non-physicians, the AMA's establishment of a sub-specialty by three boards -- Neurology and Psychiatry, Physical Medicine, and Anesthesiology -- and their collaboration in setting standards and procedures have enabled licensed physicians to become board-certified in pain. The three member boards of the American Board of Medical Specialties (ABMS) have implemented a single set of credentialing criteria, and the pain medicine test for all three is the same. The current certification exam consists of 200 questions to be done in half a day. Starting in 2004, candidates for sub-certification were required to complete 12 months of pain management fellowship training. A committee of the American Society of Regional Anesthesia (ASRA) published a listing of anesthesiology-based fellowships (post-residency); found in 1999-2000 97 programs in anesthesiology for 292 positions; neurology/neurosurgery had 13 programs for 29 positions, and physiatry had 6 programs for 13 positions.[51]

The first stirrings on the road to certification in pain medicine in the American Medical Association began in 1983, when the American Academy of Pain Medicine was founded as the first physician group focused on pain medicine as a specialty. Since 1988 the American Academy of Pain Medicine has been a fully accredited member in the AMA House of Delegates. In 1989, specialty boards of the American Medical Association began to develop certification requirements and processes for physicians to be certified in pain medicine. In that year the American Board of

---

50. "Credential in Pain Management Program," American Academy of Pain Management at www.aapainmanage.org, accessed 11-18-15; John Burns, "Pain group certified without exam," *Modern Healthcare* (Nov. 22, 1993), .

51. Honghui Feng and Howard S. Smith, "Certification in Pain Medicine," in Warfield and Bajwa, *Pain Management*, 838-840; Robin J. Hamill-Ruth, President of the American Board of Pain Medicine, "Open Letter to all ABPM Diplomates," from www.abpm.org/uploads/files/openletter.pdf, accessed 9-22-15.

Anesthesiology (ABA) notified the American Board of Medical Specialties (ABMS) of its intent to offer such certification. The ABMS suggested that the ABA contact other specialty boards to gauge their interest in doing the same.[52]

The 1990s were the launch decade for the new specialty. Fittingly, it was within anesthesiology that pain medicine was first designated as a specialty. In 1991 the American Board of Anesthesiology offered its first exam for qualification in pain management. In 1993 the ABPM created board certification in pain medicine to enable board-certified anesthesiologists, neurologists, neurosurgeons, psychiatrists, and physical medicine/rehabilitation specialists to become board certified following credentialing and examination. In that same year the American Academy of Pain Medicine gained a seat as a separate medical specialty in the AMA. In 1998 the American Board of Physical Rehabilitation (ABPM&R) and the American Board of Psychiatry and Neurology (ABPN) submitted a joint proposal to offer their certification in pain management, and their first was issued in 2001.[53]

Since 2000, requirements for training in pain medicine have expanded and training opportunities have grown as well. In 2000 the American Board of Psychiatry and Neurology (ABPN) and American Board of Physical Medicine and Rehabilitation (ABPMR) applied to be able to issue subspecialty certificates in pain management. Residency and fellowship requirements for pain medicine have been developed conjointly by the AAPM and ABPM, which have also made recommendations to the ACGME. In 2001 the ABMS proposed a curriculum for 2- and 3-year primary residencies in pain medicine, called Essentials of Accredited Training Programs in Graduate Medical Education: Institutional and Program Requirements for Pain Medicine Training Programs. In 2006 the ACGME approved new standards for pain management fellowships that

52. Gallagher and Fishman, "Pain Medicine," 638-9.
53. Gallagher and Fishman, "Pain Medicine," 639; Dubois and Follett, "Pain Medicine," 864, 866; Lippe, "Conceptual Construct," 183; Feng and Smith, "Certification in Pain Medicine," 838-840.]

require multispecialty faculty (anesthesiology, neurology, physiatry, and psychiatry) beginning in 2007.[54]

The emergence of pain medicine as a recognized sub-specialty has ratified pain as a distinct clinical entity and focus of practice. At the same time, the forms of that emergence have retained elements of pain's historical ambiguity within medical practice. Establishment of the specialty within multiple certifying boards has shown that the description of pain as "familiar in many disciplines but at home in none" has retained salience. The existence of dual paths to certification, with one for physicians only and the other for clinicians of many kinds, has been both a triumph of the IASP multidisciplinary model and an affirmation of pain's poor fit with a biomedical model. At the same time, pain's "arrival" as a sub-specialty has not led to increased focus on pain in medical training. An Institute of Medicine report in 2011 described pre-professional education in pain as extremely limited and asserted that many primary care clinicians felt unprepared to manage pain. A Canadian study showed that (in 2007) the average number of teaching hours devoted to pain in medical school was 15. In dental school the number was 16, pharmacy training averaged 13 hours. The numbers were higher in education for nursing, occupational therapy, and physical therapy, where a focus on pain averaged 31, 28, and 41 hours respectively. Reflecting the continued importance of animal studies in pain research, as well as the political salience of animal rights and ethical limitations on pain research in humans, the study found that veterinary schools averaged 87 hours across the curriculum. Even as it recognized progress in the understanding and treatment of pain, the IOM report expressed the view that efforts to address the United States' "enormous burden" of pain will require a "cultural transformation" in how clinicians understand, assess, and

54. Gallagher and Fishman, "Pain Medicine," John L. Quintner, Milton L. Cohen, David Buchanan, James D. Katz, and Owen D. Williamson, "Pain Medicine and Its Models: Helping or Hindering?" *Pain Medicine*, Volume 9, Number 7 (2008): 824-834.

treat pain. As a sub-specialty and the focus of very limited time in medical training, the IASP model of pain and its practice in clinical medicine remain in productive, yet still formative, tension.[55]

55. Institute of Medicine, *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research* (Washington, DC: National Academies Press, 2011); Patricia Morley-Forster and Jolanta Karpinski, "Pain Medicine: A New Credential in Canada," *Pain Medicine* 16 (2015): 1038-1044.

## Conclusion

By 1993, when the first pain-medicine specialists were certified by the American Board of Anesthesiology, decades of change had refashioned pain's clinical status. Forty years earlier, Bonica's *Management of Pain* had delineated a nascent field and challenged the medical profession to rethink pain. In 1993 it had been 36 years since Darvon appeared on the U.S. market, 28 years since publication of Melzack and Wall's gate control theory (GCT); two decades since the founding of the International Association for the Study of Pain (IASP), and 18 years since the McGill Pain Questionnaire (MPQ) was introduced.[1]

*A Disease Itself* began with a question: If, as pain researcher Sean McKay asserted in 2013, Descartes' model of pain had been shown to be so defective, what accounted for more than 300 years of its dominance in medicine? Part of the answer is the Cartesian model's depiction of pain as rooted in biology and not in the workings of the divine. This was a conceptual departure that, if not wholly original, became a defining statement, gave impetus to the gradual secularization of pain, and was interpreted to fit comfortably within a biomedical model of disease. A biomedical paradigm privileged direct links between organic causes and clinical effects as well as the diagnostic value of recurring patterns of intensity, duration, and presentation in the courses of disease and injury. This concept in fact matched many forms of acute pain, relegated psychological factors in pain to irrelevance, and, in maximizing pain's addressability by equating it with chronic pain, became a conceptual framework within which pain had been marginalized, clinically and organizationally, within the medical profession by 1945.

---

1. Bonica, *Management of Pain*, x-xiv. Professional and personal connections joined all four events and activities in a growing, global pain field after World War II. As with the history of anesthesiology, what started as individual pursuits of a small group of clinicians became a substantial, self-aware medical field across the 20th century. See John J. Bonica, *The Management of Pain* (Philadelphia: Lea and Fibiger, 1953); Melzack and Wall, "A new theory of pain," 277-299.

By 1945, this marginality was predicated on several widely perceived attributes of pain. First was its enduring quandaries, including phantom-limb pain, headache, and the existence of pain in the absence of injury or illness. Pain was familiar in many specialties but "home" in none, an organizational limbo that impeded understanding of pain as a medical challenge in its own right. Pain had, with much justification, been apprehended widely as a symptom of, and accompaniment to, many conditions. Clinicians had long noted pain's variability, including diverse responses to comparable pharmaceutical regimens even when people had the "same" medical issues. Pain had historically been neglected in medical training; in 2014, journalist Judith Foreman found four medical schools in the United States that offered a course on pain. Success in treating acute pain had worked against the salience and urgency of chronic pain, as a procession of new pain relievers after 1900 had expanded options for combatting pain's diversity. These attributes shaped an entrenched concept of pain among mid-century clinicians as marginal on the merits. At mid-century, pain was largely perceived as simple, rote, symptomatic, understood, and increasingly treatable.[2]

My dissertation has shown how a fundamental transformation in the clinical status of pain was conceived, articulated, and operationalized in the five decades that followed the end of World War II. This shift displaced the Cartesian model and refashioned clinical pain as complex, chronic, variable, and decisively subjective. The new model was premised on the inseparability of physiology and psychology in the experience of pain as well as the value of multidisciplinary and alternative treatment regimens. The change was driven by and reflected in the professionalization of pain, which took two main forms: the 1973 establishment of a scientific society, the IASP, focused on the study and treatment of pain, and the recognition of pain medicine in 1993 as an official sub-specialty within American medicine. Advances in pain measurement, management, and organizational structure revised pain's marginality by promoting an inclusive model of pain, by

2. Foreman, *A Nation in Pain*, 5.

showing the capabilities of alternative and multidisciplinary treatments, and by providing global venues (e.g., publications, meetings) in which new ideas about pain were developed, debated, refined, and tested.

*A Disease Itself* has described how bodily pain became a complex, decisively personal amalgam of organic conditions, personal history, cognitive and emotional influences, and individual circumstances. The shift changed how people experienced pain, how healers treated it, the dynamics between patients and clinicians, legislative actions, and the fortunes of pharmaceutical companies. After the middle of the twentieth century, a long-simmering challenge to a dominant model of pain, given direction by the gate-control theory of pain (1965), promoted pain and its treatment as a distinct clinical specialty and an urgent, cross-disciplinary professional focus defined by fundamental subjectivity. After 1945, the MPQ operationalized; Darvon embodied; and the IASP coordinated a shift in dominance between these two models of pain's origins, nature, and treatment.[3]

The eclipse of a dominant model of pain was more than an event within medicine and science. It reflected substantial cultural turmoil around ideas and practices of identity, selfhood, authority, and autonomy. After 1945, insurgent ideas about pain drew on wider cultural currents that contested prevailing ideas about selfhood, identity, authority, and individual autonomy. Previously robust sources of authority in many professions, including medicine, became objects of disfavor and cynicism. The ascent of a revised model of pain as variable and subjective benefited from cultural turmoil in which new forms of individuality, identity formation, and personal autonomy found expression in the growth of alternative and increasingly customized pain-treatment regimens. A

3. Professional and personal connections joined all four events and activities in a growing, global pain field after World War II. As with the history of anesthesiology, what started as individual pursuits of a small group of clinicians became a substantial, self-aware medical field across the 20th century. See Melzack and Wall, "A new theory of pain," 277-299; *Oral History Interview with Michael J. Cousins,* 19 October 1997 (Ms. Coll. No. 127.10), John C. Liebeskind History of Pain Collection, History & Special Collections for the Sciences, UCLA Library Special Collections, 23-29, 31-35; *Patrick D. Wall,* UCLA History of Pain Collection, 37-43; Bourke, *Story of Pain,* 10-12, 290-302.

broad, fundamental challenge to established authority on diverse professional and political fronts helped new concepts of pain and its relief look plausible and exciting. A concept of the individual as in possession of distinctive abilities to understand and react to medical events in his or her life bore particularly on pain and how to manage it.[4]

As part of a belief in the shortcomings of medicine's engagement with pain, the challenge to a prevailing model included an ethical dimension. For Bonica and others, marginalization and neglect of pain, for whatever reasons, was a moral failure that haunted the heart of the profession, an abdication of a fundamental duty, a denial of patients' most frequent complaint to doctors. Early leaders of the IASP saw the treatment of pain as essential to medical practice. They believed that refocusing clinical attention on chronic pain hardly marginalized the acute form; in their view it elevated the status of acute and transient pain by making it distinct. Dissenters from a prevailing pain orthodoxy believed that ongoing vigilance on acute pain was called for, among other reasons, because there was evidence that poorly treated acute pain could become chronic pain. Pain relief should be among the most developed skills among clinicians; it was inhumane to favor pharmaceuticals exclusively or excessively when combined therapies had proven their usefulness. Finally, the continued non- or under-treatment of pain, often motivated by fear of producing addiction, could become inhumane if prolonged. The ethical dimension of pain's neglect was a muted but distinct feature of a broader challenge to pain orthodoxy.[5]

---

4. Keith Wailoo captured this dimension of the success of the gate control theory. In 2014 he wondered whether and how the gate control theory's often-praised inclusiveness also had allowed it to be all things to all people, too unstructured to deliver rigorous insight. In this openness Wailoo detected an emblematic marker of its time. Wailoo, *Pain: A Political History*, 77-86; Jessica Grogan, *Encountering America: Humanistic psychology, Sixties Culture and the Shaping of the Modern Self* (New York: Harper Perennial, 2012), 27-29, 37, 53-58, 118, 318; Michael E. Staub. *Madness is Civilization: When the Diagnosis Was Social, 1948-1980* (Chicago: The University of Chicago Press, 2011), 37, citing Ernest Havermann, "The Age of Psychology in the U.S.," *Life,* January 7, 1957, 37, 68, 72.

5. The moral stance, implicit and expressed, in challenging a prevailing model of pain has only begun to be explored by historians. See Loeser, "Pain Musings," _____; Reynolds, L. A. and E. M. Tansey, ed., Innovation in Pain Management Wellcome Seminar, 13-22, 60-64.

A challenge on pain had not sprung full-blown from a post-war American setting. There had been dissenters and skeptics about received wisdom and divergent views on pain for as long as healers had debated the topic. *A Disease Itself* has argued that scientific and, professional developments, as well as wartime experiences of key clinicians, had created important preconditions for a shift in the status and understanding of pain. But controversies and debates that had started millennia ago sometimes had a familiar ring. Controversies in classical Greece and Rome remained comprehensible to contemporary students because philosophers and healers in those societies had delineated enduring questions about pain's nature and workings. Was it a sensation or an emotion? What were the roles of different bodily systems and organs? How was pain tied to perception, awareness, mind/body interaction, and the creation of meaning?

The dissertation's pre-histories sketched how developments in neurophysiology prepared the scientific ground for pain as complex and individual; how the evolution of anesthesiology as a specialty after 1900 both broadened clinicians' involvement with pain management and addressed the definition and scope of a medical specialty focused on pain; how the experiences of William Livingston, Henry Beecher, and John Bonica during World War II forged their determination to promote a revised model of and clinical engagement with pain; and how a research partnership among the federal government, academia, and pharmaceutical companies, launched in 1929, had studied the biochemical and pharmacological roots and processes of pain relief and addiction through an extensive study of morphine. This endeavor helped create and populate a growing commercial search for pain relief, forged professional networks among academia and industry, led to the creation of new therapies based on an increased understanding of morphine's structural and functional attributes.

Together these pre-histories described conditions under which a global, self-directed, scientific, and organizational challenge to pain's marginality developed. The neurophysiological foundations

of pain's complexity were based on the involvement of numerous brain sectors and areas of the spinal cord as well as electrochemical mechanisms in which responses to pain were encoded, compressed, manipulated, and reassembled as perception. Studies in anatomy and physiology that accelerated after 1800 began to reveal underlying structures and processes involved in pain. These became precursors to greater understanding of the body's multiple modulations of painful impulses. This in turn created scientific grounding for pain as complex and for inseparability of physical and psychological elements. Research confounded a concept of pain as simple and readily explained.[6]

It was fitting that the first board of the American Medical Association (AMA) to establish certification in pain management was in anesthesiology. The history of anesthesiology's emergence as a clinical discipline was a critical pre-story to the transformation of pain. More than any other specialty, anesthesiology had addressed clinical and organizational issues that involved pain as a core focus. It was within anesthesiology that a decisive reconceptualization of pain originated, as advances in nerve block and surgical techniques both expanded the ability of anesthesiologists to manage pre- and post-surgical pain while revealing the limits of such methods in managing chronic pain. After about 1920, anesthesiologists' ongoing battle for professional standing with surgeons (and in opposition to nurse anesthesiologists) had involved growing engagement with pain management. At the same time, new chemical agents and techniques in anesthesiology, along with perceived clinical opportunities in pre- and post-operative pain, spurred the growth of competing anesthesiology groups. By 1940 the American Board of Anesthesiology [ABA] had been recognized by the AMA as a specialty board. More than 70 years before the ABA approved plans for

6. Keele, *Anatomies,* 102-131; Bourke, *Story of Pain*, 10, 95-96; Rey, *History of Pain*, 132-242; Liebeskind, John C., and Linda A. Paul, "Psychological and Physiological Mechanisms of Pain." *Annual Review of Psychology* 28:1 (1977): 41-60.

certification in pain, anesthesiologists had begun to address questions about how to define and establish a new specialty in which pain featured prominently.[7]

Beginning in 1929, a collaboration among the federal government, philanthropic organizations, pharmaceutical companies, and academic institutions set a goal of understanding the biochemical origins and workings of morphine's (and its derivatives') analgesic and addictive properties. The original impetus for the effort had been to address addiction as a social problem. These efforts were focused in laboratories at the universities of Michigan and Virginia, which worked with the Addiction Research Center (ARC) at the Lexington, Kentucky federal narcotics prison that had opened in 1935. A network of scientists and prisoners investigated dozens of existing and prospective compounds in ways that helped create the scientific, commercial, and organizational foundations of pain as a discrete medical entity, the cultivation of a growing pain "market" by pharmaceutical companies, and institutional structures in which diverse ideas about pain could be developed and refined.[8]

The wartime experiences of three clinicians were pivotal in demonstrating the diversity of pain conditions, the influence of circumstances on organic conditions, and the basis for a challenge to what they had been taught about pain in their medical training. After the war Livingston, Beecher, and Bonica developed strong ties to organizations and certifying boards in anesthesiology, surgery, and neurology as well as to academic departments in these fields. Those ties contributed to the growth of the IASP and to the establishment of certification programs in pain medicine by three of the AMA's 24 specialty sections – Neurology and Psychiatry, Physical Medicine and Rehabilitation,

---

7. The history of anesthesiology as a specialty prefigured the later development of pain management as a recognized discipline by the American Medical Association. Anesthesiology may have been less global in the first decades of the twentieth century than the IASP would be in its launch in the 1970s. M. Swerdlow, M. D. Mehta, and S. Lipton, "The role of the anesthetist in chronic pain management," *Anaesthesia*, 1978, Volume 33, 250-257; Douglas R. Bacon, "Gaston Labat, John Lundy, Emery Rovenstine, and the Mayo Clinic: The spread of Regional Anesthesia in America Between the World Wars," *Journal of Clinical Anesthesia* 14:315-320, 2002.
8. Campbell, *Discovering Addiction*, 68-187; Acker, "Planning and Serendipity," 139-157; Acker, "Addiction and the Laboratory," 167-193.

and Anesthesiology. Bonica provided conceptual and organizational direction, based in part on his experiences with anesthesiology groups, and the three clinicians raised important and difficult questions about how pain medicine might be organized and how a multidisciplinary approach to pain could be given an organizational or institutional structure.[9]

The dissertation's case studies showed how an insurgent model took shape and was implemented after 1945. It has contended that the MPQ operationalized, Darvon reflected, and the IASP organized a challenge to pain's marginality, and that the impacts of all three were both accretive and mutually reinforcing. Individually and together, the activities and events that "surrounded" the MPQ, Darvon, and the IASP -- scientific and clinical, governmental, and global -- advanced an insurgent concept of pain and unseated a model that had prevailed for three centuries.

How did changes in measuring pain contribute to, and embody, this more fundamental shift after 1945? While the MPQ was not the only pain measurement tool that sought to help patients articulate what pain felt like and how it was affecting them, its long career, its ties to the gate control theory, and its attempt to meld the physiological and psychological components of pain – sensation and affect – into one assessment device made the MPQ a microcosm of larger changes in pain measurement. The MPQ succeeded through the reputation of the author, the questions it asked, the categories it used, and assumptions it made about what contributed to formation of a pain experience. The numerical weighting of patient input in the MPQ sought to make pain intensity a clinically useful proxy for the pain experience. But its innovation and wide deployment did not make the MPQ a universal method or tool that reliably crossed disciplines and conditions readily and successfully. After 1975, the MPQ spurred the growth of pain measurement in

9. Beecher, Henry K., "The Measurement of Pain: Prototype for the Quantitative Study of Subjective Responses," *Pharmacological Reviews* 9:1 (1957): 59-209; Bonica, John J., "Pain research and therapy: past and current status and future needs," In *Pain, Discomfort and Humanitarian Care*, edited by L. K. Y. Ng and John J. Bonica, 1-46. New York: Elsevier-North Holland, 1980;
Bonica, John J. "Evolution and Current Status of Pain Programs." Journal of Pain and Symptom Management, Vol. 5, No. 6 (December 1990): 368-374.

evaluating pain relievers and in assessing how patients presented and reported on their pain. Shortcomings in measurement, whether structural or operational, themselves suggested the salience of qualitative and affective dimensions. The failures of measurement methods to provide a clinically robust tool opened a conceptual door to elements of pain as beyond measurement. The inability of the MPQ, or any other tool, to achieve anything close to universality supported a notion of pain as variable and individual. Different pain measurement methods were developed and used for different conditions. such as back pain or headache.[10]

What did Darvon's clinical ambiguity reveal about wider debates over pain and how to treat it? A combination of Darvon's pervasiveness and variability in the responses it evoked itself communicated a concept pain as personal and circumstantial. The ambiguity of Darvon mirrored more than the diversity of conditions against which it was deployed, in billions of doses, after 1957. It showed the fluidity of conditions, pain intensities, side effects, and therapeutic effectiveness. In controversies over its standalone effectiveness and safety from its earliest days, and the ambiguity it showed in both with equal tenacity, Darvon displayed how many forms pain could take. Darvon achieved consistent commercial success in the face of murky standalone capabilities either as an analgesic or as an agent of addiction; it had narcotic elements but didn't require a narcotic prescription until 1973. Darvon enabled people to inscribe their experiences on it in ways that other analgesics didn't. It was seen as a low-reward, low-risk pain reliever. Unlike virtually all other pain relievers, Darvon has had a scant history as a drug of abuse.

10. Ronald Melzack, "The McGill pain questionnaire: major properties and scoring methods," Pain 1 (1975): 277-299; Kenneth A. Holroyd et al., "A multi-center evaluation of the McGill Pain Questionnaire: results from more than 1700 chronic pain patients," Pain, 48 (1992) 301-311; Ronald Melzack and Joel Katz, "Pain Measurement in Adult Patients," 305-314 in Stephen McMahon, Irene Tracey, and Dennis C. Turk, ed., *Melzack and Wall's Textbook of Pain, Sixth Edition* (New York: Elsevier, 2013), 305-314; Melzack and Wall, *Textbook of Pain*, 39-42, 260, 276, 278-279; Baszanger, *Inventing Pain Medicine*, 52. Journalistic accounts of pain's post-1945 emergence as a discrete medical syndrome include Judy Foreman. *A Nation in Pain: Solving America's Biggest Public Health Problem* (Oxford: Oxford University Press, 2014; Jean E. Jackson. *"Camp Pain:" Talking with Chronic Pain Patients* (Philadelphia: University of Pennsylvania Press, 2000).

Eight years after publication of the gate control theory, and simultaneous with publication of findings on endogenous pain-management systems, the IASP coordinated a global challenge to a dominant paradigm of pain by working to build a scientific society based on an insurgent model. The IASP was a multidisciplinary organization that aggressively sought to expand the number and range of medical and scientific disciplines were represented in its membership. In its publications, meetings, pain taxonomies, interactions with governments and the United Nations, the IASP developed an institutional "home" for pain that ended its historical limbo and institutionally embodied chronic pain as a distinct medical condition. The IASP expanded the networks that the 1929 research collaboration and the growth of anesthesiology as a specialty had put into motion.

After 1993, the growth of pain medicine as a specialty would extend and ratify the rise of a formerly outcast conception of pain. Pain became a recognized sub-specialty by three AMA specialty boards between 1993 and 2006, with perhaps 9-10,000 clinicians currently certified. Through the American Academy of Pain Management, founded in 1983, non-board certification had been available to licensed physicians as well as scientists and researchers in many disciplines. The existence of pain management clinics, departments, and programs in the United States by 2010 attested to the triumph of multidisciplinary treatment approaches. By 2014, some 70 journals and 30 pain organizations, including the IASP at nearly 7,000 members in 130 countries, suggested the reach of professional and scientific global networks in the pain field. By the early years of the twenty-first century, pain had become a full-fledged specialty.[11]

The histories of the case studies in *A Disease Itself* have continued to unfold and to reflect the intractability of debates and paradoxes in the understanding and treatment of pain. In late 2010 the FDA announced that manufacturers had agreed to a phased withdrawal of propoxyphene

11. DuBois and Follett, "Pain Medicine," 863-866; Philip Lippe, "Conceptual Construct of the Specialty of Pain Medicine," *The Clinical Journal of Pain* Volume 13(3) (September 1997): 183-185; Gallagher and Fishman, "Pain Medicine," 633-639.

products from the United States market, the same decision European regulators had reached in 2005. In announcing their action the FDA acknowledged the ambiguity of the research, both current and past, and the variability of the effects of Darvon on patients. The terms in which the decision was announced showed that Darvon's clinical and social ambiguity would span its entire career. In 2014 the president of the American Academy of Pain Management -- the group that has certified clinicians of diverse specialties in pain management since the early 1990s -- noted that debates over clinicians' deployment of opioids; the training and skills needed to practice pain management; and political concerns over an opiate "epidemic" showed that the status of pain management as a discipline, and the professional standing of practitioners, remained contested. In 2014 IASP had close to 7,000 members who represented more than 130 countries; there were 20 special-interest groups, the journal *Pain* was in its 40th year of continuous publication, world congresses were well attended. The MPQ's use has dropped off substantially since the 1990s, when managed care plans ratcheted up time pressures on many physicians. The ability to spend the time that the MPQ required to learn about a patient's pain experience and history has become an enviable and long-vanished ideal to many practitioners.[12]

But changes in the commercial, scientific, and cultural fortunes of the MPQ, Darvon, and the IASP have left ineradicable tracks across the history of pain. Their trajectories differed, but they all advanced a concept of pain that Livingston, Bonica, and others had begun to grasp and articulate in after 1945. In this view pain was irreducibly complex and personal, not just influenced by individual traits and histories but decisively shaped by them. The activities and events captured in the dissertation's case studies promoted a concept of pain as deeply psychological and contingent. The MPQ and the work of the IASP incorporated and sought to reconcile findings in the neurophysiology of pain with behavioral and cognitive perspectives. The MPQ, as well as Darvon's

12. Hammill-Ruth, Robin J., "Open Letter to all ABPM Diplomates," from www.abpm.org/uploads/files/openletter.pdf, accessed 9-22-15; Fernando Cervero, "IASP 2014 Annual Report."

variable effects, brought patient input and individual factors to new prominence in clinical assessment. Proponents of an insurgent concept of pain attributed crucial significance to such factors while believing that they could be quantified in clinically useful ways. .

Changes in measurement, management, and professional organization thus facilitated and reflected a fundamental shift in the core identity and clinical status of pain. The ascent of the model was not total, as the dominance of the prior model had not been, but by 2016 a concept of pain as fundamentally complex was as entrenched in medicine and culture to a degree that matched the level of dominance that a former model had once enjoyed. In unseating a Cartesian paradigm and establishing a fundamental subjectivity in the experience of pain, an insurgent model both elevated the significance of the individual and raised fresh questions about what such subjectivity meant and entailed. How did a particular mix of personal history, attitudes, beliefs, and organic conditions find expression and form in different ways among different people? Was pain infinitely variable, or did that concept too harshly dismiss recognized patterns in pain associated with specific injuries, illnesses, and procedures? In becoming fundamentally subjective, pain and its treatment have been individualized in ways that embody new concepts of identity and selfhood. In this they have embodied contests over the sources and nature of medical expertise and authority that took shape after World War II. By the 1970s, distrust and skepticism about institutions, public actors, and the integrity of legally constituted authority encouraged people to look within for new sources of authority. The grounding of pain in subjectivity, the triumph of an insurgent concept of pain, has led to a shift in the locus of decisive authority from social and institutional centers to private experience, perception, and judgment. The individual has become a more critical and authoritative social actor, a new standard against which ascendant professional and cultural expertise was increasingly measured. Pain has been privatized.

*A Disease Itself* has traced how the understanding of pain was fundamentally transformed after 1945. A larger historical arc within which this change took place can be described as encompassing the evolution of pain from secular to scientific to subjective. A hypothetical "next" chapter of *A Disease Itself* would explore the forms and meanings of this subjectivity, both in individuals and in the clinical assessment and management of pain. It would look at the growing molecularization of pain, the search for ultimate, irreducible units in the individuality of genetic inheritance and operations, and how this has affected, altered, or undermined the shift that the dissertation has traced. Molecularization and geneticization can be seen as epistemological and scientific outgrowths of concepts of individuality and subjectivity. At bottom, further exploration of the paths of the dissertation would engage with the full variability of pain, the many-headed clinical reality of nearly endless forms and varieties. Descartes may have oversimplified the physiological mechanisms of the body's responses to noxious stimuli. But in nudging the understanding of pain beyond the spiritual realm and grounding it in biology, Descartes had set the understanding of pain on a course that led to its subjectification in ways that continue to evolve.[13]

13. John G. Cawelti. *Apostles of the Self-made Man: Changing Concepts of Success in America* (Chicago: The University of Chicago Press, 1965), 2, 12, 73, 202. The book examines changes in the meaning and interpretations of the self-made man as a constant in American history. In American people began to think of themselves "not as members of a traditionally defined group with an established social role but as individuals with the capacity to choose between social roles, or create new ones; finally, it meant that the individual was no longer given an identity by birth, but that he had to create one for himself." "As Weber demonstrates, the major Protestant creeds and the ethos of middle-class enterprise emphasized an individualistic spirit, the diligent pursuit of a calling, self-discipline, and temperance." Cawelti described President Abraham Lincoln as the nation's ultimate epic of self-development, and Ralph Waldo Emerson as its greatest philosopher. "David Riesman's 'other-directed' character type, Whyte's 'organization man,' Packard's ' status seeker,' and Mills's 'new middle class' offered in common the observation that Americans no longer danced to the tune of individualistic achievement."

# BIBLIOGRAPHY

Primary sources for *A Disease Itself* comprised the records of federal agencies (Food and Drug Administration; Department of Health, Education, and Welfare; Drug Enforcement Administration) pertaining to reviews and decision-making on Darvon between 1957 and 1980. In addition, organizational records of the International Association for the Study of Pain and documents generated by early leaders and members were crucial to Chapter 4. These sources were bolstered by an extensive clinical literature on propoxyphene and related substances; abundant studies on clinical applications of the McGill Pain Questionnaire and other pain assessment tools after 1975; and a wide, cross-disciplinary literature on social, cultural, and existential issues related to the experience and history of pain.

The UCLA *History of Pain Collection* is part of the History and Special Collections Division at the Louise M. Darling Biomedical Library at the University of California, Los Angeles. It includes archival records of the International Association for the Study of Pain, the American Pain Society, founded in 1977 as the U.S. chapter of the IASP, and the American Academy of Pain Management (1988-1997). It includes the personal papers of anesthesiologist and IASP founder John Bonica, surgeon William K. Livingston, and surgeon Willem Noordenbos, as well as more than 40 oral history interviews with clinicians and researchers and a range of journals and bibliographies related to the history of pain.

The Wood Library-Museum of Anesthesiology is housed at the American Society of Anesthesiology in Park Ridge, Illinois. The Library-Museum focuses on the science, art, and history

of anesthesia. It includes manuscripts, membership lists, organization records, legal documents, newsletters, legal documents and other items related to the history of anesthesiology. It houses the records of John Bonica's presidency of the World Federation of Societies of Anesthesiologists (1963-1968).

The Arthur E. Guedel Memorial Anesthesia Center at UC-San Francisco opened in its current location in 1970 at the former San Francisco site of the Stanford-Lane Medical School. It is named for an anesthesiologist whose contributions to clinical anesthesia were significant. He identified key signs of anesthetic effects and became known as the "motorcycle anesthetist" in France during World War I. The Guedel Center houses the papers of Dr. Chauncey Leake, UC-SF Professor of Anesthesiology; the papers and correspondence of other early leaders in anesthesiology, including Ralph Waters; rare books on the history and development of anesthesia; and historical artifacts.

## PRIMARY SOURCES


Bonica, John, Editorial, "The Need of a Taxonomy," and "Pain Terms: A List With Definitions and Notes on Usage, as Recommended by the IASP Subcommittee on Taxonomy.); Pain, 6 (1979): 247-263.

Burrows, E. A., Regulatory Affairs Associate, Eli Lilly & Company, letter to Ronald Kartzinel on propoxyphene preparations, November 22, 1978.

Califano, Joseph A., "Statement by Joseph A. Califano, Jr., Secretary of Health, Education and Welfare," February 15, 1979.

Califano, Joseph A., "United States Department of Health, Education and Welfare, Office of the Secretary, In re: Petition to Suspend New Drug Applications for Propoxyphene, Order of the Secretary Denying Petition," February 15, 1979.

Califano, Joseph R., Health Research Group, February 28, 2006 petition and letter to Andrew von Eschenbach, Acting Commissioner, FDA.

Casey, Kenneth L., Oral History Interview with Kenneth L. Casey, 20-21 April 2000 (Ms. Coll. No. 127.53), John C. Liebeskind History of Pain Collection,, History & Special Collections for the Sciences, UCLA Library Special Collections.

Cooper, Theodore, "Scheduling Recommendations for Dextropropoxyphene," letter and memorandum to Peter Bensinger of the Drug Enforcement Administration, August 12, 1976.

Cousins, Michael. J., Oral History Interview with Michael J. Cousins, 19 October 1997 (Ms. Coll. No. 127.10), John C. Liebeskind History of Pain Collection, History & Special Collections for the Sciences, UCLA Library Special Collections.

Crout, J. Richard, "Memorandum of Telephone Conversation with Sidney Wolfe," December 15, 1978.

Crue, Benjamin L. Jr., Oral History Interview with Benjamin L. Crue, Jr., 9-10 May 1996 (Ms. Coll. No. 127.11), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Library Special Collections, Louise M. Darling Biomedical Library, University of California, Los Angeles.

Kartzinel, Ronald, Director, Division of Neuropharmacological Drug Products, "Evaluation of Propoxyphene – Action Memorandum," from Director, Division of Neuropharmacological Drug Products, Department of Health, Education, and Welfare, to Director, Bureau of Drugs, Department of Health, Education, and Welfare, January 15, 1979.

Federal Register, Volume 34, Number 6264, "Drugs for Human Use: Drug Efficacy Study Implementation," April 8, 1969.

Federal Register, Volume 42, Number 19, 8636, "Placement of Dextropropoxyphene in Schedule IV," February 11, 1977.

Foley, Kathleen, Oral History Interview with Kathleen Foley, 25 June 1996 (Ms. Coll. No. 127.14), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise B. Darling Biomedical Library, University of California, Los Angeles.

Hamill-Ruth, Robin J., "Open Letter to all ABPM Diplomates," from www.abpm.org/uploads/files/openletter.pdf, accessed 9-22-15.

Health Research Group, November 21, 1978, "Petition Requesting Transfer of the Narcotic Dextropropoxyphene (Darvon) and Its Salts from Controlled Substances Schedule IV to Schedule II," submitted to US Attorney General Griffin Bell and DEA Administrator Peter Bensinger;

Herr, E. B., Jr., letter to Joseph Califano, Secretary of Health, Education, and Welfare, December 13, 1978.

Jones, Louisa E., Oral History Interview with Louisa E. Jones, 11 July 1993 (Ms. Coll. No. 127.18), John C. Liebeskind History of Pain Collection, History & Special Collections for the Sciences, UCLA Library Special Collections.

Kartzinel, Ronald, Director, Division of Neuropharmacological Drug Products, "Phone request for additional information on propoxyphene use," to Commissioner, Food and Drug Administration, January 26, 1979.

Liebeskind, John C., Oral History Interview with John C. Liebeskind, 17-19 July 1995 (Ms. Coll. No. 127.21), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise M. Darling Biomedical Library, University of California, Los Angeles.

Eli Lilly and Company, "Preliminary Submission of Eli Lilly & Company Concerning the Health Research Group's Letter of November 21, 1978 to Secretary Califano," submitted December 28, 1978.

Loeser, John D., Oral History Interview with John D. Loeser, 12 July 1993 (Ms. Coll. No. 127.24), John C. Liebeskind History of Pain Collection, History & Special Collections for the Sciences, UCLA Library Special Collections.

Melzack, Ronald and Patrick D. Wall, "Pain mechanisms: a new theory," Science 150 (1965): 971-979.

Melzack, Ronald, "The McGill pain questionnaire: major properties and scoring methods," Pain 1:3 (1975): 277-99.

Merskey, Harold, ed., Thoughts and Findings on Pain: The Hebb-Bishop correspondence and a selection of papers. (Vancouver: The Canadian Pain Society and the American Pain Society. 1996).

Testimony to Monopoly and Anticompetitive Activities Subcommittee of the U.S. Senate Select Committee on Small Business, January 31-February 1, and February 5, 1979, by Sidney M. Wolfe, Charles G. Moertel, Arthur McBay, Larry V. Lewman, Page Hudson, Kenneth A. Durrin, William T. Beaver, Morris Boynoff, Micahel A. Newman, John Adriani, Donald Kennedy, Robert H. Furman, Bryan S. Finkle, and Louis Lasagna.

Morris, Louis, "Comments on Lilly's Second Quarterly Darvon Report Submitted to FDA January 24, 1980," February 5, 1980.

US Department of Commerce Report #981, 1946.

Memorandum from Judith K. Jones, Director of Drug Experience, Department of Health, Education, and Welfare, to Robert Wetherell, Edward melton, and Henry Dausch, Legislative Services, January 29, 1979.

Kennedy, Donald M., Commissioner of the Food and Drug Administration, letter to Sidney M. Wolfe, January 22, 1979.

Letter from Edward Press, State Public Health Officer, State of Oregon, to Edward C. Tocos, Chief, Drug Abuse Staff, Bureau of Drugs, Food and Drug Administration, November 28, 1978.

"Forensic Toxicology of Propoxyphene Fatalities," statement by Randall C. Baselt, Department of Pathology, University of California, Davis, to public hearing of the Food and Drug Administration, April 6, 1979.

Morris, Louis. Comments on Lilly's Second Quarterly Darvon Report Submitted to FDA January 24, 1980. February 5, 1980.

Rappaport, Bob A., Memorandum from FDA Center for Drug Evaluation and Research, to FDA Anesthetic and Life Support Drugs Advisory Committee, January 15, 2009.

Rheinstein, Peter H., Director, Division of Drug Advertising, Department of Health, Education, and Welfare, "The Popularity of Darvon – Promotion of Darvon as a Non-Narcotic," to Office of Legislative Services, Department of Health, Education, and Welfare, January 30, 1979.

Wall, Patrick D., Oral History Interview with Patrcik D. Wall, 10 August 1993 (Ms. Coll. No. 127.2), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise M. Darling Biomedical Library, University of California, Los Angeles.

Wolfe, Sidney M. and Public Citizen Health Research Group, "Petition Requesting Transfer of the Narcotic Dextrpropoxyphene (Darvon) and its Salts From Controlled Substances Schedule IV to Schedule II," to Griffin Bell, Attorney General, and Peter Bensinger, Department of Justice, November 21, 1978.

Wolfe, Sidney M. and Public Citizen Health Research Group, "Memo to Secretary Califano," November 22, 1978.

Wolfe, Sidney M., letter to Donald M. Kennedy, Commissioner, Food and Drug Administration, December 18, 1978.

Wolff, B. Berthold, Oral History Interview with B. Berthold Wolff, 5-6 November 1993 (Ms. Coll. No. 127.39), John C. Liebeskind History of Pain Collection, History & Special Collections Division, Louise B. Darling Biomedical Library, University of California, Los Angeles.

## SECONDARY SOURCES

Acker, Caroline Jean. "Planning and Serendipity in the Search for a Nonaddicting Opiate Analgesic," in *The Inside Story of Medicines: A Symposium*, edited by Gregory J. Higby and Elaine C. Stroud, 139-157. Madison: American Institute of the History of Pharmacy, 1997.

Acker, Caroline Jean. "Take as Directed: The Dilemmas of Regulating Addictive Analgesics and Other Psychoactive Drugs," in *Opioids and Pain Relief: A Historical Perspective. Progress in Pain Research and Management, Vol. 25*, edited by Marcia L. Meldrum, 35-55. Seattle: IASP Press, 2003.

Acker, Caroline Jean. "From All Purpose Anodyne to Marker of Deviance: Physicians' Attitudes Towards Opiates in the US From 1890 to 1940," in *Drugs and Narcotics in History*, edited by Roy Porter and Mikulas Teich, 114-132. Cambridge: Cambridge University Press, 1995.

Acker, Caroline Jean. *Creating the American Junkie: Addiction Research in the Classic Era of Narcotic Control*. Baltimore: Johns Hopkins University Press, 2002.

Acker, Caroline Jean. *Addiction and the Laboratory: The Work of the National Research Council's Committee on Drug Addiction, 1928-1939*. *Isis*, Vol. 86, No. 2 (June 1995): 167-193.

Angell, Marcia. *The Truth About Drug Companies: How They Deceive Us and What To Do About It*. New York: Random House, 2005.

Apple, Rima D. *Vitamania: Vitamins in American Culture*. New Brunswick, NJ: Rutgers University Press, 1996.

Arner, Staffan. "Opioids and long-lasting pain conditions: 25-year perspective on mechanism-based treatment strategies." *Pain Reviews* 7 (2000): 81-96.

Aronoff, Gerald M. *Pain Centers: A Revolution in Health Care*. New York: Raven Press, 1988.

Aronoff, Gerald M., Wayne O. Evans, and Pamela L. Enders, "A Review of Follow-Up Studies of Multidisciplinary Pain Units." *Pain* 16(1983): 1-11.

Avorn, Jerry. *Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs*. New York: Vintage Books, 2005.

Aydede, Murat, ed. *Pain: New Essays on Its Nature and the Methodology of Its Study*. Cambridge, MA: The MIT Press, 2005.

Bacon, Douglas R. "Gaston Labat, John Lundy, Emery Rovenstine, and the Mayo Clinic: The spread of Regional Anesthesia in America Between the World Wars." *Journal of Clinical Anesthesia* 14 (2002): 315-320.

Balkin, Jack M. "Nested Oppositions." *Faculty Scholarship Series*, paper 281 (1990): http://digitalcommons.lawyale.edu/fss_papers/281.

Balkin, J. M, *Cultural Software: A Theory of Ideology*. New Haven and London: Yale University Press, 1998.

Bakan, David. *Disease, Pain, Sacrifice*. Chicago: U. of Chicago Press, 1968.

Banning, A, P. Sjogren, and H. Henriksen, "Pain causes in 200 patients referred to a multidisciplinary cancer pain clinic." *Pain* 45 (1991): 45-48.

Baszanger, Isabelle. *Inventing Pain Medicine: From the Laboratory to the Clinic*. New Brunswick: Rutgers University Press, 1988.

Baszanger, Isabelle. "Deciphering chronic pain." *Sociology of Health & Illness* Vol. 14, No. 2 (1992): 181-214.

Baszanger, Isabelle. "Pain: Its Experience and Treatments." *Social Science and Medicine* Vol. 29, No. 3 (1989): 425-434.

Bauerie, J. E. "New Non-Narcotic Analgesics." *Journal of the San Antonio District Dental Society* 13:6 (1958).

Bear, Mark F. "Bidirectional Synaptic Plasticity: From Theory to Reality." *Philosophical Transactions: Biological Sciences* Vol. 358, No. 1432 (April 29, 2003): 649-655.

Beaver, W. T. "Are Synthetic Narcotics Adequate Substitutes for Opium-Derived Alkaloids?" *Advances in Neurology* 4 (1974): 519-525.

Beecher, Henry K. "The Pain of Men Wounded in Battle." *Annals of Surgery* 123:1 (1946): 96-105.

Beecher, Henry K. "The Measurement of Pain: Prototype for the Quantitative Study of Subjective Responses." *Pharmacological Reviews* 9:1 (1957): 59-209.

Beecher, Henry K. *Measurement of Subjective Responses: Quantitative Effects of Drugs*. New York: Oxford University Press, 1959.

Beecher, Henry K. *Pain and Some Factors That Modify It*. , _____, Vol. 12 (September 1951): 633-641.

Bennett, I. F. "Misuse of Propoxyphene." *JAMA* 235(16) (1976): 1686.

Betcher, Albert M., "Historical Development of the American Society of Anesthesiologists, Inc." In *The Genesis of Contemporary American Anesthesiology*, edited by P. Volpitto and L. D. Vandam, 85-121. Springfield, IL: Charles C. Thomas, 1982.

Betcher, Albert M., Benjamin J. Ciliberti, Paul M. Wood, and Lewis H. Wright. "The Jubilee Year of Organized Anesthesia." *Anesthesia and Analgesia* Vol. 17 (March 1956): 226-264.

Biro, David. *The Language of Pain: Finding Words, Compassion and Relief*. New York: W. W. Norton & Company, 2010.

Bliss, Michael. *The Discovery of Insulin*. Chicago: The University of Chicago Press, 2007.

Boddice, Rob, ed. *Pain and Emotion in Modern History*. New York: Palgrave Macmillan, 2014.

Bogduk, Nikolai. "Taxonomy." In *Encyclopedia of Pain, Volume 3*, edited by Robert F. Schmidt and William D. Willis, 2396-2398. Berlin: Springer-Verlag, 2007.

Bond, Michael R. *Pain: Its Nature, Analysis and Treatment, Second Edition*. Edinburgh: Churchill Livingstone, 1984.

Bond, Michael R., Ronald Dubner, Louisa E. Jones, and Marcia L. Meldrum. "The History of the IASP: Progress in Pain Since 1975." In The Paths of Pain, 1975-2005, edited by Harold Merskey, John D. Loeser, and Ronald R. Dubner, 23-33. Seattle: IASP Press, 2005.

Bonica, John J. "Pain research and therapy: past and current status and future needs." In *Pain, Discomfort and Humanitarian Care*, edited by L. K. Y. Ng and John J. Bonica, 1-46. New York: Elsevier-North Holland, 1980.

Bonica, John J. "Evolution and Current Status of Pain Programs." *Journal of Pain and Symptom Management*, Vol. 5, No. 6 (December 1990): 368-374.

Bonica, John J., Denise G. Albe-Fesard, B. Raymond Fink, and Louisa E. Jones, editors. *Advances in Pain Research and Therapy, Volume 1: Proceedings of the First World Congress on Pain*. New York: Raven Press, 1976.

Bonica, John, Editorial, "The Need of a Taxonomy," and "Pain Terms: A List With Definitions and Notes on Usage, as Recommended by the IASP Subcommittee on Taxonomy." *Pain* 6 (1979): 247-263.

Boring, Edwin G. *Sensation and Perception in the History of Experimental Psychology*. New York: Appleton Century Crofts, Inc., 1942.

Bourke, Joanna. *The Story of Pain: From Prayer to Painkillers*. Oxford: Oxford University Press, 2014.

Bourke, Joanna. "The History of Medicine as the History of Pain," *History Today*. Volume 61, Issue 4 (April 2011).

Bowsher, David. Letter to the editor. *Pain* 113 (2005): 430.

Brandman, Otto. "Clinical Evaluation of the Effectiveness and Safety of a New Analgesic." *The American Journal of the Medical Sciences* (December 1961): 694-701.

Brandt, Allan M. *The Cigarette Century: The Rise, Fall, and Deadly Persistence of the Product that Defined America*. New York: Basic Books, 2009.

Breivik, Else Kristine, Gudmundur Bjornsson, and Eva Skovlund. "A Comparison of Pain Rating Scales by Sampling from Clinical Trial Data." *The Clinical Journal of Pain* Vol. 16(1) (March 2000): 22-28.

Brena, Steven M. ed. *Chronic Pain: America's Hidden Epidemic*. New York: Atheneum/SMI, 1978.

Brieger, Gert. "The Historiography of Medicine." In *Companion Encyclopedia of the History of Medicine*, edited by William F. Bynum and Roy Porter, 24-45. London: Routledge, 1993.

Burns, John. "Pain group certified without exam." *Modern Healthcare* (Nov. 22, 1993).

Bynum, W. F. *Science and the Practice of Medicine in the Nineteenth Century*. Cambridge: Cambridge University Press, 1994.

Campbell, Nancy D. *Discovering Addiction: The Science and Politics of Substance Abuse Research*. Ann Arbor: The University of Michigan Press, 2007.

Campbell, Nancy, J.P. Olsen, and Luke Walden. *The Narcotic Farm: The Rise and Fall of America's First Prison for Drug Addicts*. New York: Abrams, 2008.

Canguilhem, Georges. *The Normal and the Pathological*. New York: Zone Books, 1991.

Carnwath, Tom and Ian Smith. *Heroin Century*. New York: Routledge, 2002.

Carpenter, Daniel. *Reputation and Power: Organizational Image and Pharmaceutical Regulation at the FDA*. Princeton: Princeton University Press, 2010.

Carr, Daniel B. "Ideal Pain Terminology Is Parsimonious, Jargon-free, and Scale-appropriate." *Pain Forum* 6(2) (1997): 95-97.

Cartwright, Nancy. *Nature's Capacities and Their Measurement.* Oxford: Clarendon Press, 1989.

Casey, Kenneth L. ""Learning to Live With the Language of Pain." *Pain Forum* 6(2) (1997): 98-100.

Caton, Donald. "The Secularization of Pain." Anesthesiology 62 (1985):493-501.

Cawelti, John G. *Apostles of the Self-Made Man: Changing Concepts of Success in America* Chicago: The University of Chicago Press, 1965.

Cervero, Fernando. *Understanding Pain: Exploring the Perception of Pain*. Cambridge: The MIT Press, 2012.

Cervero, Fernando. "The Gate Theory, Then and Now." In *The Paths of Pain, 1975-2005*, edited by Harold Merskey, John D. Loeser, and Ronald R. Dubner, 33-46. Seattle: IASP Press, 2005.

Chambers, Carl D., Arthur D. Moffett, and Walter R. Cuskey. "Five Patterns of Darvon Abuse." *The International Journal of the Addictions* 6(1) (1971): 173-189.

Chandler, Alfred D. *Shaping the Industrial Century: The Remarkable Story of the Evolution of the Modern Chemical and Pharmaceutical Industries*. Cambridge, MA and London: Harvard University Press, 2005.

Chaplan, Sandra R. and Linda S. Sorkin. "Agonizing Over Pain Terminology." Pain Forum 6(2) (1997): 81-87.

Chapman, C. Richard and John D. Loeser, ed. *Advances in Pain Research and Therapy: Issues in Measurement, Volume 12*. New York: Raven Press, 1989.

Chapman, C. R., K. L. Casey, R. Dubner, K. M. Foley, R. H. Gracely, A. E. Reading. "Pain Measurement: An Overview." *Pain* 22 (1985): 1-31.

Clarke, M. C. and J. E. Morin. "Pain Clinic Records: A Comprehensive Form and Computerized Database." *The Clinical Journal of Pain* 9 (1993):131-134.

Coakley, Sarah and Kay Kaufman Shelemay, ed. *Pain and Its Transformations: The Interface of Biology and Culture*. Cambridge: Harvard University Press, 2007.

Cohen, Mitchell J. M. James Campbell, ed. *Progress in Pain Research and Management, Volume 7: Pain Treatment Centers at a Crossroads: A Practical and Conceptual Reappraisal*. Seattle: IASP Press, 1996.

Cole, Debra S. *Pain Management Solutions: Managing Pain in Stages*. Bloomington: iUniverse, Inc., 2012.

Conrad, Peter. "Eliot Freidson's revolution in medical sociology." *Health: An Interdisciplinary Journal for the Study of Health, Illness, and Medicine* Vol. 11(2): 1141-1144.

Cooper, Steven J. "Donald O. Hebb's synapse and learning rule: a history and commentary." *Neuroscience and Behavioral Reviews* 28 (2005): 851-874.

Cooter, Roger and John Pickstone, ed. *Medicine in the Twentieth Century*. Sydney: Harwood Academic Publishers, 2000.

Courtwright, David T. *Dark Paradise: A History of Opiate Addiction in America*. Cambridge, MA: Harvard University Press, 2001.

Courtwright, David T. *Forces of Habit: Drugs and the Making of the Modern World*. Cambridge, MA: Harvard University Press, 2001.

Cowan, J.L. *Pleasure and Pain: A Study in Philosophical Psychology*. New York: St. Martin's Press, 1968.

Crawford, Cassandra S. "From pleasure to pain: The role of the MPQ in the language of phantom limb pain." *Social Science & Medicine* 69 (2009): 655-661.

Crease, Robert P. *World in the Balance: The Historic Quest for an Absolute System of Measurement*. New York: W. W. Norton & Company, 2011.

Crue, Benjamin L. Jr. "Multidisciplinary Pain Treatment Programs: Current Status." *The Clinical Journal of Pain* Vol. 1, No. 1 (1985): 31-38.

Crue, Benjamin L. Jr., ed. *Pain Research and Treatment*. New York: Academic Press, 1975.

Daemmrich, Arthur A. Pharmacopolitics: Drug Regulation in the United States and Germany. Chapel Hill and London: The University of North Carolina Press, 2004.

Dallenbach, Karl M. "Pain: History and Present Status." *The American Journal of Psychology* Vol. 52, No. 3 (July 1939): 331-347.

Dallenbach, Karl M. "Somesthesis." In *Introduction to Psychology*, edited by Edward G. Boring, H. S. Langfeld, and H. P. Weld, 608-625. New York: Wiley and Sons, 1939.

Danziger, Kurt. *Constructing the Subject: Historical Origins of Psychological Research*. Cambridge: Cambridge University Press, 1990.

Daut, Randall L., Charles S. Cleeland, and Randall C. Flanery. "Development of the Wisconsin Brief Pain Questionnaire to Assess Pain in Cancer and Other Diseases." *Pain* 17 (1983): 197-210.

DeGrandpe, Richard. *The Cult of Pharmacology: How America Became The World's Most Troubled Drug Culture*. Durham: Duke University Press, 2006.

de Moulin, Daniel. "A Historical-Phenomenological Study of Bodily Pain in Western Man." *Bulletin of the History of Medicine* 48:4 (1974: Winter): 540-570.

Denton, Jane E., and Henry K. Beecher. "New Analgesics: A Comparison of the Side Effects of Morphine, Methadone, and Methadone's Isomers in Man, Parts 1-3." *Journal of the American Medical Association* 141 (1949abc): 1051-1057, 1146-1153.

Dingwall, Robert. *Essays on Professions*. Burlington, VT: Ashgate Publishing Company, 2008.

Dixon, Thomas. *From Passions to Emotions: The Creation of a Secular Psychological Category*. Cambridge: Cambridge University Press, 2003.

Doleys, Daniel M. *Pain: Dynamics and Complexities.* Oxford: Oxford University Press, 2014

Dormandy, Thomas. The Worst of Evils: The Fight Against Pain. New Haven: Yale University Press, 2006.

Dubois, Michel Y. and Kenneth A. Follett "Pain Medicine: The Case for an Independent Medical Specialty and Training Programs." *Academic Medicine* Vol. 89, No. 6 (June 2014): 863-868.

Dumit, Joseph. *Drugs for Life: How Pharmaceutical Companies Define Our Health*. Durham: Duke University Press, 2012.

Eddy, Nathan B. and Everette L. May. "The Search for a Better Analgesic." *Science* Vol. 181, 3 (August 1973): 407-414.

Eddy, Nathan B. "The Search for New Analgesics." *Journal of Chronic Disease*, Volume 4, Number 1 (July 1956): 59-71.

Elson, A. and E.F. Domino. "Dextro Propoxyphene Addiction: Observations of a Case." *Journal of the American Medical Association* 183 (1963): 482.

Engel, George L. "'Psychogenic' Pain and the Pain-Prone Patient." *American Journal of Medicine* 26:6 (1959): 899-918.

Escohotado, Antonio. *A Brief History of Drugs: From the Stone Age to the Stoned Age*. Rochester, VT: Park Street Press, 1999.

Eyzaguirre, Carlos. *Physiology of the Nervous System: An Introductory Text.* Chicago: Year Book Medical Publishers, 1969.

Fagerhaugh, Shizuko Y., and Anselm Strauss. *Politics of Pain Management: Staff-Patient Interaction*. Menlo Park, CA: Addison-Wesley Publishing Company, 1977.

Feinberg, Steven. "The Pain Medicine Specialist as a Physician-Healer." *The Clinical Journal of Pain* Vol. 12(1) (March 1996): 3-5.

Feng, Honghui and Howard S. Smith. "Certification in Pain Medicine." In Warfield, Carol A. and Zahid H. Bajwa, *Principles and Practices of Pain Medicine, Second Edition*, Carol A. Warfield and Zahid H. BaJwa, 581-811. New York: McGraw-Hill Medical Publishing Division, 2004.

Fernandez, Ephrem and Stuart Towery. "A parsimonious set of verbal descriptors of pain sensation derived from the McGill Pain Questionnaire." *Pain*, 66 (1996): 31-37.

Fernandez, Ephrem and Gregory J. Boyle. "Affective and Evaluative Descriptors of Pain in the McGill Pain Questionnaire: Reduction and Reorganization." *The Journal of Pain*, Vol. 2, No. 6 (December, 2001): 318-325.

Feudtner, Chris. *Bittersweet: Diabetes, Insulin, and the Transformation of Illness*. Chapel Hill: The University of North Carolina Press, 2003.

Flor, Herta, Thomas Fydrich, and Dennis C. Turk. "Efficacy of multidisciplinary pain treatment centers: a meta-analytic review." *Pain* 49 (1992): 221-230.

Foreman, Judy. *A Nation in Pain: Solving America's Biggest Public Health Problem*. Oxford: Oxford University Press, 2014.

Forsyth, Patrick B. and Thomas J. Danisiewicz. "Toward a Theory of Profesionalization." *Work and Occupations* Vol. 12, No. 1 (February 1985): 59-76.

Foucault, Michel. *Power/Knowledge: Selected Interviews and Other Writings, 1972-1977*. New York: Pantheon Books, 1980.

Fraser, H. F. and Harris Isbell. "Pharmacology and addiction liability of dl- and d-propoxyphene." *Bulletin on Narcotics*, Issue 1 (1960).

Freidson, Eliot. *Profession of Medicine: A Study of the Sociology of Applied Knowledge*. New York: Dodd, Mead & Company, 1970).

Gallagher, Rollin M. and Scott M. Fishman. "Pain Medicine: History, Emergence as a Medical Specialty, and Evolution of the Multidisciplinary Approach." In *Neural Blockade in Clinical Anesthesia and Pain Medicine, Fourth Edition*, edited by Michael J. Cousins, Phillip O. Bridenbaugh, Daniel B. Carr, and Terese T. Horlocker, 633-639. Philadelphia: Wolters Kluwer / Lippincott William & Wilkins, 2009.

Gerbershagen, H.U., R. Frey, F. Magin, W. Scholl and N. Muller-Suur. "The Pain Clinic: An Interdisciplinary Team Approach to the Problem of Pain." *British Journal of Anaesthesia* (1975): 47, 526.

Gevitz, Norman, ed. *Other Healers: Unorthodox Medicine in America*. Baltimore: The Johns Hopkins University Press, 1988.

Ghaemi, S. Nassir. *The Rise and Fall of the Biopsychosocial Model: Reconciling Art & Science in Psychiatry*. Baltimore: The Johns Hopkins University Press, 2010.

Goldacre, Ben. *Bad Pharma: How Drug Companies Mislead Doctors and Harm Patients*. New York: Faber and Faber, Inc., 2012.

Good, Mary-Jo Delvechhio, Paul E. Brodwin, Byron J. Good, and Arthur Kleinman ed. *Pain as Human Experience: An Anthropological Perspective*. Berkeley: University of California Press, 1992.

Gracely, Richard H. "Evaluation of Pain Sensations." In *The Paths of Pain, 1975-2005*, edited by Harold Merskey, John D. Loeser, and Ronald R. Dubner, 271-285. Seattle: IASP Press, 2005.

Grantham, Dewey W. *The United States Since 1945: The Ordeal of Power*. New York: McGraw-Hill Book Company, 1976.

Greene, Jeremy A. *Prescribing by Numbers: Drugs and the Definition of Disease*. Baltimore: The Johns Hopkins University Press, 2007.

Greene, Jeremy A. and Elizabeth Watkins, ed. *Prescribed: Writing, Filling, Using, and Abusing the Prescription in Modern America*. Baltimore: The Johns Hopkins University Press, 2012.

Greene, Jeremy A. and Scott Podolsky. "Keeping Modern in Medicine: Pharmaceutical Promotion and Physician Education in Postwar America.," *Bulletin of the History of Medicine* 83, No. 2 (2009): 331-377.

Griffith, Harold R. "History of the World Federation of Anesthesiologists." *Anesthesia & Analgesia* 42 (1963): 389-397.

Grogan, Jessica. *Encountering America: Humanistic Psychology, Sixties Culture & The Shaping of the Modern Self*. New York: HarperCollins, 2013.

Hacking, Ian. *The Taming of Chance*. Cambridge: Cambridge University Press, 1990.

Hadjistavropoulos, Thomas and Kenneth D. Craig, ed. *Pain: Psychological Perspectives*. Mahwah, NJ: Lawrence Erlbaum Associates, 2004.

Hafferty, Frederic W. and Donald W. Light. "Professional Dynamics and the Changing Nature of Medical Work." *Journal of Health and Social Behavior*, Vol. 35, Extra Issue: Forty Years of Medical Sociology: The State of the Art and Directions for the Future (1995): 132-153.

Halliwell, Martin. *Therapeutic Revolutions: Medicine, Psychiatry, and American Culture, 1945-1970*. New Brunswick, NJ: Rutgers University Press, 2013.

Halpern, Lawrence M. "Analgesic Drugs in the Management of Pain." *Archives of Surgery* 112 (July 1977): 861-869.

Harcus, A.W., R. B. Smith, and B. A. Whittle, ed. *Pain: New Perspectives in Measurement and Management*. Edinburgh: Churchill Livingstone, 1977.

Hardy, James D., Harold G. Wolff, and Helen Goodell. *Pain Sensations and Reactions*. Baltimore: The Williams and Wilkins Company, 1952.

Hardy, James D.; Wolff, Harold G.; Goodell, Helen. "Studies on Pain. A New Method for Measuring Pain Threshold: Observations on Spatial Summation of Pain." *The Journal of Clinical Investigation* 19:6 (1940): 659-80.

Haugen, Frederick P., and Livingston, William K. "Experiences with the Hardy-Wolff-Goodell Dolorimeter." *Anesthesiology* 14:2 (1953): 109-16.

Hawthorn, Jan and Kathy Redmond. *Pain: Its Causes and Management*. Oxford, UK: Blackwell Science, 1998.

Healy, David. *Pharmageddon*. Berkeley: University of California Press, 2012.

Hebb, D. O. "Neuropsychology: Retrospect and Prospect." Canadian Journal of Psychology 37 (1) (1983): 4-7.

Hebb, D. O. "Drives and the C.N.S. (Conceptual Nervous System)." *The Psychological Review*, Vol. 62, No. 4 (July 1955): 243-254.

Hebb, D. O. "What Psychology is About." *American Psychologist* (February 1974).

Hebb, D. O. "Consider Mind as a Biological Problem." *Neuroscience* Vol. 6, No. 12 (1981): 2419-2422.

Herzberg, David. *Happy Pills in America: From Miltown to Prozac*. Baltimore: The Johns Hopkins University Press, 2009.

Higby, Gregory J. and Elaine C. Stroud, ed. *Pill Peddlers: Essays on the History of the Pharmaceutical Industry*. Madison, WI: American Institute of the History of Pharmacy, 1987.

Hilts, Philip J. *Protecting America's Health: The FDA, Business, and One Hundred Years of Regulation*. Chapel Hill: The University of North Carolina Press, 2003.

History of Anesthsiology … Anesthesia Organizations. Park Ridge, IL: American Society of Anesthesiology, ___.)

Hodgson, Barbara. *Opium: A Portrait of the Heavenly Demon*. Vancouver: Greystone Books, 1999.

Holroyd, Kenneth A., Jeffrey E. Holm, Francis J. Keefe, Judith A. Turner, Laurence A. Bradley, William D. Murphy, Patrick Johnson, Karen Anderson, Andrew L. Hinkle, and W. Brian O'Malley. "A multi-center evaluation of the McGill Pain Questionnaire: results from more than 1700 chronic pain patients." *Pain* 48 (1992): 301-311.

Hornbrook, Mark C. "Prescription Drugs: Problems for Public Policy." *Current History*. (May-June 1977): 215-229.

Hudson, Joseph S. and Thomas Pratt. "Pain Clinics: Their Value to the General Practitioner." *Southern Medical Journal*, Vol. 72, No. 7 (July 1979): 845-847.

Hughes, Everett. *Men and Their Work*. New York: The Free Press of Glencoe, 1958.

Hughes, Richard and Robert Brewin. *The Tranquilizing of America: Pill Popping and the American Way of Life*. (New York: Warner Books, 1979).

Huisman, Frank and John Harley Warner, ed. *Locating Medical History: The Stories and Their Meanings*. Baltimore: The Johns Hopkins University Press, 2004.

Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington, DC: National Academies Press, 2011.

Jackson, Jean E. *"'Camp Pain':" Talking with Chronic Pain Patients*. Philadelphia: University of Pennsylvania Press, 2000.

Jackson, Marni. *Pain: The Science and Culture of Why We Hurt*. London: Bloomsbury, 2002.

Jauhar, Sandeep. *Doctored: The Disillusionment of an American Physician*. New York: Farrar, Straus and Giroux, 2014.

Jensen, Mark P., Paul Karoly, Eoghan F. O'Riordan, Frank Bland, Jr., and Ronald S. Burns. "The Subjective Experience of Acute Pain: An Assessment of the Utility of 10 Indices." *The Clinical Journal of Pain* 5 (1989): 153-159.

Jensen, Mark P., Leslie Miller, and Lloyd D. Fisher. "Assessment of Pain During Medical Procedures: A Comparison of Three Scales." *The Clinical Journal of Pain* 14(4) (December 1988): 343-349.

Johnson, Robert A. *Trends in the Incidence of Drug Use in the United States, 1919-1992*. Rockville, MD: U.S. Department of Health and Human Services Substance Abuse and Mental Health Service Administration Office of Applied Studies, March 1996.

Jonnes, Jill. *Hep-Cats, Narcs, and Pipe Dreams: A History of America's Romance with Illegal Drugs*. New York: Scribner, 1996.

Kalwak, Weronika, Dominika Brol, Jaonna Durlik, Marcin Koculak, Wiktoria Koziol, Sylwia Latacz, Joanna Luczynska, Bartosz Majchrowicz, Katarzyna Siuda, Radoslaw Stupak, and Anna Zymelka, "'My Pain is more like a noun:' Linguistic issues concerning the usage of the McGill Pain Questionnaire." Paper presented at 3rd Global Conference, "Pain: A Making Sense of Project," May 19-21, 2012, Prague, Czech Republic.

Keele, K. D. *Anatomies of Pain*. Springfield, IL: Charles C. Thomas, 1957.

Klegon, Douglas. "The Sociology of Professions: An Emerging Perspective." *Sociology of Work and Occupations* Vol. 5., No. 3 (August 1978): 267-279.

Klein, Axel. *Drugs and the World*. London: Reaktion Books, 2008.

Klein, Raymond M., "Donald Olding Hebb," at www/scholarpedia.org/article/Donald_Olding_Hebb, accessed 6-15-16.

Kleinke, Chris L. "Patients' Preferences for Pain Treatment Modalities in a Multidisciplinary Pain Clinic." *Rehabilitation Psychology*, Vol. 32, No. 2 (1987): 113-120.

Kotarba, Joseph. *Chronic Pain: Its Social Dimensions*. Beverly Hills: Sage, 1983.

Kula, Witold, trans. Richard Sretzer. *Measures and Men*. Princeton: Princeton University Press, 1986.

Labat, Gaston L. "Regional Anaesthesia." *Annals of Surgery* 73 (1921): 165-169.

Lasagna, Louis. "The Clinical Evaluation of Morphine and Its Substitutes as Analgesics." *Pharmacology Review* 16 (1964): 73-75.

Laveaga, Gabriela Soto. *Jungle Laboratories: Mexican Peasants, National Projects, and the Making of the Pill*. Durham and London: Duke University Press, 2009.

Lee, Martin A. and Bruce Schlain. *Acid Dreams: The Complete Social History of LSD; The CIA, the Sixties, and Beyond*. New York: Grove Weidenfeld, 1985.

Le Fanu, James. *The Rise and Fall of Modern Medicine*. London: Abacus, 2011.

Lenoir, Timothy. *Instituting Science: The Cultural Production of Scientific Knowledge*. Stanford, CA: Stanford University Press, 1997.

Lenson, David. *On Drugs*. Minneapolis: University of Minnesota Press, 1995.

Lesch, John E. *The First Miracle Drugs: How the Sulfa Drugs Transformed Medicine*. Oxford: Oxford University Press, 2007.

Lewis, Milton J. *Medicine and the Care of the Dying: A Modern History*. Oxford: Oxford University Press, 2007.

Lewis, Thomas. *Pain*. New York: The Macmillan Company, 1942.

Liebenau, Jonathan. *Medical Science and Medical Industry: The Formation of the American Pharmaceutical Industry*. Baltimore: The Johns Hopkins University Press, 1987.

Liebeskind, John C., and Linda A. Paul. "Psychological and Physiological Mechanisms of Pain." *Annual Review of Psychology* 28:1 (1977): 41-60.

Lindblom, Ulf and Richard Tegner. "Are the Endorphins Active in Clinical Pain States? Narcotic Antagonism in Chronic Pain Patients." *Pain* 7 (1979): 65-68.

Livingston, William K., edited by Howard L. Fields. *Pain and Suffering*. Seattle: IASP Press, 1998.

Lippe, Philip. "Conceptual Construct of the Specialty of Pain Medicine." *The Clinical Journal of Pain* Volume 13(3) (September 1997): 183-185.

Loe, Meika. *The Rise of Viagra: How the Little Blue Pill Changed Sex in America*. New York and London: New York University Press, 2004.

Loeser, John D. "Pain History Musings." *Pain Forum* 4(2) (1995): 134-135.

Loeser, John D. and Richard G. Black. "A Taxonomy of Pain." *Pain* 1 (1975): 81.

Lucas, Scott. *The FDA*. Millbrae, CA: Celestial Arts, 1978.

Lukacs, John. *The Future of History*. New Haven: Yale University Press, 2011.

Mace, Dave. "Re: Safety of 130 mg of propoxyphene Hydrochloride." In *Perspective from an IDIS Subscriber*, Iowa Drug Information Service, n.d.

Main, Chris J. and Spanswick, Chris C. *Pain Management: An Interdisciplinary Approach*. Edinburgh: Churchill Livingstone, 2000.

"Credential in Pain Management Program," American Academy of Pain Management at www.aapainmanage.org, accessed 11-18-15.

Mandler, George. *A History of Modern Experimental Psychology*. Cambridge, MA: The MIT Press, 2007.

Manicas, Peter T. *A History & Philosophy of the Social Sciences*. Oxford: Basil Blackwell, 1988.

Marks, Harry M. *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900-1990*. Cambridge, UK: Cambridge University Press, 1997.

McCleane, Gary J. *Pain Management: Expanding the Pharmacological Options*. Oxford, UK: Wiley-Blackwell, 2008.

McCoy, Alfred W. *The Politics of Heroin: CIA Complicity in the Global Drug Trade, Revised Edition*. Chicago: Lawrence Hill Books, 2003.

McDowell, Ian. *Measuring Health: A Guide to Rating Scales and Questionnaires*. Oxford: Oxford University Press, 2006.

McNeill, William H. *Plagues and Peoples*. New York: Anchor Books, 1976.

McTavish, Jan R. *Pain and Profits: The History of the Headache and Its Remedies in America*. New Brunswick, NJ and London: Rutgers University Press, 2004.

Maletzky, Barry M. "Addiction to Propoxyphene (Darvon): A Second Look." *The International Journal of the Addictions* 9(6) (1974): 775-784.

Meldrum, Marcia L. "A Capsule History of Pain Management." *Journal of the American Medical Association* Vol. 290, No. 18 (November 12, 2003): 2470-2475.

Melzack, Ronald and Joel Katz. "Pain Measurement in Adult Patients." In *Melzack and Wall's Textbook of Pain, Sixth Edition*, edited by Stephen McMahon, Irene Tracey, and Dennis C. Turk, 305-314. New York: Elsevier, 2013.

Melzack, Ronald and Joel Katz. "The Gate Control Theory: Reaching for the Brain." In *Pain: Psychological Perspectives*, edited by Thomas Hadjistavropoulos and Kenneth D. Craig, 13-35. Mahwah, NJ: Lawrence Erlbaum Associates, 2004.

Melzack, Ronald and Patrick Wall. *The Challenge of Pain, Updated Second Edition*. New York: Penguin Books, 1991.

Melzack, Ronald. "From the gate to the neuromatrix." *Pain Supplement* 6 (1999): S121-S126.

Melzack, Ronald. "Evolution of the Neuromatrix Theory of Pain: The Prithvi Raj Lecture, Presented at the Third World Congress of World Institute of Pain." *Pain Practice*, Volume 5, Issue 2 (2005): 85-94.

Melzack, Ronald and Warren S. Torgerson. "On the Language of Pain." *Anesthesiology*, Volume 34, Number 1 (1971): 50-59.

Melzack, Ronald. "Phantom Limbs, the Self and the Brain." D. O. Hebb Memorial Lecture, *Canadian Psychology* 30:1 (1989): 1-16.

Merskey, Harold. "Some Features of the History of the Idea of Pain." *Pain* 9 (1980): 3-8.

Merskey, Harold. "The Perception and Measurement of Pain." *Journal of Psychosomatic Research* Vol. 17 (1973): 251-255.

Merskey, Harold, ed. *Thoughts and Findings on Pain: The Hebb-Bishop correspondence and a selection of papers*. Vancouver: The Canadian Pain Society and the American Pain Society. 1996.

Merskey, Harold, John Loeser, and Ronald Dubner, ed. *The Paths of Pain, 1975-2005*. Seattle: IASP Press, 2005.

Merskey, H. "Development of a Universal Language of Pain Syndromes." In *Advances in Pain Research and Therapy, Vol. 5, Proceedings of the Third World Congress on Pain*, edited by John J. Bonica, Ulf Lindblom, and Ainsley Iggo, _____. New York: Raven Press, 1983.

Merskey, Harold. "Terms and Taxonomy: Paper Tools at the Cutting Edge of Study." In *The Paths of Pain, 1975-2005*, edited by Harold Merskey, John D. Loeser, and Ronald Dubner, 329-337. Seattle: IASP Press, 2005.

Merskey, Harold. "Don't Agonize." *Pain Forum* 6(2) (1997): 92-94.

Milner, Peter M. "Obituary, Donald Olding Hebb (1904-1985)." Elsevier (August 1986): 347-351.

Milner, Peter M. "The Brain and Behavior: Donald O. Hebb," at https://brain-health-neurology.knoji.com/the-brain-and-behavior-donald-o-hebb, accessed 6-15-16.

Milner, Peter M. "The Mind and Donald O. Hebb." *Scientific American* (January 1993): 124-129.

Mohamed, S. N., G. M. Weisz, and E. M. Waring. "The Relationship of Chronic Pain to Depression, Marital Adjustment, and Family Dynamics." *Pain* 5 (1978): 285-292.

Moore, Joseph Earle and David Seegal, ed. "Announcement." *The Journal of Chronic Diseases*, Vol. 1, No. 1 (January 1955): 1-11.

Morris, David B. *Illness and Culture in the Postmodern Age*. (Berkeley: University of California Press, 2000.

Morris, David B. *The Culture of Pain: Illness in the Postmodern World*. Berkeley: University of California Press, 1988.

Moscoso, Javier. trans. Sarah Thomas and Paul House. *Pain: A Cultural History*. London: Palgrave Macmillan, 2012.

Musto, David F. *The American Disease: Origins of Narcotic Control, Third Edition*. Oxford: Oxford University Press, 1999.

Musto, David F., editor. *Drugs in America: A Documentary History*. New York: New York University Press, 2002.

Nakamura, Yoshio and C. Richard Chapman., "Measuring pain: An introspective look at introspection." *Consciousness and Cognition* 11(2002): 582-592.

Napoli, Donald S. *Architects of Adjustment: The History of the Psychological Profession in the United States*. Port Washington, NY: Kennikat Press, 1981.

Neal, Helen. *The Politics of Pain*. New York: McGraw-Hill, 1978.

Nielson, Warren R. "The Concept of Pain." *The Clinical Journal of Pain* Vol. 17, No. 4 (Supplement 2001):S5-S7.

Noble, Bill, David Clark, Marcia Meldrum, Henk ten Have, Jane Seymour, Michelle Winslow, and Silvia Paz. "The Measurement of Pain, 1945-2000." *Journal of Pain and Symptom Management* Vol. 29, No. 1 (January 2005): 14-21.

Numbers, Ronald L. "The Fall and Rise of the American Medical Profession," in *The Professions in American History*, edited by Nathan O. Hatch, 51-72. Notre Dame, IN: University of Notre Dame Press, 1988.

O'Donnell, John M. *The Origins of Behaviorism: American Psychology, 1870-1920*. New York: New York University Press, 1985.

Okifuil, Akiko. "Interdisciplinary Pain Management with Pain Patients: Evidence for Its Effectiveness." *Seminars in Pain Medicine* Vol. 1, No. 2 (2003): 110-119.

Pearce, Joanne and Stephen Morley. "An experimental investigation of the construct validity of the McGill Pain Questionnaire." *Pain* 39 (1989): 115-121.

Peck, Robert E. "A Precise Technique for the Measurement of Pain." *The Journal of Head and Face Pain* Vol. 6, Issue 4 (January 1967): 189-194.

Pepitone-Rockwell, Fran, Richard Rosenblatt, and Guy Corkill. "Pain Clinic Model for Community Practice." The Western Journal of Medicine 131 (August 1979):166-170.

Perl, Edward R. "Ideas about pain: a historical view." *Nature Reviews/Neuroscience* Vol. 8 (January 2007): 71-80.

Perlstein, Rick. *Nixonland: The Rise of a President and the Fracturing of America*. New York: Scribner, 2009.

Perlstein, Rick. *The Invisible Bridge: The Fall of Nixon and the Rise of Reagan*. New York: Simon and Schuster, 2014.

Pernick, Martin S. *A Calculus of Suffering: Pain and Anesthesia in Nineteenth-Century America*. New York: Columbia University Press, 1985.

Perrone, Michael. "FDA pulls Darvon," November 19, 2010; "Excerpts from the chronology of U.S. FDA inaction on Propoxyphene (Darvon, Darvocet)," published by Public Citizen, Nov. 19, 2010.

Petrie, Asenath. *Individuality in Pain and Suffering*. Chicago: U. of Chicago Press, 1967.

Petryna, Adriana, Andrew Lakoff, and Arthur Kleinman, ed. *Global Pharmaceuticals: Ethics, Markets, Practices*. Durham, NC and London: Duke University Press, 2006.

Pickstone, John V. *Ways of Knowing: A New History of Science, Technology and Medicine*. Chicago: The University of Chicago Press, 2000.

Pilowsky, I., C. Richard Chapman, and John J. Bonica. "Pain, Depression, and Illness Behavior in a Pain Clinic Population." Pain 4 (1977): 183-192.

Portenoy, Russell K. "Opioid Therapy for Chronic Nonmalignant Pain: Clinicians' Perspective." *Journal of Law, Medicine & Ethics* 24, no. 4 (1996): 296-309.

Porter, Roy. *The Greatest Benefit to Mankind: A Medical History of Humanity*. New York: W. W. Norton & Company, 1997.

Power, Mike. *Drugs Unlimited: The Web Revolution That's Changing How the World Gets High*. New York: Thomas Dunne Books, 2013.

Price, Donald D. and Stephen W. Harkins. "Combined Use of Experimental Pain and Visual Analogue Scales in Providing Standardized Measurement of Clinical Pain." *The Clinical Journal of Pain* 3 (1987):1-8.

Price, Donald D., Francis M. Bush, Stephen Long, and Stephen W. Harkins. "A comparison of pain measurement characteristics of mechanical visual analogue and simple numerical rating scales." *Pain* 56(1994): 217-226.

Quinones, Sam. *Dreamland: The True Tale of America's Opiate Epidemic*. New York: Bloomsbury Press, 2015.

Quintner, John L., Milton L. Cohen, David Buchanan, James D. Katz, and Owen D. Williamson. "Pain Medicine and Its Models: Helping or Hindering?" *Pain Medicine* Volume 9, Number 7 (2008): 824-834.

Rangell, Leo. "Psychiatric Aspects of Pain." *Psychosomatic Medicine* 15:1 (1953): 22-37.

Reading, Anthony E. "Pain Measurement and Experience." *Journal of Psychosomatic Research* Vol. 27, No. 5 (1983): 415-420.

Reekie, W. Duncan and Michael H. Weber. *Profits, Politics and Drugs*. New York: Holmes & Meier Publishers, Inc., 1979.

Rey, Roselyne. trans. Louise Elliott Wallace, J. A. Cadden, and S. W. Cadden. *The History of Pain*. Cambridge: Harvard University Press, 1998.

Reynolds, L. A. and E. M. Tansey, editors. Innovation in Pain Management: the transcript of a Witness Seminar, Wellcome Trust Centre for the History of Medicine, 2004, held at University College London (UCL), December 12, 2002.

Riddoch, George. "Central Pain." Lancet, 1 (1938):1150-1156, 1205-1209.

Riddoch, George. "Phantom Limbs and Body Shape." *Brain* 64 (1941):197-222.

Robinson, Daniel N. *An Intellectual History of Psychology, Third Edition*. Madison: The University of Wisconsin Press, 1995.

Rose, Nikolas and Joelle M. Abi-Rached. *Neuro: The New Brain Sciences and the Management of the Mind*. Princeton: Princeton University Press, 2013.

Rosen, George. "Disease and Social Criticism: A Contribution to the Theory of Medical History." *Bulletin of the History of Medicine* (January 1941): 5-15.

Rosen, George. "Levels of Integration in Medical Historiography: A Review." *Journal of the History of Medicine* (Autumn 1949): 460-467.

Rovenstine, E. A. and H. M. Wertheim. "Therapeutic Nerve Block." *The Journal of the American Medical Association* Vol. 117, No. 19 (Nov. 8, 1941): 1599-1603.

Ruiz, Teofilo F. *The Terror of History: On the Uncertainties of Life in Western Civilization*. Princeton: Princeton University Press, 2011.

Ruth, Henry S. "Diagnostic, Prognostic and Therapeutic Nerve Blocks." *The Journal of the American Medical Association* Vol. 102, No. 6 (February 10, 1934): 419-425.

Saks, Mike. "Medicine and the Counter Culture." in Medicine in the Twentieth Century, edited by Roger Cooter and John Pickstone, 113-124. Sydney: Harwood Academic Publishers, 2000.

Sandbrook, Dominick. *Mad as Hell: The Crisis of the 1970s and the Rise of the Populist Right*. New York: Anchor Books, 2011.

Scarry, Elaine. *The Body in Pain*. New York: Oxford University Press, 1985.

Sen, Surjya, David P. Martin, Douglas R. Bacon. "Exploring Origins: Was John Bonica's Model of Modern-Day Pain Management Influenced by John Lundy's Earlier Work?" *Regional Anesthesia and Pain Medicine* Volume 32, Number 3 (May-June 2007): 258-262.

Shainbaum, Mark. "The king of (understanding) pain." *McGill Reporter*, November 17, 2008.

Sinclair, Christian, "Are You Glad Darvocet Got Pulled by the FDA? Are You Sure?" on Pallimed: A Hospice & Palliative Medicine Blog, posted Nov. 30, 2010.

Skevington, Suzanne M. "Pain control and mechanisms for the measurement of pain." *Journal of Psychopharmacology* 5 (1991): 360-370.

Smith, W. Lynn, Harold Merskey, and Steven C. Gross. *Pain: Meaning and Management*. New York: SP Medical & Scientific Books, 1980.

Soumerai, Stephen B., Jerry Avorn, Steven Gortmaker, and Sharon Hawley. "Effect of Government and Commercial Warnings on Reducing Prescription Misuse: The Case of Propoxyphene." *American Journal of Public Health* Vol. 77, No. 12 (1987), 1518-1523.

Spanswick, Christopher and Chris Main. *Pain Management: An Interdisciplinary Approach*. London: Palgrave Macmillan, 2000.

Starr, Paul. *The Social Transformation of American Medicine*. New York: Basic Books, 1982.

Staub, Michael E. *Madness is Civilization: When the Diagnosis Was Social, 1948-1980*. Chicago: The University of Chicago Press, 2011.

Stephen, C. Ronald. "Anaesthetists' Travel Club, 1929-1952: An Historical Review." St. Louis: Academy of Anesthesiology, 1992.

Stevens, Jay. *Storming Heaven: LSD and the American Dream*. New York: Grove Press, 1987.

Stevens, Rosemary. *American Medicine and the Public Interest, Updated Edition with a New Introduction*. Berkeley: University of California Press, 1998.

Stiller, Richard. *Pain: Why It Hurts Where It Hurts When It Hurts*. Nashville, TN: Thomas Nelson Inc., 1975.

Stimmel, B. "The Emperor's New Clothes: The Reality of Darvon-N." *American Journal of Drug and Alcohol Abuse* 1(1) (1974): 137-140.

Strumpf, Michael, Anne Willweber-Strumpf, and Michael Zenz. "Economic considerations in chronic pain." *Bailliere's Clinical Anesthesiology* Vol. 12, No. 1 (March 1998): 89-102.

Swann, John P. *Academic Scientists and the Pharmaceutical Industry: Cooperative Research in 20th Century America*. Baltimore: The Johns Hopkins University Press, 1988.

Swerdlow, M., M. D. Mehta, and S. Lipton. "The role of the anesthetist in chronic pain management." *Anaesthesia* Volume 33 (1978): 250-257.

Sykes, Keith with John Bunker, contributing ed. *Anaesthesia and the Practice of Medicine: Historical Perspectives*. London: The Royal Society of Medicine Press, 2007.

Taylor, Charles. *Sources of the Self: The Making of the Modern Identity*. Cambridge: Harvard University Press, 1989.

Temin, Peter. *Taking Your Medicine: Drug Regulation in the United States*. Cambridge: Harvard University Press, 1980.

Thernstrom, Melanie. *The Pain Chronicles: Cures, Myths, Mysteries, Prayers, Diaries, Brain Scans, Healing, and The Science of Suffering*. New York: Farrar, Straus and Giroux, 2010.

Titchener, Edward B. "Notes from the psychological laboratory of Cornell University." *American Journal of Psychology* 31 (1920): 212.

Tobbell, Dominique A. *Pills, Power, and Policy: The Struggle for Drug Reform in Cold War America and Its Consequences*. Berkeley: University of California Press and New York: Milbank Memorial Fund, 2012.

Tone, Andrea. *The Age of Anxiety: A History of America's Turbulent Affair with Tranquilizers*. New York: Basic Books, 2009.

Tone, Andrea and Elizabeth Siegel Watkins, ed. *Medicating Modern America: Prescription Drugs in History*. New York: New York University Press, 2007.

Torgoff, Martin. *Can't Find My Way Home: America in the Great Stoned Age 1945-2000*. New York: Simon and Schuster, 2004.

Tousignant, Noemi. "The Rise and Fall of the Dolorimeter: Pain, Analgesics, and the Management of Subjectivity in Mid-twentieth-Century United States." *Journal of the History of Medicine* Vol. 66 (April 2011): 145-179.

Tousignant, Noemi, "A Quantity of Suffering: Measuring Pain as Emotion in the Mid-Twentieth-Century USA," in Pain and Emotion in Modern History, edited by. Rob Boddice, 112- (New York: Palgrave Macmillan, 2014), 111-129.

Towery, Stuart and Ephrem Fernandez. "Reclassification and rescaling of McGill Pain Questionnaire verbal descriptors of pain sensation: a replication." *Clinical Journal of Pain* 12(4) (December 1996): 270-6.

Tracy, Sarah W. and Caroline Jean Acker, ed. *Altering American Consciousness: The History of Alcohol and Drug Use in the United States, 1800-2000*. Amherst and Boston: University of Massachusetts Press, 2004.

Trout, Kimberly K. "The Neuromatrix Theory of Pain: Implications for Selected Nonpharmacologic Methods of Pain Relief." *Journal of Midwifery & Women's Health* Volume 49, Number 6 (November/December 2004): 482-488.

Turk, D. C. "Chronic Pain: Models and Treatment Approaches," in *International Encyclopedia of the Social and Behavioral Sciences*, edited by Neil J. Smelser and Paul B. Baltes. New York: Elsevier Science Ltd., 2001.

Turk, Dennis C., Thomas E. Rudy, Peter Salovey. "The McGill Pain Questionnaire Reconsidered: Confirming the Factor Structure and Examining Appropriate Uses." *Pain* 21 (1985): 385-397.

Turk, Dennis C. "Assessment of Pain: The Elusiveness of Latent Constructs," in Advances in Pain Research and Therapy, Volume 12: Issues in Pain Measurement, edited by Chapman, C. Richard and John D. Loeser, 267-280. New York: Raven Press, 1989.

Tursky, Bernard, Larry D. Jamner, and Richard Friedman. The Pain Perception Profile: A Psychophysical Approach to the Assessment of Pain Report." *Behavior Therapy* 13 (1982): 376-394.

Vos, Rein. *Drugs Looking for Diseases: Innovative Drug Research and the Development of the Beta Blockers and the Calcium Antagonists*. Dordrecht, Boston, and London: Kluwer Academic Publishers, 1991.

Vrancken, Mariet A. E. "Schools of Thought on Pain." *Social Sciences and Medicine*, Vol. 29, No. 3 (1989): 435-444.

Wailoo, Keith. Pain: A Political History. Baltimore: Johns Hopkins University Press, 2014.

Wall, Patrick D. *Pain: The Science of Suffering*. New York: Columbia University Press, 2000.

Wall, Patrick D., "Modulation of pain by nonpainful events," in Proceedings of the First World Congress on Pain, Advances in Pain Research and Therapy, Volume 1, edited by John J. Bonica and Denise G. Albe-Fessard, 1-16. New York: Raven Press, 1976.

Wall, Patrick D. "25 Volumes of Pain" Pain 25 (1986): 1-4.

Wall, Patrick D. and Ronald Melzack, ed. *The Textbook of Pain, 2nd edition*. Edinburgh: Churchill Livingstone, 1989.

Wall, Patrick D. and William H. Sweet. "Temporary Abolition of Pain in Man." Science, New Series, Vol. 135, No. 3758 (Jan. 6, 1967): 108-109.

Wallace, Mark S. and Peter S. Staats, ed. *Pain Medicine and Management: Just the Facts*. New York: McGraw-Hill, 2005.

Warfield, Carol A. and Zahid H. Bajwa. *Principles and Practices of Pain Medicine, Second Edition*. (New York: McGraw-Hill Medical Publishing Division, 2004.

Watkins, Elizabeth Siegel. "From History of Pharmacy to Pharmaceutical History," Keynote Address, American Institute for the History of Pharmacy meeting, University of Wisconsin, Madison, October 17-18, 2008.

Wells, J. C. D. "The place of the pain clinic." *Bailliere's Clinical Rheumatology*, Vol. 1, No. 1 (April 1987).

Wheen, Francis. *Strange Days Indeed: The 1970s – The Golden Age of Paranoia*. New York: Public Affairs, 2009.

White, James C. and William H. Sweet. *Pain and the Neurosurgeon: A Forty-Year Experience*. (Springfield, IL: Charles C. Thomas, 1969.

White, William L. *Slaying the Dragon: The History of Addiction Treatment and Recovery in America*. (Normal, IL: Chestnut Health Systems/Lighthouse Institute, 1998), 260-1.

Wikler, Abraham, Helen Goodell, and Harold G. Wolff. "Studies on Pain: The Effects of Analgesic Agents on Sensations Other than Pain." *Journal of Pharmacology and Experimental Therapeutics* 83.4 (1945): 294-99.

Wilkie, Diana J., Marilyn C. Savedria, William L. Holzemer, Mary D. Tesler, and Steven M. Paul. "Use of the McGill Pain Questionnaire to Measure Pain: A Meta-Analysis." *Nursing Research*, Vol. 39, No. 1 (January/February 1990): 36-41.

Willis, William D. Jr. "Physiology and Anatomy of the Spinal Cord Pain System." in Harold Merskey, John D. Loeser, and Ronald Dubner, ed. *The Paths of Pain, 1975-2005* (Seattle: IASP Press, 2005).

Wolff, Harold G. and James D. Hardy. "On the Nature of Pain." *Physiological Reviews*, Vol. 27, No. 2 (April 1947): 167-199.

Woodbridge, Philip D. "Therapeutic Nerve Block with Procaine and Alcohol." *American Journal of Surgery* (August 1939): 278-288.

Yeamans, D. C., et al., "Pain, Management of," *International Encyclopedia of the Social & Behavioral Sciences, 2001 edition*, ed. (New York: Elsevier, 2001), 10996-11000.

Young, James Harvey. *The Toadstool Millionaires: A Social History of Patent Medicines in America before Federal Regulation*. Princeton: Princeton University Press, 1961.

Zborowski, Mark. *People in Pain.* San Francisco: Jossey-Bass, 1969.

Zimmermann, Manfred, "The History of Pain Concepts and Treatment before IASP," in The Paths of Pain, 1975-2005, ed. Harold Merskey, John Loeser, and Ronald Dubner (Seattle: IASP Press, 2005), 19.

Zinsser, Hans. *Rats, Lice and History*. New Brunswick, NJ: Transaction Publishers, 2008.

Zwillich, Todd, "FDA Panel Urges Ban of Pain Drug," January 30, 2009, WebMD Health News, reviewed by Louise Chang, MD, http://www.medicinenet.com/script/main/art.asp?articlekey=97355

---

**Publishing Agreement**

*It is the policy of the University to encourage the distribution of all theses, dissertations, and manuscripts. Copies of all UCSF theses, dissertations, and manuscripts will be routed to the library via the Graduate Division. The library will make all theses, dissertations, and manuscripts accessible to the public and will preserve these to the best of their abilities, in perpetuity.*

***Please sign the following statement:***

*I hereby grant permission to the Graduate Division of the University of California, San Francisco to release copies of my thesis, dissertation, or manuscript to the Campus Library to provide access and preservation, in whole or in part, in perpetuity.*

Stephan Baiter
Author Signature

9/1/16
Date