Power Shifts: How Patient Activism Shapes the Practice of Medicine

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For my children
Wilson, Willa, and Oscar

Abstract

This dissertation examines specific phenomena that illustrate a unique aspect of the role of patient activism in shaping the practice of medicine. Each chapter focuses on a specific example. The four examples are the rise of Morgellons disease, activism by sufferers of chronic Lyme disease, research subject activism, and the use of patients to market Paxil for social phobia. I use these examples to examine various shifts of power that have occurred in medicine over the last few decades. These shifts can be generally divided into two types: a shift in power from physicians to patients and an overlapping shift in power from professional medicine to various corporate entities. In the past thirty years, patients have taken more and more control over their own medical care. Over this same time period the pharmaceutical industry became a highly profitable business, increasing its economic and political power and research has become more commercialized. The older fee-for-service model of medical practice has been replaced with a corporate model and the influence of professional medical bodies has waned. Each of the shifts documented here has its own moral story, but together they also point to larger trends in medicine that have important moral consequences. In the conclusion I point to four different points of tension for ethics: a shift in the locus of moral expertise, the changing physician-patient relationship, ambiguity in the goals of medicine, and the role of bioethicists as watchdogs for patients.

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INTRODUCTION

A woman comes to an appointment with a dermatologist armed with dozens of pages printed off the internet, claiming that she has fibers growing under her skin. A patient with a history of a tick bite and uncertain diagnosis requests that his physician prescribe long-term antibiotics. Testifying in front of an FDA panel, a cancer patient representing a patient group funded by a pharmaceutical company explains why it is so important that the latest cancer drug be approved. A shy college professor asks her doctor for a prescription for Paxil after identifying with a public awareness poster that asked her to "Imagine Being Allergic to Life." Each of these examples involves patient activism—individual patients and patient groups making demands for power that end up shaping the practice of medicine. In this dissertation I use these examples to examine various shifts of power that have occurred in medicine over the last few decades. Most of the shifts have empowered patients, but we will see that other groups, such as pharmaceutical companies, have exploited the power of patients for their own benefit.

Aim and Scope of the Dissertation

Each chapter examines a specific phenomenon that illustrates a unique aspect of the role of patient activism in shaping medicine. The four examples are the rise of Morgellons disease, activism by sufferers of chronic Lyme disease, research subject activism, and the use of patients to market Paxil for social phobia. This dissertation will add depth to this literature by examining these examples individually and as a class,

with a particular emphasis on the role of power. The project is both descriptive and normative. In each chapter I point out particular tensions that have arisen and ask how these tensions came about, giving a description in response. Each chapter also raises important normative questions, which I raise and address at the end of each chapter. Rather than trying to answer questions of clinical ethics, such as how physicians should respond to the requests of patients, which will depend on the details of each particular case, I have tried to place these questions in a larger social context that will make them easier to interpret. The concluding chapter looks at these normative questions in a more comprehensive and systematic way, pointing to larger shifts in medicine.

Taking a comprehensive view of these aspects highlights larger moral implications of the shift in power to patients. Respect for autonomy is important, but can patients genuinely become knowledgeable enough about health and illness to make the best healthcare decisions? Can they be knowledgeable enough to protect themselves from those who want to exploit them for profit? Does this change in the context of psychiatric illness? The conclusion of the dissertation will take up a larger question: now that doctors have begun to lose their authority and clinical practice has begun to lose its traditional moral content, where does that leave medicine?

A recent study published in *BMJ* found that half of physicians routinely prescribe placebos for their patients.[1] On the surface, this could be taken as evidence that medicine has not really changed all that much over the last few decades. Physicians deceive their patients because they think they are acting in the patients' best

[1] Tilburt, Jon C. et al. "Prescribing 'Placebo Treatments': Results of a National Survey of US Internists and Rheumatologists." *BMJ*, 337 (2008): a1938.

interests; the old model of medical authoritarianism is still strong. The work in this dissertation will suggest a different interpretation: rushed physicians, who do not have a long-standing relationship with their patients, prescribe placebos in response to patients' *desires*, not their *needs*.

Summary of Chapters

Chapter One: Morgellons Disease

The phenomenon of Morgellons disease seemed to come out of nowhere in 2003 when Mary Leitao, a Pennsylvania mother and former hospital laboratory technician, set up a website in hopes of determining what was ailing her two-year-old son, who appeared to have fibers coming from sores on his mouth. She named the condition Morgellons disease after a similar sounding condition reported in French medical journals in the eighteenth century. Since then, alarming news reports have warned people of a new, mysterious disease, and nearly 13,000 sufferers of Morgellons disease have registered on her website. Many believe that they are suffering from an infectious disease that gives them the tingling sensation of fibers crawling under their skin. These patients have banded together, trying to get the medical establishment to take their concerns seriously.

After much lobbying by members of Congress, who were inundated by mail from constituents, the CDC has launched an investigation into Morgellons disease. In general, however, the activism of Morgellons disease patients has not been very successful yet, primarily because the majority of physicians do not believe their claims. They think, instead, that these people are suffering from delusional parasitosis (DP), a

previously recognized mental disorder. In this chapter I use the work of the philosopher of science Ian Hacking on transient mental illness to try to explain what might be going on in the case of Morgellons disease. I also use Morgellons disease as an example of the limits of patient activism, because so far, the efforts of activists have had only minimal practical effect. Patients may be making demands of their physicians, but few physicians are giving in to them.

Chapter Two: Chronic Lyme Disease

In the 1970s patient activists were instrumental in the discovery of acute Lyme disease, an infectious disease transmitted by tick bite, by helping researchers discover the tick-borne bacterium that causes the disease. Later, however, many Lyme disease patients began to complain of symptoms long after the original infection, and ask their physicians for more antibiotic treatment. Chronic Lyme disease refers to a condition in which a patient has received standard antibiotic treatment for acute Lyme disease, but whose symptoms return months or even years later. Most researchers think the condition is rare, but a large and increasingly powerful group of patients, along with sympathetic physicians, think otherwise.

The story of chronic Lyme disease illustrates just how powerful some patient advocacy groups have become. Chronic Lyme disease activists have marshaled a remarkable amount of political and social power, despite objections from leading Lyme disease authorities. The debates over chronic Lyme disease have also taken place during the rise of evidence-based medicine (EBM). While EBM describes a new paradigm for medicine, with research guiding practice, the story of chronic Lyme

disease describes a competing paradigm, driven primarily by the experiences of patients.

Chapter Three: Research Ethics

Accounts of patient activism often start with the story of AIDS activists in the 1980s, who protested in order to get access to clinical trials testing drugs for AIDS. Prior to the era of AIDS activism, research ethicists had been concerned mainly with the risks of medical research. AIDS activism led them to look more closely at the benefits. This shift turned the standard model for protecting human subjects on its head, leading to new regulations aimed at increasing access to medical research. By 2003, the Abigail Alliance, a patient advocacy group, sued the FDA demanding that terminally ill patients have access to experimental drugs.

This chapter explores two major shifts of power in medical research. The first shift is the one brought about by AIDS activists, in which power was transferred from medical researchers to research subjects. The second shift in power, which is less well-known, but equally important, was from academic health centers to the private sector. During the 1990s, clinical trials became much more commercialized, as pharmaceutical companies began to partner with Contract Research Organizations rather than academic researchers. At the same time pharmaceutical companies also made alliances with patient groups, using patients to advocate for things like increased research funding and quicker FDA approval for experimental drugs. This second shift of power raises concerns about whether research subjects are being exploited.

Chapter Four: Paxil and Social Phobia

In 1999 Paxil (paroxetine) became the first drug approved by the FDA for treating social anxiety disorder. Paxil soon became an enormous financial success for its manufacturer, GlaxoSmithKline. Yet only twenty years previously, the illness of social anxiety disorder did not officially exist. Today social anxiety disorder is estimated to be the third most common mental disorder in the United States, behind depression and substance abuse. How did social anxiety disorder become so widespread, and the treatment for it so profitable?

In this chapter, I will argue that the marketing of Paxil for social anxiety disorder was intimately connected to the growing power of patients. Its success came at a time just after restrictions on Direct-to-Consumer (DTC) advertising had been loosened, and when the power of patient advocacy groups was on the rise. GlaxoSmithKline marketed Paxil by going over the heads of physicians and reaching to patients themselves. The marketing campaign depended on the medicalization of shyness as social anxiety disorder, a process begun when social anxiety disorder made its debut as "social phobia" in the American Psychiatric Association diagnostic manual, *DSM-III (Diagnostic and Statistical Manual-3rd edition)* in 1980.

I will also argue that the story of Paxil demonstrates a potential danger connected to the growing power of patients. In 2004, the FDA placed a "black box warning" on Paxil and other antidepressants, warning that the drugs could lead to an increase in suicidal thoughts. The risk of suicide in patients taking Paxil or other antidepressants may be justifiable if the person taking the medication is being treated

for major depression, which itself is associated with an increased risk of suicide. But the risks of Paxil are much more questionable when it is being used to treat shyness.

Conclusion

In the conclusion I will reflect on how the shifts of power documented throughout this dissertation correspond with larger changes in medicine. The four changes I identify and discuss all have important moral consequences. First, a shift in the locus of medical expertise challenges the authority of physicians and opens up a divide between physicians and patient activists. Second, this is also closely related to a shift in the physician-patient relationship. This traditionally authoritarian relationship has been replaced with a consumer model that damages the moral content of the physician-patient relationship. Third, a shift in the goals of medicine raises questions about the moral content of medicine and whether medicine is primarily about serving patients' needs or patients' desires. Finally, I will examine some of the broader implications for the field of bioethics.

CHAPTER ONE

Morgellons Disease

Abstract

In 2003 a patient activist attributed the term Morgellons disease to the symptoms of her two-year-old son who appeared to have fibers coming from sores on his mouth. Shunned by medical professionals, Mary Leitao turned to the Internet to help figure out what was going on with her son. Since then almost 13,000 families have registered at the Morgellons Research Foundation website, founded by Leitao. Many of these people believe they are afflicted with an emerging infectious disease that involves subcutaneous fibers and severe itching, as well as neurological impairment in some cases. A majority of physicians think they know exactly what these people are suffering from: a mental disorder called delusional parasitosis. This chapter explores the emerging phenomenon of Morgellons disease, looking closely at the role of patient activism in bringing about what many patients think is a new disease. People who identify themselves as Morgellons disease sufferers have so far had limited success in gaining credibility from the medical field. The CDC is currently conducting an investigation, but primarily at the behest of politicians. I use Ian Hacking's work on transient mental illnesses and ecological niches to explore Morgellons disease and conclude with a discussion of the role of social contagion and the power of diagnosis in Morgellons disease.

Introduction

Sue Law was working in her basement on a typical day in October 2004 when all of a sudden she felt like she was being attacked by bees. There was intense itching and stinging on her back and she screamed for her husband to come help her. Her husband Tom came racing down the stairs and lifted up her shirt but did not see anything—no bees or other bugs that would explain what was going on. Law did not believe her husband—there must be something biting her. To prove it to her Tom stuck strips of packing tape on her back and then pealed them off. They both examined the tape with a magnifying eyepiece and saw that the adhesive was covered with tiny red

fibers. Neither of them had ever seen anything like it. Sue said, "You automatically think clothing. But I wasn't wearing anything red."[1] Sue's itching grew worse and "it felt as if thousands of tiny bugs were crawling under her skin, stinging and biting."[2] She was miserable.

They considered causes like flees and mold, but tearing up all the carpet and wallpaper and calling an exterminator did not help. In the morning she would discover black specks on her side of the bed and droplets of blood where the specks seemed to be coming out of her body. Law developed painful lesions all over her body and she developed other symptoms as well like joint pain and neurological symptoms like forgetfulness. Her hair started to fall out and her teeth started to rot. She told a reporter that one day she coughed up a springtail fly and a pink worm came out of one her eyeballs. Law said "That's when I thought, 'I'm really going to kill myself'."[3] She visited a dermatologist who said that he did not know what was wrong. She went to a number of other doctors, but many of them thought she was delusional. Her family practice physician wrote in her chart that "She says she's coughing up bugs and worms."[4] Law admits that she probably was acting a little crazy when she saw some of these physicians, but that was only because she was so frustrated and in so much agony.

News articles and online chat boards are filled with similar accounts. For example, Lynn Sebold, a former ICU nurse, describes mysterious symptoms beginning in 1989 when she experienced night sweats, acne and fatigue. These symptoms

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[1] Schulte, Brigid. "Figments of the Imagination?" *Washington Post*, 20 January 2008, W10.
[2] Ibid.
[3] Ibid.
[4] Ibid.

continued for over a decade until 2003 when she also developed rashes, lesions that would not heal, itchiness, brain fog, and the sensation that sharp granules were working their way out of the skin on her neck. After years of going to doctors and getting no answers, she turned to the Internet and found a diagnosis.[5]

Miles Lawrence, a landscaper in Texas was packing for a trip when he noticed his finger was tingling. He stared at his finger as "little spiny things" seemed to sprout out of his skin in the same place where he had recently removed a splinter. Lawrence grasped one of the spines with a tweezers and pulled and when he did, he felt a huge bolt of pain race up his arm. He pulled at another one, and felt a spike of pain up his neck. He said, "It felt like bugs under the skin of my arms, in my joints. I freaked out."[6] Lawrence went to the emergency room and was diagnosed with delusional parasitosis, a psychiatric disorder characterized by the mistaken belief that one is being infested by parasites like lice, mites, bacteria, or other organisms. His caregivers told him that the spines he saw coming out of his skin were just dirt. Things got worse and worse. Anytime he scratched his elbows more fibers and little black specks would show up.[7]

John Amber of Little Neck, New York claims that he felt like bugs were crawling on his legs and head and he saw something green and fuzzy that looked like lint coming out of his skin. He called an exterminator and washed all of his clothes, but the feeling of bugs crawling around his body did not go away. Amber went to a dermatologist who gave him a topical cream that did not make any difference. He went

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[5] "AKA 'Morgellons': The CDC Launches an Investigation," *American Journal of Nursing*, 108(5) (2008): 25-6.
[6] Chertoff, Benjamin. "Making Their Skin Crawl," *Popular Mechanics*, June 2005.
[7] Ibid.

back to the dermatologist who then told Amber that he was just imagining things and this was all in his mind. Since then "he's tried homemade remedies like wrapping himself in plastic bags or sleeping outdoors."[8]

Morgellons Disease

Similar experiences, symptoms, and frustrations with medical professionals have led thousands of people to the internet, but it was Mary Leitao who first officially staked out this new territory by giving it a name and a presence on the Internet.[9] In 2003 Mary Leitao picked a piece of fluff from a sore under her two-year-old son Drew's mouth. Drew developed more sores with fibers sticking out of them. Leitao took her son to pediatricians, dermatologists, and allergists. The physicians ruled out eczema and allergies. Sometimes the fibers were different colors like white, red, black, or blue. Drew also believed that insects were crawling under his skin. He would point to his lips and say "bugs." Leitao was extremely frustrated; not only was she not getting a diagnosis, but no one believed her. An infectious disease specialist at Johns Hopkins University reviewed Drew's medical history, refused to clinically examine him, and wrote in Drew's medical chart that Mary Leitao suffers from Munchausen's by proxy (a psychiatric disorder where a parent pretends a child is sick or makes the child sick in order to get attention).[10]

Leitao grew increasingly frustrated and decided that the only way to help her son was by taking things into her own hands. While researching, she came across a

[8] Goulding, Susan Christina. "Does Your Skin Crawl?," *People*, 18 December 2006, 127-8.
[9] Devita-Raeburn, Elizabeth. "The Morgellons Mystery," *Psychology Today*, March/April 2007.
[10] Ibid.

description of Morgellons disease in a 17th century French medical journal that described a condition where black hairs came out of children's skin.[11] This sounded similar to what she observed in her son, so Leitao decided to refer to Drew's condition as Morgellons disease. She set up a website describing the symptoms in hopes that medical researchers and physicians might view it and be able to offer assistance and insights. But instead of hearing from scientists, she started to hear from hundreds and then thousands of people who claimed to be afflicted with the same ailment.

The website of the Morgellons Research Foundation (MRF), founded by Mary Leitao, lists the symptoms of Morgellons disease as including "crawling, biting and stinging sensations; granules, threads or black speck like materials on or beneath the skin; and/or skin lesions (e.g. rashes or sores) and some sufferers also report systematic manifestations such as fatigue, mental confusion, short term memory loss, joint pain, and changes in vision."[12] As of August 2008, 12,804 families have registered at the MRF website. Of the more than 12,000 people who have self-reported on the site, 37% of these reports involve multiple family members and 15% of individuals are under the age of thirteen.[13] Many of these people claim that they have been suffering from the associated symptoms of Morgellons disease for many years and have never been taken seriously by physicians and the medical establishment. The power and effects of giving this list of symptoms the specific name, Morgellons disease, cannot be understated. Leitao does not claim that the Morgellons disease of the 21st century is the same as the Morgellons disease of the 17th century. If anything, she was just looking for something

[11] Ibid.
[12] Morgellons Research Foundation. "Case Definition," Accessed 25 October 2008. Available from http://www.morgellons.org/.
[13] Ibid. and Schulte.

to call what she observed. But by staking out a term, she offered some sense of unity to the experiences of thousands of people. Anyone searching the web for terms like "itchy", "bugs", or "fibers" is going to come across Morgellons disease. Not only will they come across websites and chat boards devoted to Morgellons disease, but they will also find links to numerous news reports in the last few years. MRF's web presence and local and national news reports on this "mysterious illness" have given these people a sense that they are no longer suffering alone.

The MRF case definition has been adopted by anyone referring to "Morgellons disease." MRF says that it is developing a new case definition, under the guidance of its medical board, but it would be surprising if the new definition departs significantly from the current one. The current case definition has been extremely powerful and plays a central role in shaping Morgellons disease. Just as the first appearance of social anxiety disorder in psychiatry's diagnostic manual eventually led to a broader definition, a similar thing has happened with Morgellons disease. Leitao began simply enough by describing her son's symptoms. In our Google culture, it should not be surprising that others quickly found her site and more significantly, found familiarity with her descriptions of her son's condition. The dermatological symptoms (crawling, biting and stinging sensations; granules, threads or black speck like materials on or beneath the skin; and/or skin lesions (e.g. rashes or sores)) were the first identified by Leitao, but as she heard from more and more people, it became apparent that many who exhibit the dermatological symptoms also experience the neurological symptoms as well (fatigue,

mental confusion, short term memory loss, joint pain, and changes in vision) and they were added to the definition.[14]

Most people who claim to suffer from Morgellons disease have not been taken seriously by their physicians and many of them have seen multiple, even dozens, of physicians in an attempt to get answers and relief. People who claim to suffer from Morgellons disease or who describe symptoms consistent with Morgellons disease often visit a dermatologist because their symptoms are skin related. Many physicians, especially dermatologists, think that what these people describe is most consistent with delusional parasitosis.[15] Delusional parasitosis (DP) is a mental disorder where a person claims to feel subcutaneous bugs.[16] They literally believe that bugs are crawling under their skin. Many dermatologists and psychiatrists are taught to look for the "matchbox sign". Patients with delusional parasitosis will often bring to their appointment a matchbox (this has also been updated to the "Ziploc sign") filled with evidence. Morgellons sufferers bring collections of fibers they report to have pulled from their skin. Many physicians believe that these fibers are just placed in the sores by the patients themselves. The patient is really in a catch: no one takes her seriously, so she brings what she understands to be evidence and documentation of the claims she is making. But the very fact that she is bringing this evidence makes the physician immediately reject everything she is saying and attribute her symptoms to delusional

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[14] Schulte
[15] See Koblenzer, Caroline S. "The Challenge of Morgellons Disease," *Journal of the American Academy of Dermatology* 55;5 (2006): 920-922.
[16] See Walker, Carl and Linda Papadopoulos. *Psychodermatology*. New York: Cambridge University Press, 2005.

parasitosis. Many of the patients interviewed in various news articles claim that most physicians do not even physically examine them and refuse to run any laboratory tests.[17]

Dermatology and psychiatry have a strong association with one another. Mental distress often has dermatological effects like in the case of anxiety causing blushing or perspiration. One meta-analysis indicates that "psychiatric disturbance and psychosocial impairment is reported in at least 30% of patients who have dermatologic disorders."[18] In other instances, psychiatric disorders can have dermatologic effects. For instance, obsessive compulsive disorder may be exhibited by someone obsessively picking at her skin. Delusional parasitosis falls into this second category. It is classified under delusional disorder, somatic type in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR).*[19] Arnold notes that "delusional parasitosis appears to be uncommon, with an equal sex distribution in patients younger than 50 years and a female-to-male ratio of 3:1 in patients ages 50 years and older."[20] Although the dermatology and psychiatry literatures both indicate that delusional parasitosis is relatively uncommon, there is evidence that it is frequently misdiagnosed. The Mayo Clinic found that for half of the 175 patients in a five year period who originally presented at the clinic with a diagnosis of delusional parasitosis, further testing and examination discovered a nonpsychiatric cause of their symptoms.[21] While it would be fallacious to assume that fifty percent of

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[17] See Schulte, Devita-Raeburn, and Goulding.
[18] Fried, Richard G., Madhulika A. Gupta, and Aditya K. Gupta. "Depression and Skin Disease." *Dermatologic Clinics*, 23 (2005): 657-664, 657.
[19] American Psychiatric Association, American Psychiatric Publishing, 2000.
[20] Arnold, Lesley M. "Dermatology." In *Textbook of Psychosomatic Medicine*, ed. James L Levenson, 629-646. Washington, D.C.: American Psychiatric Publishing, 2005.
[21] Schulte

all diagnoses of DP are incorrect, this does suggest that we should at least be a little skeptical.

The original definitions of DP say nothing about fibers, but dermatologists have latched onto this idea. The handful of recent articles by dermatologists that discuss Morgellons disease strictly follow a DP script.[22] While some dermatologists chastise their colleagues for being insensitive to patients' psychiatric needs, the general line is that anything a patient calls Morgellons disease is actually DP. But one of the issues is that DP is a diagnosis of exclusion, which means that it is a diagnosis arrived at by ruling everything else out. If a patient presents to a dermatologist and describes a sensation of bugs crawling under her skin, or reports seeing colored fibers coming out of an open sore, this information does not align with anything the dermatologist has ever seen. And once obvious possibilities like parasites are ruled out, the only thing left is a diagnosis of DP.

The Mayo Clinic website is the only medical organization to include any information about Morgellons disease. The entry begins, "Morgellons disease is a mysterious skin disorder characterized by disfiguring sores and crawling sensations on and under the skin. Although Morgellons disease isn't widely recognized as a medical diagnosis, experts from the Centers for Disease Control and Prevention (CDC) are investigating reports of the condition."[23] The signs and symptoms identified are taken from the Morgellons Research Foundation. The site goes on to say that "Morgellons disease shares characteristics with various recognized conditions, including attention-

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[22] See Koblenzer

[23] Mayo Clinic. "Morgellons Disease: Managing a Mysterious Skin Condition." Accessed 25 October 2008. Available from http://www.mayoclinic.com/health/morgellons-disease/SN00043.

deficit disorder, chronic fatigue syndrome, Lyme disease, obsessive-compulsive disorder and a mental illness involving false believes about infestation by parasites (delusional parasitosis)."[24] The entry takes a neutral stance on the Morgellons controversy, but acknowledges the debate by describing attitudes as falling into three categories:

- Some health professionals believe that Morgellons disease is a specific condition likely to be confirmed by future research.
- Some health professionals believe that signs and symptoms of Morgellons disease are caused by another condition, often mental illness.
- Other health professionals don't acknowledge Morgellons disease or are reserving judgment until more is known about the condition.[25]

The site acknowledges that "Some people who suspect Morgellons disease claim that they've been ignored, criticized as delusional or dismissed as fakers. In contrast, some doctors say that people who report signs and symptoms of Morgellons disease typically resist other explanations for their condition."[26] People who think they have the signs and symptoms of Morgellons disease are encouraged to find a health care professional who acknowledges their concerns and performs a thorough physical examination. But people are also encouraged to keep an open mind and to "consider various causes for your signs and symptoms, and follow your doctor's recommendations for treatment—which may include long-term mental health therapy."[27]

The response of healthcare providers has been mixed. On one end there are those who think that all of these people have DP and refuse to consider anything else.

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[24] Ibid.
[25] Ibid.
[26] Ibid.
[27] Ibid.

Most clinicians fall a little short of that. They feel deep compassion for their suffering patients, but with little evidence to go on feel very perplexed. On the other end are those few clinicians who firmly believe that Morgellons disease is an infectious disease. Clinicians like Virginia Savely and Raphael Stricker who have devoted their careers to people with chronic Lyme disease have now taken on Morgellons disease as well."[28]

Because the literature is still small compared with established diseases, it is possible to take a comprehensive look at both the medical literature and media reports of Morgellons disease. In doing this, the impact of the MRF case definition of Morgellons disease is striking. The discussion of the Mayo Clinic website entry above illustrates this. Whenever *anyone* refers to Morgellons disease, they cite the MRF case definition because that is absolutely all anyone has to go on. Everything comes from the MRF case definition and this is what everyone cites, which is circular. Part of this is completely out of necessity. It has only been five years since Mary Leitao attributed the term to a list of symptoms and despite some claims that this is a mysterious infectious disease, there is still scant evidence to support this.

The accounts of many people who claim to suffer from Morgellons disease are heart breaking. First, descriptions of the symptoms, especially the itching and feeling that bugs are under your skin, are enough to keep even the most rational person up at night.[29] Imagine that your life is going along smoothly when all of a sudden one day you feel like you are under attack and you are experiencing things you have never heard

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[28] Savely, Virginia, Mary Leitao and Raphael Stricker. "The Mystery of Morgellons Disease: Infection or Delusion?" *American Journal of Clinical Dermatology,* 7;1 (2006): 1-5.

[29] See Gawande, Atul. "The Itch." *New Yorker,* 30 June 2008. While not about Morgellons disease, Gawande's description of patients with insufferable itches is fascinating.

of or seen happen to anyone else. If you actually saw fibers oozing out of your skin, of course you would be terrified and run to see your physician. But, second, besides the terrible and frightening experience of the symptoms themselves, you find that when you seek treatment no one actually believes you. You are told that it is all in your head; you are just making this up to get attention, or this indicates a serious mental illness. You search the web and find a description of Morgellons disease. The symptoms sound familiar and people's frustration with the medical field sounds especially familiar. You even come across some news articles reporting on a new mysterious illness called Morgellons disease. The vast majority of the news articles are alarmist, claiming that thousands and thousands of people are suffering from this new disease and no one knows the cause. It is predictable that anyone in this situation would latch onto this label.

Initially, it seems like questions about Morgellons disease should be easy to settle. How hard can it be to determine if a person actually has bugs crawling under her skin? Or fibers sprouting out of a scab? The explanations for these phenomena range from the plausible to the absurd. Among the absurd, a browsing of websites and chat boards devoted to Morgellons disease includes theories which identify the cause as nanotechnology, genetically modified crops, and space aliens. Some conspiracy theorists blame the U.S. government for unleashing devastating microbes. Others blame foreign governments: "Who's saying it wasn't the Chinese who developed this and it's in the clothes they make or the food they manufacture. This is why I refuse to buy anything made in China, think of the other issues this country has had from goods

that came from China: Lead paint! Pet Foods! What next?"[30] Among the plausible, perhaps this is an emerging infectious disease. Or maybe the emergency room physician that examined Miles Lawrence was right and it is delusional parasitosis.

Medicine and Politics

MRF has teamed with a few researchers and distributes research grants, but they do not have the resources for a thorough epidemiological investigation. From the beginning of Mary Leitao's efforts, she has tried to get public health authorities interested in investigating what she termed Morgellons disease. As I will examine in other chapters in this dissertation, when sufferers get frustrated with the medical establishment, they often turn to politicians. Increasingly frustrated with the lack of attention paid to Morgellons disease, MRF has encouraged people over the past couple of years to actively petition their senators, congress people, and the federal agency Centers for Disease Control and Prevention (CDC). Morgellons disease has been reported in all 50 states, but California and Texas seem to have the largest total numbers of self-reported cases (in part, it is likely, because they are so populous).[31] In October 2003, having being alerted to clusters of Morgellons disease in California, the Infectious Diseases Branch of the California Department of Health Services conferred with CDC about the cases of Morgellons disease reported in California. The two agencies decided that a public health investigation was not warranted. At the prompting of Senator Cornyn the following spring, the Infectious Disease Epidemiology and Surveillance

[30] Washington Post Comment Board on Schulte's article. Accessed 25 October 2008. Available from http://www.washingtonpost.com/wp-dyn/content/article/2008/01/16/AR2008011603134_Comments.html.
[31] Schulte

Unit of the Texas Department of State health services also conferred with CDC about reported cases of Morgellons disease in Texas. Again, it was decided that a public health investigation was not warranted. Increasingly over the next year, U.S. Senators heard from constituents complaining that CDC was not taking this new disease seriously and calling for a full investigation. CDC responded to the senators that there was no need for alarm and that further investigation was not justified. In 2006 several senators, including Senator Feinstein of California and Senators Clinton and Schumer from New York sent strongly worded letters to CDC asking it to expedite its investigation into Morgellons disease.[32]

Responding to political pressure, CDC announced in August 2006 that an official CDC investigation of Morgellons disease would be launched in California.[33] 24% of those registered with MRF live in California with a clustering in the San Francisco area. In July 2007 CDC announced that it would contract with Kaiser Permanente, Northern California to conduct the investigation. The investigation began in January 2008 and is expected to last twelve months or longer. Protocol eligibility requires that: “one must reside in the Northern California area, be at least 13 years old, have been a health plan member of Kaiser Permanente California during July 2006 through December 2007, and have compatible signs and symptoms of the condition as described in the investigation protocol."[34] The signs and symptoms are those in the MRF case definition. The study has two parts. In the first part, eligible participants

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[32] Ibid.
[33] MRF. "Background information on the involvement of the Centers for Disease Control and Prevention (CDC) in the investigation of Morgellons disease in the U.S." Accessed 25 October 2008. Available from http://www.morgellons.org/cdc.htm.
[34] CDC, "Unexplained Dermopathy (aka 'Morgellons'): CDC Investigation." Accessed 25 October 2008. Available from http://www.cdc.gov/unexplaineddermopathy/investigation.html.

will be identified and detailed information about study participants' symptoms and potential exposures and other factors that could contribute to the condition will be collected. Participants will be identified through records review. In the second part of the study, "participants will undergo detailed clinical evaluations, including a general medical examination, a dermatology examination, a mental health examination, skin biopsies, and multiple blood tests."[35] The CDC investigation is the biggest development to date in debates over Morgellons disease. Many Morgellons disease sufferers believe this is the first major step in gaining disease recognition. But recognition is just the first step leading to what sufferers think is much more important: developing treatments.

It seems like it should be easy to prove what is actually going on here. Randy Wymore is a molecular biologist at Oklahoma State University.[36] In 2005 he stumbled across Morgellons websites and became interested in investigating the phenomena. He assumed it would be easy to test the fibers that sufferers were talking about and to really determine if they were from textiles or from the body. He emailed some of the people who had posted photos of their fibers and asked them for samples. Within 48 hours people from various parts of the country including Texas, Washington, Florida, California, and Pennsylvania sent him packages containing samples of fibers that all looked very similar. He was surprised that they all looked the same. He started to analyze the fibers and became convinced that they were not from textiles. At first Wymore worked with the Morgellons Foundation and he and a colleague, a pediatrician named Rhonda Casey received a $4,000 grant from the foundation to get fresh fiber

[35] Ibid.
[36] Schulte

samples from 20 patients. Casey removed the samples herself from the Morgellons patients. Wymore took the samples to the forensic lab of the Tulsa Police Department which had a database of 900 commercially available textiles used to analyze samples from crime scenes. The samples did not match anything in the police database. The scientists at the lab tried to burn one of the fibers to determine if it matched any of 85,000 known organic compounds. Nothing matched and the heat (to 700 degrees Fahrenheit) did nothing to the blue fiber. Wymore says, "We were able to reach in with a tweezers and pick it up…I don't have the foggiest idea what they are."[37] Wymore has had a falling out with Leitao and other MRF board members over management and funding issues. He has started his own foundation and continues to search for answers.[38] If Wymore's analysis of the fibers had turned up something conclusive, that would have gone a long way to shaping the debates over Morgellons disease. But instead, it opened up more uncertainty, which fuels the debates.

Hacking on Transient Mental Illnesses and Ecological Niches

It is hard to know what to make of Morgellons disease, in large part because the story is still unfolding. But it is worthwhile to think about why the Morgellons disease phenomena has grown so quickly, why so many clinicians think that it is actually delusional parasitosis, and why so many sufferers resist this diagnosis. Many of the possible answers to these questions are controversial, so I am going to look at a

[37] Ibid.
[38] See Wymore's website. Accessed 25 October 2008. Available from http://healthsciences.okstate.edu/morgellons/.

historical example that is less controversial and then ask whether there are any similarities between these cases.

In *Mad Travelers: Reflections on the Reality of Transient Mental Illness* Ian Hacking describes the fugue epidemic in the 1890s that began in France but spread throughout the continent of Europe. Dr. Philippe Tissié met Albert in 1886 on Dr. Albert Pitres's ward in the Bordeaux hospital Saint-André. Dr. Tissié noticed the twenty-six year old Albert, a gas fitter from Bordeaux, who was exhausted from a long journey on foot, weeping on his bed. He was upset because he could not prevent himself from taking off on trips whenever he felt compelled. He would desert his family and work and just start walking until eventually "he would be arrested for vagrancy and thrown in prison."[39] These were not just little day trips that he would take, either. Albert's accounts included adventures to Algeria, Moscow, and Constantinople. When he "came to" or snapped out of his fugue state, he had no idea where he had been, but under hypnosis he could recall most everything, which sometimes included lost years.

Albert was born May 10, 1860 to Marie Dumear and Romain Dadas. Marie died of pneumonia in 1877. The Dadas men worked for gas companies. Romain demonstrated mental instability throughout his life and was a hypochondriac who died in 1881 of paresis and softening of the brain. Albert had two brothers—one who did well and became the manager of a gas company, but then died of meningitis at the age of thirty-five. His second brother was a hypochondriac like his father who worked for a gas company and suffered from headaches. Albert also had a sister who was in good

[39] Hacking, Ian. *Mad Travelers: Reflections on the Reality of Transient Mental Illness.* Charlottesville, VA: University Press of Virginia, 1998: 7.

health and married to a gas worker. Hacking reports, "These were solid artisans, respectable, seldom without work when they needed it, loyal to their employer who in turn took patronal responsibility for their welfare."[40] Albert experienced his first fugue at the young age of twelve, shortly after being apprenticed to a manufacturer of gas equipment. His brother found him in a nearby town working for a traveling umbrella salesman. His brother tapped him on the shoulder and Albert appeared to awake from a deep sleep and he was surprised to find himself in this town selling umbrellas. This became a standard pattern. Albert would have a little money, hear of a destination, and depart. When he came to, he was astonished to find himself where he was and could not remember how he got there. The family decided that Albert should enlist in the army in place of his brother, but the army did not satisfy what the family saw as his need for adventure. Instead, Albert grew bored and deserted.

Tissié's medical reports of Albert set off a small epidemic of compulsive mad travelers. Hacking's aim is to describe what made fugue a plausible diagnosis in 1890s France. While fugue still appears in the *DSM*, it is virtually never diagnosed today and we certainly do not hear about people suffering from a mental illness that compels them to travel. Hacking argues that particular cultural and social features of the time made fugue a plausible diagnosis and he explains how it came to be an epidemic in Europe, but not in Britain or America. By answering the question, "What made this illness possible?" Hacking gives us a framework for understanding transient mental illnesses—those that come and go depending on both time and place.

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[40] Ibid., 21.

Hacking argues that transient mental illnesses can best be understood using the metaphor of ecological niches. An ecological niche describes how an organism interacts with its surroundings and in particular, the features of those surroundings that makes it possible for the organism to survive. Hacking uses the metaphor to suggest that "psychological symptoms find stable homes at a given place and time in 'ecological niches' where transient illnesses flourish."[41] Hacking argues that transient mental illnesses are those that require an ecological niche and vectors. When one or more vector disappears, the illness is no longer able to find a stable home and the illness (i.e. its diagnosis) disappears. The illness may come back, but only if it has an ecological niche.

Hacking identifies four principle vectors that made fugue possible as a medical diagnosis: medical taxonomy, cultural polarity, observability, and release. Fugue fit into the medical taxonomy of the day as either hysteria, epilepsy, or both and it "did not dislodge existing symptoms of classification."[42] Tissié's reports of Albert set off great interest within the medical community and more and more fuguers were identified. But there was also a debate about whether traveling fugues were hysteria or epilepsy. This debate over diagnosis, with Jean-Martin Charcot on the epilepsy side and Tissié and his mentor Dr. Albert Pitres on the hysteria side, actually helped this new mental illness to establish itself. The polarization among professionals ensured that they would be engaged with debates and reports of mad travelers.

In 1888, one year after Tissié published his account of Albert, Charcot gave a lecture where he exhibited a mad traveler named Mén. Charcot, a neurologist, argued

[41] Ibid., 2.
[42] Ibid., 81.

that Mén was an epileptic suffering from ambulatory automation. Mén became the epileptic paradigm. This diagnosis was possible because in the previous years epilepsy was reconceptualized. It was broadened to include latent epilepsy which produced the psychological equivalents of seizures. Charcot and his followers did not deny hysterical fugues, but they thought that they were rare and of little interest. Those like Tissié who advocated for a diagnosis of hysterical fugues similarly did not deny that there were epileptic fugues, rather they maintained that there were a great number of hysterical fugues.[43]

The two diagnoses had different characteristics. Ambulatory automation referred to involuntary activity. Hacking quotes Charcot's argument for epilepsy: "An individual has a fit and in the aftermath, in the midst of postictal nightmares, becomes violent and breaks everything about him. Afterward he begins to walk about, and this is not a quiet stroll. At the first incident the police will nab him and he will awaken in the police station. These epileptics can kill people and even commit suicide, whereas our patient here probably would not have jumped into the water if he did not already know how to swim. In his case there is no evidence of hyperexcitability or violence…Nevertheless the behavioral changes of these patients…are probably the same phenomena under different guises."[44] Latent epileptics were thought to be horrid people and there was widespread fear about what epileptics might do in a state of automatism.

In contrast, hysterical fuguers were decent, nice people. There were also clinical differences that were thought to help distinguish between epileptics and fuguers.

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[43] Hacking.
[44] Ibid., 207.

Hypnotism was highly useful with hysterical fuguers. Under hypnotism, a fuguer would recall months and years of travels. Epileptics did not respond to hypnotism. Also, bromide treatment seemed to be effective for epileptics, but useless for hysterical fuguers. New cases kept appearing on both sides.[45]

The second vector that Hacking identifies as part of the ecological niche is cultural polarity: "one of the features of a new mental illness is that it embeds itself in a two-headed way in a culture. The simplest way is that there are two versions 'of the same thing,' one held to be virtuous and one held to be vicious, between which the illness insinuates itself, as fugue lives between tourism and vagrancy."[46] Tissié describes Albert as suffering from "pathological tourism." The second half of the nineteenth century was an era of popular tourism, or tourism for the masses. This is an important part of the ecological niche. It was the golden age of travel journalism and travel was seen as rebellious. Popular tourism was something viewed very positively. But at the same time France was obsessed with vagrancy. Popular tourism was the appropriate way to leave one's life and visit new places while vagrancy was the inappropriate way. To the French in the 1880s "the vagrant signified racial degeneracy, no reproduction, or reproduction of those very features that the French race ought to get rid of."[47] Vagrancy was medicalized[48] and vagrants were considered degenerates. Rene Beck, a French physician, argued that vagrants need to be eliminated from society because they are noxious, but they must be cared for because they are ill.

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[45] Ibid.
[46] Ibid., 48-49.
[47] Ibid., 68.
[48] Medicalization is a term that sociologists use to describe the transformation of certain behaviors and conditions into medical diseases or disorders. This issue will be taken up in Chapter Four.

The third principle vector Hacking identifies is observability. The observability vector of the niche for fugue was a substantial system of surveillance and detection in place in France during that time. French laws required all to carry passports and men who had been in the military had to carry their *livret* which recorded the person's time in the army and indicated the circumstances under which he could be called up again. So, French fuguers could not wander Europe unnoticed. Young men were highly scrutinized because they were suspected of being deserters.

The polarity in French society between travel and vagrancy also influenced the final principle vector Hacking calls release. Fugue was an escape. The typical qualities of fuguers--male, working poor, urban or had a trade, having a normal life style and a regular location--meant that they did not have the means for leisure travel. But their mores also kept them from crime and vagrancy. "Fugue was a space in which dysfunctional men, on the edge of freedom yet trapped, could escape."[49] Travel was the release vector of the niche of fugue.

These four vectors help explain why the epidemic of mad travelers began in France and spread to other countries in Europe. They also help explain why the epidemic did not happen in Britain and America. Britain and America did not have similar ecological niches—principle vectors were missing which made it impossible for "mad traveler" or fugue to be a mental illness. Fugue was never taken seriously as a medical entity in America. There were plenty of examples of men who exhibited the same actions of the French mad travelers, but they were always labeled as multiple personality or double consciousness. Ambulatory automatism was never diagnosed.

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[49] Ibid., 82.

Emigration was not a French way of life the way it was for Britons and Americans; this partly explains a lack of interest in fugues in the medical taxonomy.

The vector of release was also missing. In many ways, emigration itself was a release. In America, men in a fugue state were likely to head west and never be heard from again. The vector of observability was also missing. Young men on the road in Europe were highly scrutinized because European countries had conscript armies, while Britain and America did not. Any young man traveling in Europe would be suspected of being a deserter. In Britain and America a fuguer could stay invisible much more easily. In European countries, such as France, that had conscript armies "fugue was a medical entity of peace, boredom, and dull regimentation."[50] One might assume that desertion was more common during war because men wanted to get away from the dangers of fighting, but in fact the opposite was true. Conscripted armies had the biggest desertion problems during peacetime because soldiers would desert out of boredom, just as Albert did. Also, in countries with conscription "a body of medico-forensic expertise was needed to distinguish the willful deserters from those who could be excused on account of a medical condition."[51] The French, and later German and Russian army or naval authorities, tended to side with deserters, so they could establish themselves as being independent. But there is no evidence that British or American army or naval doctors favored deserters (who were volunteers).

Cultural polarity was also missing in Britain and America—there was no equivalence of France's degeneracy program, which medicalized vagrancy in France. In France, Charcot thought that distinct failings like alcoholism (chronic drinking),

[50] Ibid., 62.
[51] Ibid., 63.

dipsomania (binge drinking), epilepsy, hysteria, and neurasthenia could all be inherited. Drunkards would breed hysterics who would breed epileptics. To the French in the 1880s "the vagrant signified racial degeneracy, no reproduction, or reproduction of those very features that the French race ought to get rid of."[52] The European degeneracy program was picked up in America as eugenics, but this was after the disappearance of fugue states in Europe. The closest thing in America to the French degeneracy program was an inferiority program which focused on providing scientific proof of the inferiority of African Americans.

Between 1887 and 1909 fugue was a significant mental illness in France, but then it was not. Why did it go away in France and other countries in Europe? Hacking argues that the vectors disappeared and so the vital ingredients in the ecological niche that made fugue possible were eliminated. In the accounts of mad travelers there is always a tension between policemen and jails and physicians and hospitals. When a mad traveler was stopped without papers, he would be thrown in jail. The medical men would earn his release by explaining that the person's actions were the result of a medical illness. The medical men started to lose out in this confrontation with the police. Fugue was thought to be an antisocial act; mental diagnosis has nothing to do with it. If someone is ill and stays home, that is fine. But if he leaves home he has shown himself to be antisocial and the police take charge. This was the line of attack from those who wanted to medicalize vagrancy. But by 1910 this attack had run its course and the vagrancy scares ended—a vital ingredient in the ecological niche was eliminated.

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[52] Ibid., 68.

Other things also disappeared, the most important being the decline of fugue itself. Joseph Babinski, Charcot's star student and a powerful professional, led a sustained attack on ambulatory automatism and hysteria that started to gain a lot of ground and won many converts. Babinski argued that hysteria was caused by suggestion, "sometimes directly from a doctor and more often culturally absorbed."[53] As early as 1916 Babinski and others began to insist that hysteria has no neurological basis. Other causes for skepticism about hysteria included an influx of new types of diagnoses including dementua praecox, which was soon replaced with schizophrenia. The historian Mark Micale argues that hysteria "vanished into a hundred places in the medical textbooks."[54] One taxonomy replaced another and the symptoms of hysteria were redistributed across a new set of illnesses.

Hacking uses the historical example of hysterical fugue as a means to discuss transient mental illnesses. Hysterical fugue is an example of a transient mental illness—it appeared at a particular time and place and then faded away. All of this leads us to a main point of Hacking's inquiry: "Are analogous conclusions to be drawn about transient mental illnesses today?" Will modern disorders like multiple personality, chronic fatigue syndrome, anorexia, and social anxiety disorder turn out to be transient mental illnesses? The answer is that it is definitely possible. With hysterical fugue, we have the advantage of examining a phenomenon that had a particular end. The controversial mental illnesses of today are ongoing phenomena, so we do not have the benefit of hindsight. But Hacking argues that we can point to similar vectors that make up the ecological niche that makes these illnesses possible.

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[53] Ibid., 72.
[54] Ibid.

For example, he argues that in the case of multiple personality (or dissociative identity disorder) there was a cultural polarity beginning in the 1970s. The negative element was child abuse and one of the positive elements was "romantic challenges to ideas of identity and selfhood."[55] Medical taxonomy also adapted to reflect multiple personality and dissociative identity disorder. These diagnoses are on the books—these people suffer from whatever the diagnostic books say they do. Hacking argues that we should understand many modern mental illnesses the way we now understand the hysterical fugue epidemic of one hundred years ago. It does not really make sense to ask whether a mental illness is "real" or not. If the vectors are there, the diagnosis will be made and it will be a plausible diagnosis for that particular place and time.

Delusional Parasitosis (DP)

Do I have any idea whether people who claim to have Morgellons disease actually have delusional parasitosis? No, and at this point no one else does either (we only have specific judgments of particular patients by individual physicians). Many different answers may come out in the coming years. But one thing I can talk about is the issue of how DP came to be the most common diagnosis for many of these people. Hacking's metaphor of an ecological niche is very useful. All four vectors are in place: medical taxonomy, cultural polarity, observability, and release. It is worth taking a closer look at DP.

[55] Ibid., 96.

Thibierge, a French dermatologist, introduced the term "acarophobia" in 1894 to describe patients who were convinced they had a mite infection, but clinical examination proved they did not.[56] He distinguished two types of acarophobia: in one a patient had a history of infection and believed the infection still continued after successful treatment. In the other, there was no history of infection. Two years later another French dermatologist named Perrin introduced the term "névrodermie parasitophobique". According to Trabert, he immediately found the term misleading because the prominent feature in many cases seemed to be a delusional conviction, not phobia. In the next few decades, the disorder took on a number of different names. In Europe, it was often referred to as "präseniler Dermatozoenwahn" (presenile dermstozoic delusion), so named in 1938 by the Swedish psychiatrist Ekbom (in the 1970s it was also referred to as Ekbom's syndrome). In 1946 Wilson and Miller coined the term "delusions of parasitosis" and pointed out the syndrome's diagnostic nonspecificity. It was thought possible in "schizophrenia, involutional melancholy, dementia, toxic psychoses and 'severe psychoneurosis'."[57] Soon after Wilson and Miller's contribution there was a growing debate over the appropriate nosology of this syndrome. The peak of this debate was over a label by German psychiatrist Klaus Conrad. Conrad introduced the term "chronic tactile hallucinosis" and argued that pure delusional parasitosis was organic because it resembled alcoholic hallucinations. Other psychiatrists argued that it should be classified under late onset schizophrenia or in the context of paranoia.

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[56] Trabert, Wolfgang. "100 Years of Delusional Parasitosis: Meta-Analysis of 1,223 Case Reports," *Psychopathology* 28 (1995): 238-246.
[57] Ibid., 239.

These debates have lingered and the conception of delusional parasitosis as a subgroup of paranoia was renewed when Munro "introduced the term 'monosymptomatic hypochondriacal psychosis' and subsumed this entity under 'delusional disorders' in *DSM-III-R* and *ICD-10* [The International Statistical Classification of Diseases and Related Health Problems]."[58] The debate in psychiatry has also been shaped by professional boundaries. Psychiatrists have always been interested in this syndrome, but in reality they seldom see patients with this disorder since patients are more likely to seek care from a dermatologist and reject any psychiatric consultation. In his 1995 review "100 Years of Delusional Parasitosis," Trabert (a psychiatrist) says that it is important to take a comprehensive look at DP because so many of its reports are single cases or small samples. He also argues that these small samples have affected nosological debates, suggesting that once we take an epidemiological approach to DP, it is highly likely that "different classificatory assessments could emerge."[59]

Trabert offers a comprehensive meta-analysis of all cases with delusional parasitosis published in the last 100 years. He excludes cases that are repeated or are related to cocaine or amphetamine use. The results are 193 articles reporting a total of 1,223 patients. Interestingly, most of these articles (73.5%) were published by psychiatrists, while 16.0% were published by dermatologists. Most of the papers (81.8%) described very small patient samples (less than five) and only 3.1% described samples larger than 50 patients. DP is more frequent in older subjects and occurs more

[58] Ibid.
[59] Ibid., 240.

often in women, with the sex ratio increasing with age (after 50 years of age the proportion of females clearly increased).[60]

Of the 363 patient reports that indicated the duration of delusions, the mean time was 3-4.6 years. In 67 cases, Trabert was able to assess the social contacts of patients: "53.7% were assessed as socially isolated, 25.3% had some few relationships and only 20.8% were regarded as individuals with good and stable social contacts."[61] 50% of patients went into remission after some course of therapy. The rate of full remission increased after the beginning of the psychopharmacological era in 1960 from 33.9% to 51.9%. DP is typically treated with antipsychotic agents. Trabert's analysis of diagnostic classification (possible in 449 cases) found a high proportion of "pure" forms of DP (meaning that the DP was not secondary to some other psychiatric disorder) at 40.3%.[62]

Trabert's review provides a useful view of DP, but while the point of reviews is to provide generalizations, the information that is most interesting is found in specific case reports. First, it is interesting that Trabert found that most cases were reported by psychiatrists, although most patients with DP see dermatologists rather than psychiatrists. So it is difficult to be sure that the literature really provides a representative sample. There is also increasing debate over the frequency of DP. Some authors have argued that DP is not as uncommon as previously thought.[63]

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[60] Ibid.
[61] Ibid., 241.
[62] Ibid.
[63] See Srinivasan, T.N. et al. "Nature and Treatment of Delusional Parasitosis: A Different Experience in India." *International Journal of Dermatology*, 33;12 (2007): 851-855.

Descriptions of DP have not changed much in the last few decades. A summary presented in *JAMA* in 1966 by a dermatologist describes the matchbox sign and patients who on a first visit will "invariably [bring] a small envelope which contains bits of dirt, skin, scales, and material fibers. The patient will not be satisfied until they have been examined. Sometimes letters from laboratories may be offered as evidence that there is an organism present and responsible for all of the patient's difficulties. The delusion is so fixed and the patient so convincing that other people are led to believe that the patient is actually infested."[64] Does this sound familiar? Halprin concludes, "These patients are deeply disturbed and avoid true psychosis by means of the delusion which allows them to keep some contact with reality in other areas. They therefore cling to their delusion as if their very life depended upon it—and it often does."[65]

Trabert does not offer a geographical breakdown, but a quick Medline search indicates cases of DP reported all over the world. Besides North America and Europe, other locations include India, Thailand, Russia, and Korea.[66] This may indicate that DP is not a transient illness; Hacking describes transient illnesses as transient to particular time and *places*. But even if DP is not transient, it is still worth examining whether it is culturally bound. It is also possible that the particular vectors that provide an ecological niche for DP, might vary across different cultures. A striking example is a case report from the Bosnian war in which a woman experienced DP after the trauma of multiple

[64] Halprin, Kenneth. "The Art of Self-Mutilation II. Delusions of Parasitosis" *JAMA* 198;2 (1966): 185.
[65] Ibid.
[66] See Srinivasan and Kim, Chuleung et al. "Delusional Parasitosis as 'Folie à Deux'." *Journal of Korean Medical Science,* 18 (2003): 462-5.

rapes.[67] Clearly the "release" desired by this patient is very different than the "release" that DP might provide a suburban housewife in New Jersey.

Unfortunately Trabert does not report how many cases exhibited "folie á deux", which means madness shared by two or "folie á famille", madness of the family. But in 1978 Skott's review of 354 cases found that 25% exhibited "folie á deux" suggesting that DP can be a contagious mental state.[68] DP can also lead to very dangerous behavior. In 1987 Hunt and Blacker reported the case of a 70 year old man who set fire to his flat, and then flooded his replacement accommodations in an attempt to get rid of the infestation of bugs that he believed were plaguing him.[69] There are also reports of dangerousness attached to cases of "folie á deux". In 1992 Bourgeois et al. reported a case that began in the 1960s of delusional parasitosis that involves folie á deux and attempted murder of a family doctor.[70] A 58 year-old French woman tried to kill her general practitioner after he had refused to treat her for what she believed were small animals swarming under her scalp and crawling under her skin. She was "compulsorily admitted to hospital in 1967 after twice shooting (and missing) her family doctor with a hunting gun. Following the attempts, she proceeded to inflict minor injuries to his head with a stick."[71] Apparently the doctor did not press charges, but the patient was admitted to a mental hospital where she had been since the follow-up by Bourgeois et al. 24 years later. Until she was admitted to the hospital, her husband shared her beliefs

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[67] Oruc, Lilijana and Pamela Bell. "Multiple Rape Trauma Followed by Delusional Parasitosis: A Aase Report from the Bosnian War." *Schizophrenia Research*, 16 (1995): 173-4.
[68] Skott, A.. "Delusion of Infestation: Ekbom's Syndrome." *Report No. 13 from the Psychiatric Research Center*, University of Goteborg. 1978.
[69] Hunt, N. J. and V. R. Blacker. "Delusional Parasitosis." *British Journal of Psychiatry*, 150 (1987): 713-714.
[70] Bourgeois, M. L., P. Duhamel and H. Verdoux. "Delusional Parasitosis: Folie a Deux and Attempted Murder of a Family Doctor." *British Journal of Psychiatry* 161 (1992): 709-711.
[71] Ibid., 710.

and he had threatened the doctor himself. Attempts were made to treat and release her, but without success. She had tried to commit suicide several times and she suffered from cognitive impairment and tardive dyskinesia. Bourgeois et al. also report anecdotally about a woman in Alameda County who killed her doctor after he referred her to a psychiatrist. These cases are shocking and certainly rare, but they do speak to the desperation that many patients feel.

Other cases seem much more typical. A 53-year-old male chemical engineer presented to a dermatologist with a five month history of "pruritic rash that was characterized by pink patches with excoriation on his upper and lower extremities."[72] He reported that the rash began after cleaning out the house of his recently dead mother. There was mold in the basement and the house smelled "damp." Two weeks after cleaning the house he became increasingly itchy on his upper extremities and trunk. "He believed that he had inhaled 'mole spores' that, after having infected his entire body, were causing the pruritus. He subsequently removed some of his skin with a sharp blade and examined it under a microscope, revealing white spots that he believed were 'fungus'."[73] The first dermatologists he saw for treatment prescribed topical treatments, which did not relieve his suffering. When he presented at the clinic of Meehan et al. he brought his laptop and a showed a prepared presentation of photographs of his skin. The doctors examined skin scrapings and found no evidence of organisms. "He was diagnosed as having delusions of infestation and irritant dermatitis

[72] Meehan, William J., Sonia Badreshia, and Christine L. Mackley. " Successful Treatment of Delusions of Parasitosis with Olanzapine." Archives of Dermatology, 142 (2006): 352-355.
[73] Ibid., 352-353.

caused by frequent washing."[74] The patient responded well to treatment with olanzapine and at a three month follow-up appointment reported no rash and no remaining concern with fungal infection.

What would Hacking say about this case? Without any direct interaction with the patient himself, one of the most salient features of the case description seems to be the fact that this was connected with cleaning out his deceased mother's home. Traumatic events can trigger all sorts of different psychological reactions. But why did this patient develop DP instead of mild depression or anxiety? The vectors were certainly in place. DP is widely known and recognized as a disorder. What about cultural polarity? In DP, cultural polarity probably changes depending on the situation, but it is certainly culturally bound. Environmental illnesses like mold poisoning have increasingly gained attention. Maybe this played a role for this patient. Probably the most important vector for this particular patient was "release." Given the death of his mother, his psyche might have been directed to a physical release like a rash as a way of avoiding mental anguish. Of course, all of this is speculation, but when we look at a variety of mental illnesses that seem to be transient, or at least culturally bound, it is not uncommon to find some sort of "trigger" experience that was the beginning causal event for a particular patient.

What can we say more generally about DP and ecological niches? It seems entirely possible that DP is a plausible diagnosis for many people who claim to suffer from Morgellons disease. It may not be transient in the way that Hacking characterizes hysterical fugues, but it can be understood as culturally bound. There are a few reasons

[74] Ibid., 353.

for thinking that it is not transient, although we can only make such definite claims with the benefit of historical hindsight. DP, or something similar to DP, has been part of the medical taxonomy for at least a hundred years and has been reported in a wide variety of places. It is entirely possible that in fifty years, DP will disappear as a diagnosis the same way that hysterical fugue did. It's also possible that DP is not as closely tied to place as hysterical fugue was tied to Europe. This may have to do with the breaking down of cultural and geographical boundaries, or it could have more to do with the nature of the ecological niche that DP finds.

How do the vectors of medical taxonomy, cultural polarity, observability, and release play out for DP? Medical taxonomy is pretty straight forward—this is a diagnosis that has been discussed and recognized for more than a hundred years. It is clear that psychiatrists and dermatologists are interested in this disorder, although their interest may be for different reasons. The emergence of Morgellons disease has invigorated new discussion in dermatology, in particular, with renewed attention to dermatology's understanding of mental disorders and the often close interaction between dermatologic and psychiatric disorders. The distinction between primary and secondary DP also affects the taxonomy issue. DP can be secondary to some other psychiatric illness, like schizophrenia. But it is also quite often diagnosed as "pure" or "primary" meaning that it comes about on its own, not caused by some other psychiatric illness. If most cases of DP were secondary, it would be more likely that the taxonomy would shift and DP would be subsumed by the illnesses to which it is secondary.

The vector cultural polarity is a little more difficult to identify. Cultural polarity might vary for DP depending on location. The cultural polarity that helps provide a

niche for DP in Thailand may be different from the cultural polarity that helps provide a niche for DP in San Francisco. But one possibility is to think about what Hacking calls a "romantic opening up of possibilities."[75] For a fuguer like Albert, travel provided such a thing. In the 1970s, "worries about identity and the plethora of new identity options" provided such a thing for multiple personality disorder. These are on the romance/virtue end. Today, remarkable advances in technology provide a romantic opening up of possibilities. But at the vice end are fears about pollution, unhealthy food, uncleanness, and the danger of drug resistant bacteria that could take over the whole world. Throw in speculation about rogue nanotechnology and we have a great horror film.

Observability and release are easier to talk about. First, observability is very straightforward in DP. Patients present with lesions, sores, and rashes. The evidence collected by patients is also part of observability. A patient presents evidence to her physician in the form of fibers, but the physician dismisses it as illegitimate. The release vector may also vary, but like other modern controversial diagnoses like fibromyalgia and chronic fatigue syndrome, it is plausible that DP offers a release from the pressures of modern life.

One of the most fascinating aspects of Hacking's discussion is one that he barely dwells on. It was not Albert himself who started a small epidemic of mad travelers in Europe, it was Tissié's *reporting* of Albert that set off the epidemic. This has two aspects. One is that Tissié's reports influenced other physicians to be on the lookout for similar patients. But the other is that stories of mad travelers started to circulate among

[75] Hacking, 96.

common people, which gave men like Albert the very idea (whether consciously or unconsciously) to set off on their own fugue induced travels. Now we call this social contagion—the study of how ideas spread.[76]

A common question is whether those who identify themselves as having Morgellons disease actually have the same diagnosis in common or whether there are a number of different things going on and the symptoms just happen to overlap. Some people say that the fact that so many different people across the country and across the world describe the exact same symptoms and experiences is proof that sufferers are not making this up. If people were making it up, there wouldn't be so much coherency and such strong parallels between the stories (unless people develop the symptoms of Morgellons disease only *after* learning about it—i.e. social contagion).

This is the primary question the CDC investigation is supposed to answer. The idea is that if there really is something going on here, an epidemiological study will find certain markers and characteristics that cannot be explained away by just epidemiological happenstance. In some ways, this sounds similar to the early days of Lyme disease (which is the topic of the next chapter), before there was clear evidence and a specific case definition. But Morgellons disease is also different because it seems to be shaped by things like the Internet (one medium for the spread of ideas). In the 1970s Polly Murray, who helped discover Lyme disease, had to scour her community

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[76] For historical accounts see Mackay, Charles. *Memoirs of Extraordinary Popular Delusions.* London 1841. Contemporary accounts include Gladwell, Malcolm. *The Tipping Point: How Little Things Can Make a Big Difference*. New York: Back Bay Books, 2002. Lynch, Aaron. *Thought Contagion: How Belief Spreads Through Society.* New York: Basic Books, 1996. Micale, Mark S. *Approaching Hysteria.* Princeton, NJ: Princeton University Press, 1994. Showalter, Elaine. *Hystories: Hysterical Epidemics and Modern Media.* New York: Columbia University Press, 1998.

searching for families with similar symptoms and experiences. In 2003 Mary Leitao started a website and within months found hundreds of others from all over the country who claimed to be experiencing the exact same thing as her son. Maybe the real difference is the way the Internet can bring things about more quickly, but there is a concern that these things feed on one another. By the early 1990s the self-help movement in the United States was very strong, and much of this was evidenced by the proliferation of support groups from everything from addiction to infertility and cancer. These were groups that brought strangers together to share a similar experience and people often found great strength and benefit from these groups. But as the Internet became more prominent, online support groups began replacing face to face support groups. This is partly explained by the convenience of the Internet; in many cases, the Internet makes it much easier to bridge geographical divides. Maybe I do not know of anyone in my local community who suffers the same symptoms I do, but I can log onto a Morgellons chat board and find a whole community waiting for me. But it also raises concerns that people are grasping onto a Google diagnosis. And as we will see with chronic Lyme disease, maybe it will not matter what experts say people have because they have already grasped onto a diagnosis of "Morgellons disease."

It is unlikely that the CDC investigation will settle the debate. What would be the best possible outcome? I think that many who claim to suffer from Morgellons disease would say that the best outcome would be the discovery of evidence that validates their reports: this is "real" and people are not making this up. And then actually discovering the cause which could lead to a cure, or at least some sort of treatment. But this is an unlikely outcome given everything we know so far. It is

probably much more likely that this first investigation will raise more questions than it answers.

Social Contagion, Medical Hysteria, and the Power of Diagnosis

What if it is not really true that people experienced symptoms, looked at the internet, and then had a name for their symptoms? What if what really happens--at least in some cases—is a person comes across Morgellons disease on the Internet or watches a report on Fox News, and *then* develops the symptoms? The history of medicine includes all sorts of phenomena that sounded like psychiatric ailments at first, but are now linked to invasive pathogens. For example, we now know that ulcers are caused by spirochetes and not stress. Syphilis is caused by a bacterial infection, not insanity. And tuberculosis is an infectious disease, not a psychosomatic one. But there are also plenty of examples of phenomena that were originally thought to be infectious or to have some sort of biological basis, but that turned out to be fanned by mass hysteria. At the beginning of the twentieth century it was popular to have all your teeth pulled because you could be suffering from autointoxication from infected root canals."[77] At the time of World War One there was a trend to have much of one's colon removed "on the grounds that your feces were leaking out of your colon and poisoning the rest of your body."[78] These examples sound silly today, but at the time must have struck those who chose them as perfectly reasonable.

[77] Shorter, Edward. *From Paralysis to Fatigue: A History of Psychosomatic Illness in the Modern Era.* New York: Free Press, 1993.
[78] Ibid.

Charles Rosenberg, a medical historian, describes the history and power of diagnosis in medicine. While most people mark the emergence of the germ theory of disease as the transformative moment, he argues that most of the conceptual change had already occurred by the 1860s. Rosenberg explains, "Mastering a vocabulary of disease pictures and being able to distinguish among them have long been fundamental to the physician's role, as such knowledge underlies the socially indispensable tasks of diagnosis and prognosis and the rationalization of therapeutic practice."[79] Disease categories "have always linked knowledge and practice."[80] Germ theories of disease, first articulated in the 1860s and 1870s, proposed that disease and infection were caused by living organisms. These new theories argued for a reductionist and mechanism-oriented way of understanding the body and disease that still dominates medicine today. In order to understand cancer, researchers look at what is causing mutations at a microscopic level. By the end of the 19th century, "a vocabulary of named disease pictures had already become a widespread and largely unquestioned component of Western medicine."[81] Rosenberg argues that diagnosis has always been important in the history of medicine, in particular because it is the mode for linking patient and physician, it legitimates physicians' and the medical system's authority, and it connects the emotional with the physical.

According to Rosenberg specific disease entities are powerful because of their social traction—"their ability to acquire social texture and circumstantiality, to structure and legitimate practice patterns, to shape institutional decisions, and to determine the

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[79] Rosenberg, Charles E. "The Tyranny of Diagnosis: Specific Entities and Individual Experience" *The Milbank Quarterly*, 80;2 (2002): 237-260.
[80] Ibid.
[81] Ibid., 247.

treatment of particular patients."[82] So, while it is common to think of diseases as having some sort of ontological status (people think about cancer as being "real" and something that can be separated from the person who has cancer), the act of diagnosis has incredible social power. It confers social approval on certain sickness roles and structures various bureaucratic interactions. The fact that so many diagnoses are contested (e.g. chronic fatigue syndrome and fibromyalgia) illustrates both the "cultural centrality of the mechanism-defined disease entity as an explanatory category as much as for the moral and political resonance" of these particular illnesses.[83]

Diagnosis plays the function of linking an individual to a social system. Only with a specific diagnosis, does a patient have a specific entry into the medical establishment. Without it, patients wander around from doctor to doctor trying to figure out their ailments. There is no specific connection. But once a diagnosis is conferred, this uncertainty is replaced "by a structured narrative."[84] "Diagnosis is a cognitively and emotionally necessary ritual connecting medical ideas and personnel to the men and women who are its clients. Such linkages between the collective and the uniquely individual are necessary in every society, and in ours the role of medicine is central to such negotiated perceptions and identities. The system of disease categories and diagnosis is both a metaphor for our society and a microcosm of it. Diagnosis is a substantive element in this system, a key to the repertoire of passwords that provide access to the institutional software that manages contemporary medicine."[85]

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[82] Ibid., 250.
[83] Ibid., 246.
[84] Ibid., 255.
[85] Ibid., 256-257.

In the case of Morgellons disease, the power of diagnosis takes on different dimensions. First, the diagnosis itself or the definition of the disease did not come from researchers and physicians. It first came from Mary Leitao, acting out of desperation. She was looking for a way into the medical establishment because she knew that is what she needed to get help for her son. But all of her efforts had been spurned and nothing that the medical establishment was telling her, like "he's fine" or "you're just making this up for attention", fit with her own narrative. The power of naming a list of symptoms is highly evident. There is a huge difference between saying "I have Morgellons disease" and "No one is sure what I have, but it feels like there are bugs crawling under my skin and sometimes I see fibers sprouting out of sores on my arms and legs."

I have suggested that we can use the idea of social contagion and Hacking's understanding of ecological niches and vectors to help us understand what *might* be going on in the case of Morgellons disease and delusional parasitosis. People will resist explanations that do not fit with their already established framework. This was not the case for Albert. He was frustrated by his condition, but there is no evidence that he felt stigmatized by it the way that many people seem to feel stigmatized by DP. The Internet has sped up the process of establishing a narrative framework for people who claim to suffer from Morgellons disease. People need frameworks to make sense of their experiences. People turn to physicians for treatment, but they are also seeking explanations. When reading through many of the various news accounts of Morgellons disease many of the interviews with sufferers are striking. The narratives have much in common. A person begins to experience bizarre symptoms including sores that will not

heal with fibers coming out of them, and feeling like bugs are crawling under their skin. He or she (usually a she) immediately seeks medical treatment, but does not find relief. This then turns into a series of different doctor visits, with growing frustration. And then this person sits down at her computer and types in a search for "sores and colored fibers." All sorts of sites devoted to Morgellons disease pop-up and the person finally has an explanation. Now armed with information, she makes another appointment and arrives at the clinic armed with an explanatory framework. But now her doctor does not trust her—she claims to have a disease that he has never heard of and he is skeptical of any medical information found online. But for the patient, the Morgellons framework is the only thing she has found that makes sense of her experience—both her physical symptoms and also her secondary experiences with a skeptical medical system.

A common remark found in these interviews is that when someone gets diagnosed with DP they often say something like, "Why would I make this up? Before this happened I was healthy, happy, and full of energy. Now I can barely function. If you knew me before this happened, you would not recognize me now." It is unfair to psychologize individuals based on a news media interview, but these accounts share similarities with other diseases, disorders, and syndromes of the last twenty years. When what was eventually called chronic fatigue syndrome first emerged in the early 1990s it was disparagingly called "yuppie flu."[86] The idea was that in American culture, it is unacceptable to just want to take a break from the pressures to succeed and produce more and earn more. But if you are "sick", you have a legitimate reason to

[86] Shorter, 310.

take a break. The symptoms are very real in that the person is actually experiencing them (the symptoms themselves are not delusions), but they may be psychosomatic. Similarly, the physical symptoms of anxiety are very "real", e.g. a red face, excessive perspiration, and a dry mouth, but they are caused by psychic distress. When I was in first grade I had a stomach ache every single day. The pain in my stomach felt very real, but undoubtedly it was caused by the anxiety and dread I felt about going to school. Having a physical symptom gave me a legitimate reason to avoid the unpleasant (for a little while at least until my parents caught on, took me to a doctor to make sure there was not anything physically wrong with me, and then insisted I go to school even with a stomach ache). Physical maladies give us legitimate excuses. And often the underlying reasons are unknown to the person him or herself. Maybe this is what is going on with a lot of people who identify as having Morgellons disease. The fact that someone does not think they have a mental illness or does not want to have a mental illness, does not dismiss the possibility that Morgellons disease and DP have found a home in a particular ecological niche. Questions about how patients and cultures shape diagnosis and treatments will remain central in the following chapters of this dissertation.

CHAPTER TWO

Chronic Lyme Disease

Abstract

Lyme disease was first identified in Connecticut in 1977 through collaboration between patients and researchers. It is a bacterial infection spread to humans by deer ticks. Since its discovery, a great amount of research has been done, improving diagnosis and treatment of acute Lyme disease, but there is much debate over chronic Lyme disease. Chronic Lyme disease refers to a condition where a patient has been treated for acute Lyme disease using standard treatment protocols, but who still experiences some of the symptoms associated with acute Lyme disease (such as headache, fatigue, and joint pain). A majority of Lyme researchers and treating physicians believe that the definition of chronic Lyme disease is far too wide, and that in fact the condition is extremely rare. They argue that these patients are suffering from something else—it is not related to Lyme disease. But over the last two decades a growing movement involving patients, their physicians, and some politicians, have argued that these researchers and clinicians who reject chronic Lyme disease are wrong. The activism of these patients plays an enormous role in this debate, just like we saw in the previous discussion of Morgellons disease, but what is unique in the story of chronic Lyme disease is the *way* that patients have marshaled a tremendous amount of legal and social power and brought it to bear on the practice of medicine. This chapter begins with the story of acute Lyme disease and the role of patients in its discovery. Next, I look at some of the key debates over chronic Lyme disease, in which patients play a central role, but I also emphasize how debates in the medical literature between physicians and the role of financial interests have shaped this debate. Finally, I examine the way that chronic Lyme disease patients and their physicians have claimed a large amount of social power and how this power has produced specific political and legal gains. I conclude the chapter by discussing the effects of chronic Lyme disease on the practice of medicine and the moral authority of physicians.

Introduction

On August 5, 1993 the Senate Labor and Human Resources Committee held a hearing “to examine problems associated with diagnosis and treatment of Lyme

disease" and assess prevention and control activities.[1] A young boy in a wheelchair appeared at the hearing wearing headphones to block out other voices, which sound deafening because of neurological damage from a Lyme spirochete. Referring to chronic Lyme disease patients, the boy spoke into a microphone, "We can't think. We can't sleep. We need you."[2] Dr. Allen Steere, the discoverer and leading researcher on Lyme disease, tried to explain why misdiagnosis of chronic Lyme disease is so prevalent only to be interrupted by shouts from the gallery: "He's wrong! He's wrong!"[3]

By 1993, scientific and medical debates over acute Lyme disease were becoming more and more settled. Nearly 20 years earlier, in 1975, Dr. Steere, then a rheumatology fellow at Yale University, had begun to investigate reports of sick children in various parts of Connecticut. Children and adults were reporting symptoms including rashes, swollen knees, stiff joints, and sore throat. Many of the children were being diagnosed with juvenile rheumatoid arthritis, but it did not make sense to Steere that so many children in one particular area would have this rare disease. Two years later, Steere and his team gave the condition the name Lyme disease (named after the endemic area of Lyme Connecticut) and suspected it was caused by infected deer ticks. In 1982 Willy Burgdorfer's group at the Rocky Mountain Labs identified the transmitted bacterium *Borrelia burgdorferi* in the intestinal track of an adult deer tick.

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[1] "Lyme Disease: A Diagnostic and Treatment Dilemma." Committee on Labor and Human Resources. Senate Hearing, 5 August 1993.
[2] Grann, David. "Stalking Dr. Steere Over Lyme Disease." *New York Times*, 17 June 2001.
[3] Ibid.

The CDC began disease surveillance in 1982 and in 1991 Lyme disease was classified as a nationally reportable disease.[4]

Today, acute Lyme disease refers to standard cases caught early, while late Lyme disease refers to cases caught late, with the main experiential difference between the two being that neurological symptoms appear more common in late Lyme disease.[5] Standard therapy in both acute and late cases is a brief course of antibiotics. At the time of the Senate hearings, however, an increasingly vocal and active group of Lyme disease patients and physicians were claiming that the standard course of therapy did not cure their disease and they were actually suffering from chronic Lyme disease. These were the people shouting down Dr. Steere.

People such as those at the Senate hearings are often desperate for relief from debilitating ailments which they firmly believe are caused by chronic Lyme disease. Typically, such a person was diagnosed with acute Lyme disease, received the standard antibiotic treatment, and initially felt better, only to have some of the symptoms return months or years later. Because the symptoms are similar to their experience with acute Lyme disease, they often assume that their present condition can be explained by the same cause. For most, laboratory tests for an active Lyme spirochete have proven negative (even if their acute Lyme disease was confirmed with a positive test) and they have been to many doctors seeking answers. Some who shouted from the gallery that day at the Senate hearing participate in organized Lyme disease support groups in various parts of the country and on the Internet. At these meetings and via online

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[4] Edlow, Jonathan A. *Bull's Eye: Unraveling the Medical Mystery of Lyme Disease*. New Haven and London: Yale University Press, 2003. Weintraub, Pamela. *Cure Unknown: Inside the Lyme Epidemic*. New York: St. Martin's Press, 2008.

[5] Centers for Disease Control and Prevention. "Surveillance Summaries." *MMWR* 57 (2008): 1-9.

discussion boards, people who believe they are suffering from chronic Lyme disease share advice on the doctors who are most willing to take their cases seriously, and in particular, which doctors positively receive their requests for long-term antibiotics (or which physicians are themselves advocates for long term antibiotic therapy). Many see antibiotics as their lifeline: the only treatment that gives them enough energy to get out of bed. Yet a diagnosis of chronic Lyme disease also seems to be a lifeline of another sort: a lifeline to their identity as a victim of a debilitating disease.

Since the Senate hearings in 1993, the debate over chronic Lyme disease has made little progress. If anything, the two sides have become more entrenched in their positions. To understand why this is so, it is necessary to understand how patient activism challenges traditional medical authority. This challenge was also evident in the story of Morgellons disease, of course. But Lyme disease is unique in that patients also played a central role in the discovery of the acute disease, the cause and pathophysiology of which is relatively undisputed. Lyme disease started as a story about the great benefits of patient activism and patient-physician collaboration. But at some point that collaboration went seriously wrong.

Chronic Lyme disease is not just like Morgellons disease on a larger scale, with a longer timeline; patient activism is just one part of the story. Chronic Lyme disease differs from Morgellons disease in several important ways, which I will illustrate in this chapter. These differences show how chronic Lyme disease has in many ways rewritten the rules of medicine. The unique aspects of chronic Lyme disease include the role of acute Lyme disease in its genesis, genuine debates in the medical literature between physicians, and the role of financial interests in the spread of the disease. These factors

have led to the most significant feature of the rise of chronic Lyme disease: the way that patients have marshaled social and legislative power and brought it to bear on the practice of medicine.

Acute Lyme Disease and Patient Activism

The discovery of acute Lyme disease is a classic case of medical detective work that benefited from close collaboration between researchers and patients.[6] Early sufferers of what came to be termed Lyme disease were active in its identification. Frustrated sick people petitioned doctors and public health officials for help, unwilling to take no for an answer. One of these sufferers was Polly Murray, of Lyme, Connecticut, who had been sick since the 1960s with symptoms including rashes, swollen knees, stiff joints, and sore throat.[7] By 1975 she had consulted over two dozen doctors before seeing Dr. Steere. Murray's story did not make sense to Dr. Steere. Her symptoms did not fit any known pathology. She was sick with something going undetected by standard medical tests and she had collections of case histories she had collected on her own. Murray had been keeping detailed records of her symptoms as well as her children's for years. And she was not the only one who was sick; these case histories indicated that whatever was going on was also prevalent among her neighbors.[8] Many of the physicians Murray visited dismissed her concerns as those of a hysterical woman. Once when she suggested to a physician that there must be something larger going on since everyone in her family had the same symptoms, the

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[6] See Roueche, Berton. *The Medical Detectives.* New York: Plume, 1991.
[7] See Murray, Polly. *The Widening Circle: A Lyme Disease Pioneer Tells Her Story.* New York: St. Martin's Press, 1996.
[8] See Murray chapters 6-10 and Weintraub 43-47.

physician sarcastically retorted, "You know, Mrs. Murray, sometimes people subconsciously want to be sick."[9] But Murray believed that there must be something larger going on—she just needed to find someone who would take her concerns seriously. Steere was the first physician who was interested in all of her information. As he tried to piece together this puzzle, Steere relied on Murray's authority as patient.

At the same time Judith Mensch (also of Lyme, Connecticut), trying to understand why her daughter and other children in the neighborhood were being diagnosed as having juvenile rheumatoid arthritis (JRA), contacted the state health authorities in Connecticut and the CDC.[10] She was also referred to Steere.[11] He began a formal study of the clusters of children diagnosed with JRA. To guide the study, Steere came up with a definition of the disease. To be entered into the study, patients needed to have experienced arthritis, characterized by brief, recurrent attacks of swelling and pain in a few large joints. The list of symptoms was left purposely wide. Steere understood that these symptoms could describe all sorts of things, but they also appeared to be the only symptoms that these children had in common. He looked at the clusters of children diagnosed with JRA, developed a definition of the disease, and then went back to the same group of children. The first study group included thirty-nine children fitting this description and Steere quickly ruled out JRA. JRA occurs randomly in the population at a rate of 1 to 10 per 100,000, but this new disease was striking at a rate a hundred times more frequently than that. Through formal patient interviews, Steere was able to document what Murray and Mensch had already reported:

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[9] Murray, 35.
[10] Ibid., 132-133.
[11] See Aronowitz, Robert A. Making Sense of Illness: Science, Society, and Disease. Cambridge University Press, 1998, pp. 63-64.

"geographic clustering within the communities, as well as seasonal and familial clustering."[12] In this group of thirty-nine, half of the children lived on only four roads and most had become sick in the summer or early fall.

The bacterium *Borrelia burgdorferi* occurs naturally in hosts like mice, squirrels, and other small vertebrae. When deer ticks feed on the blood of infected hosts, they can then transmit the bacterium to other hosts, including humans. Deer are not infected by *Borrelia burgdorferi*, but they play a role in transporting ticks and maintaining tick populations. With suburban sprawl, humans are increasingly likely to come in contact with infected ticks which presumably helps account for the spread of Lyme disease. The symptoms first described by Murray and Mensch turned out to be a classical infectious disease.[13]

However, it quickly became clear to Steere that Lyme disease included more than just the arthritis-like symptoms he first observed. There seemed to be a common early symptom that "branded" the disease: a "bull's-eye" rash. This increased the clinical spectrum and in a 1977 publication Steere and his group reported that arthritis was just one of several possible outcomes following a bull's-eye rash. Reporting on thirty-two Lyme patients with arthritis, the rash, or both, Steere and his group also included a host of broad symptoms including malaise, fatigue, chills and fever, headache, stiff neck, backache, muscle aches, nausea, vomiting, and sore throat.[14] This list of symptoms was so general that Steere knew it could not be used to diagnose Lyme

[12] Weintraub, 49.
[13] See CDC 2008.
[14] Weintraub, 50.

disease so he instructed physicians that the most important diagnostic marker was the skin lesion and without it, geographic clustering was the most important.[15]

Early research focused on identifying the vector and bacterium, but by 1980 clinical research showed that antibiotic treatment worked for acute Lyme disease.[16] Steere and his team observed patients for four consecutive summers. During the summer epidemics of 1977 and 1979 they treated rash patients with 7 to 10 days of antibiotics, but they did not treat them during the summers of 1976 and 1978.[17] The data showed that the rash resolved more than twice as rapidly in treated patients and that treated patients developed arthritis at less than half the rate of untreated patients. Further research showed that slightly longer courses of antibiotics drastically reduced the rate of arthritis following a rash. It was also established that the arthritis is really a late manifestation of the multisystem disease. The arthritis reported by Murray and Mensch was probably the result of years of untreated infection. In cases caught and treated early, the arthritis symptoms rarely occurred.

Without the collaboration between Murray and Mensch and Steere it is possible that the discovery of Lyme disease would have been greatly delayed. The activism of Murray and Mensch brought this disease to the attention of medical researchers. But success also required a medical authority (in this case Steere) that was willing to seriously consider and listen to the concerns of lay people. But as more and more scientific evidence was produced, including the discovery of the spirochete and clinical trials showing the effectiveness of antibiotics in treating Lyme disease, the need for

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[15] Ibid.
[16] See Edlow, 119.
[17] Weintraub, 51.

patient input waned. In the discovery stage of the disease, researchers relied on sufferers to help them produce and identify the pieces of the puzzle. Once researchers thought the puzzle was essentially complete, the need for input disappeared.

As word of this new disease spread, physicians began to identify more and more cases of Lyme disease, particularly in the most endemic areas in the northeast and upper-Midwest. Many clinicians had been seeing Lyme disease in their practices for years, but now they knew what to call it and how to treat it. The CDC initiated surveillance for Lyme disease in 1980 and the first summary of 226 cases was published in 1981.[18] In the first five years of surveillance (1982-1986) the number of cases reported increased by a factor of 32, making Lyme disease a major health concern. But case definitions and reporting practices varied within states and between states. In 1991 the Council of State and Territorial Epidemiologists (CSTE) designated Lyme disease as a nationally notifiable disease and published a standardized surveillance case definition. This case definition was not meant to be used as absolute criteria for clinical diagnosis, but in reality it often is used in clinical diagnosis. The clinical description given in 1990 is "A systemic, tick-borne disease with protean manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities. The best clinical marker for the disease is the initial skin lesion, erythema migrans, that occurs among 60%-80% of patients."[19] The clinical case definition requires Erythema migrans (the bull's-eye rash described by Steere) or at least one late manifestation AND laboratory confirmation of infection. Late manifestations include things like "Recurrent, brief

[18] Centers for Disease Control and Prevention. "Lyme Disease—United States." *MMWR*, 30 (1981): 489-927.
[19] Centers for Disease Control and Prevention. "Lyme Disease—United States." *MMWR*, 39 (1990): 873-875.

attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints" and neurological involvement (but excludes headache, fatigue, and stiff neck).[20] Updated versions of the CDC definitions remain consistently the same.[21]

Acute Lyme disease is now the most common tick-borne disease in the United States. During 1992-2006, 248,074 cases of Lyme disease were reported to the CDC. The number of cases increased 101% from 9,908 in 1992 to 19,931 in 2006. It has been reported in all fifty states and is also found in parts of Europe and Asia. However, in this period (1992-2006) 93% of cases were reported from just ten states (Connecticut, Delaware, Massachusetts, Maryland, Minnesota, New Jersey, New York, Pennsylvania, Rhode Island, and Wisconsin).[22]

Clinically, the general features of Lyme disease that came out early in its discovery remain firm. Studies show that 70-80% of patients develop the characteristic bull's-eye rash at the site of the tick bite within 30 days and this rash is often accompanied by fatigue, fever, headaches, mild stiff neck, arthralgia, or myalgia. The standard treatment recommended by the Infectious Diseases Society of America (IDSA) and endorsed by a range of professional groups is two to three weeks of antibiotics treatment.[23]

The CDC also includes a definition of late Lyme disease (caught late, distinct from chronic Lyme disease), which is more pronounced. According to the CDC

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[20] Ibid.
[21] See CDC 2008.
[22] Ibid.
[23] Wormser, Gary P. et al. "Practice Guidelines for the Treatment of Lyme Disease." *Clinical Infectious Diseases,* 31 (2001): 1-14.

symptoms may not appear until weeks, months, or years after a tick bite and may include arthritis (pain and swelling in one or more large joints), nervous system involvement like nerve paralysis and meningitis, cardiovascular irregularities, and neurologic involvement like problems with memory, fatigue, headache, and sleep disturbances. Late Lyme disease sometimes requires treatment with intravenous antibiotics for four weeks or more. The rate of late Lyme disease is low compared with acute Lyme disease. The CDC emphasizes that a diagnosis of acute or late Lyme disease must take into account both a patient's clinical presentation and the results of tests for *Borrelia burgdorferi* (the bacterium).[24] The laboratory tests for the bacterium can be useful, but they are also controversial.

Laboratories use a two-step method to analyze antibodies formed against Lyme spirochetes in human blood. The first test is an enzyme-linked immunosorbent assay (ELISA). If a patient tests positive on the ELISA, then the lab will also use the Western immunoblot to test for antibodies. These tests are indirect. They do not actually show the bacterium. Developing tests that directly detect *Borrelia burgdorferi* has been difficult because the bacteria cannot be easily cultured except under very specific laboratory conditions and the bacteria are also unlikely to be found in the typical things cultured like blood, urine, and body tissues. Instead, these tests assess the body's immune response by looking for the antibodies that the body produces to fight the infection. Both tests frequently yield false negative and false positive results because the timing of the tests can play a huge role in whether the test is positive or negative. One study showed that "even patients with advanced disease and high levels of

[24] See CDC 2008.

antibody failed the Lyme ELISA between 9 and 69 percent of the time depending on the laboratory used" and patients who passed the Western blot test, failed the ELISA screening test 30 percent of the time.[25] These tests were first developed in the 1980s and unfortunately there has not been much improvement since then. The Lyme Urine Antigen Test, developed in the last few years, purports to be more accurate, but it has not been approved by the FDA and the CDC does not recommend it. Because the tests are not completely accurate, emphasis is placed on the importance of clinical diagnosis for both acute and late Lyme disease.[26]

A lot has changed since Molly Murray and Judy Mensch first collaborated with Dr. Steere in 1975. In a very short time Lyme disease awareness has increased significantly throughout the United States. Within just a few years, a disease that was completely unknown became common knowledge. Although the CDC expresses concern over the continued emergence of Lyme disease and underscores the need for tick avoidance and early treatment,[27] there is strong belief in the medical community that acute Lyme disease and the much rarer late Lyme disease are both easily diagnosed and easily treated. Patient activism made the discovery possible, but medicine has taken over by doing what it does best—diagnosing and treating an infectious disease. But an expanding group of patients and physicians do not agree that it is so straightforward. They argue that the medical community has ignored a larger and much more harmful aspect of Lyme disease—chronic Lyme disease.

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[25] Weintraub, 116.
[26] For more on the tests see Weintraub, 10-11 and 115-116. See also Edlow, 175-178.
[27] See CDC 2008.

Chronic Lyme Disease and Debates Between Physicians

Beginning in the late 1980s physicians began to see patients who had been treated for acute Lyme disease, but who either did not seem to get better or who recovered for a short time after receiving antibiotic treatment, only to relapse with the same symptoms. Some physicians began to feel angry about the state of affairs. For example, Kenneth Liegner of Armonk, New York is a critical care specialist who, in 1988, started to see a specific group of patients who did not get well. Liegner found that more and more local doctors were diagnosing patients with fibromyalgia, chronic fatigue syndrome, depression, or multiple sclerosis without considering the proper evidence. He believed that these physicians should perform "the requisite differential diagnosis for Lyme disease as an alternative, more treatable, cause of their ills."[28] Soon Liegner had patients streaming into his office who had been allowed to decline and become chronically ill with what he believed was untreated Lyme disease. He diagnosed many of these patients with Lyme disease and treated them with long courses of antibiotics, sometimes for months, and found that most of them improved. Some patients remained sick, however, and Liegner believed that this was the result of delayed treatment. They had been declining for so long that permanent damage remained from the infection.[29]

In the previous section of this chapter I described the relatively quick "settling" of debates over acute Lyme disease with the help of patient activism at the beginning of its discovery. But at the same time in the late 1980s and early 1990s that acute Lyme disease seemed to be a settled issue, concerns about chronic Lyme disease began to

[28] Weintraub, 133.
[29] Ibid.

emerge from both patient groups and some physicians like Liegner. Since the late 1980s/early 1990s, the key focus of patient concern has been on chronic Lyme disease, both its diagnosis and its treatment. Chronic Lyme disease**,** or post-Lyme disease syndrome, are terms for patients "who have chronic symptoms after what is thought to be adequate antibiotic therapy."[30] [31]

Some patients think they have chronic Lyme disease because they were first diagnosed with acute Lyme disease and recovered after standard antibiotic treatment, only to have their symptoms return weeks, months, or even years later. Of course, it is possible to become reinfected by another tick—the body does not produce immunity to Lyme disease once a patient has had it. But many people who think their symptoms have returned after a positive diagnosis find that when the lab tests are done again, the tests come back negative. This leads many physicians to conclude that what the patients are experiencing is not a return of Lyme disease. Other patients were never diagnosed with acute Lyme disease, but they become ill with the symptoms of Lyme disease (fatigue, swollen joints, headache, etc.). Either the patient comes to the conclusion that they must have Lyme disease (maybe by talking with friends who have had Lyme disease or coming across a definition on the Internet) or they visit a physician who makes the diagnosis.

At the heart of the debate over chronic Lyme disease is a disagreement about the cause and treatment of a particular group of people with unexplained symptoms. The

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[30] Rowe, P. "Chronic Lyme Disease: The Debate Goes On." *The Lancet*, 355 (2000): 1436.

[31] "Adequate antibiotic therapy" is currently identified as no more than four weeks. The CDC tracks acute Lyme disease, but its surveillance case definition does not include chronic Lyme disease and it is unclear how common the condition is. The CDC *MMWR* on surveillance for Lyme disease published October 3, 2008 makes no reference to chronic Lyme disease.

patients are clearly suffering, yet they lack the required signs and designated laboratory results for a diagnosis of Lyme disease. In addition, many of these same patients have seen physicians who have diagnosed them with conditions such as fibromyalgia, chronic fatigue syndrome, or depression. Like patients who claim to have Morgellons Disease, these patients often reject their diagnosis in favor of another one which they believe to be more accurate. Unlike the case of Morgellons Disease, however, which has been almost entirely driven by patients, the debate over chronic Lyme disease has also taken place between doctors.

Beginning in the late 1980s, physicians themselves were expressing disagreements with each other about the cause, treatment and pathophysiology of chronic Lyme disease. On one side are skeptics such as C. Ben Beard, Ph.D., chief of the Bacterial Diseases Branch of the Division of Vector-Borne Infectious Diseases of the CDC. Beard says, "These people are very sick, and we feel great compassion for them. Their lives have been destroyed, but based on their symptoms, we're just not convinced that they have Lyme disease."[32] One the other side of the debate are supporters like Dr. Brian Fallon, a psychiatrist and director of the Lyme and Tick Borne Diseases Research Center at Columbia University. He says, "Patients without objective signs can still have symptoms of Lyme disease—cognitive problems, fatigue, joint pain, mood swings. Because those symptoms weren't objectified early in the history of the disease by the specific specialties first involved, many doctors still think they don't

[32] Weintraub, 9.

count [but they do]. There are other ways of defining illness and objectifying signs and symptoms of disease."[33]

The debate between physicians came about because there was a tension between what researchers were reporting in the literature and what some physicians were seeing in their clinics. The medical literature was sending a simple and clear message: acute Lyme disease is easy to diagnose and easy to successfully treat. If a patient has a bull's-eye rash, she probably has Lyme disease and you should treat her with antibiotics. If a patient has no rash, but lives in an endemic area, has some of the symptoms like headache or fatigue, and tests positive on the ELISA and Western blot tests, she probably has Lyme disease and you should treat her with antibiotics. If a patient has some of the symptoms, but no history of rash and negative test results, it is not Lyme disease.

But physicians in endemic areas found different clinical evidence. If a patient had negative test results, but a treating physician like Dr. Liegner, suspected it was Lyme disease, he would prescribe antibiotic treatment anyway. And Liegner and others were starting to see that patients who did not meet the strict diagnosis criteria for Lyme disease, nonetheless improved with antibiotics. These were patients who resembled other Lyme disease patients in every way, except they had negative lab results. The history and symptoms fit. This anecdotal clinical evidence made them begin to suspect that there was something else going on here.[34]

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[33] Ibid.
[34] Ibid., 121-125.

In 1993 (the same year as the Senate hearings) *JAMA* published Steere's article "The Overdiagnosis of Lyme Disease."[35] Steere reported a study of 788 patients who had been referred to his clinic as Lyme disease sufferers. He concluded that 23 percent had active Lyme disease. Another 20 percent once had Lyme disease but no longer did; instead he believed that they had some other syndrome triggered by Lyme disease like chronic fatigue syndrome or fibromyalgia. Patients in this group had negative Lyme test results.[36] The remaining 57 percent never had Lyme disease at all. So, at the very time that the patient community and their sympathetic physicians were claiming that Lyme disease is drastically underdiagnosed and undertreated, the discoverer and leading researcher and expert on Lyme disease was claiming the opposite to be true.

Steere does not deny that chronic Lyme disease is possible, but he thinks that it is extremely rare and that the majority of patients who claim to have chronic Lyme disease are actually suffering from something else. As recently as 2007 Steere and others wrote in the *New England Journal of Medicine* that "Chronic Lyme disease is the latest in a series of syndromes that have been postulated in an attempt to attribute medically unexplained symptoms to particular infections."[37] Steere believes that the assumption that chronic symptoms are caused by persistent infection is not supported by laboratory studies or controlled treatment trials. He believes that chronic Lyme disease is a misnomer and that prolonged antibiotic treatments are unwarranted.

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[35] Steere, Allen et al. *JAMA*, 269 (1993): 1812-1816.

[36] Some have criticized Steere's methodology for this group in particular and argue that if he had employed a wider definition of chronic Lyme disease to start with, he would have been able to distinguish between those with chronic Lyme disease and those with something else like chronic fatigue syndrome or fibromyalgia.

[37] Feder, Henry M. et al. "A Critical Appraisal of 'Chronic Lyme Disease.'" *New England Journal of Medicine*, 357 (2007): 1422-30.

For Steere and others, the evidence against chronic Lyme disease can be categorized into signs and symptoms, laboratory tests, treatment, and a final "other" category, with various studies cited to support each claim. First, there are no objective clinical signs present (like the rash or inflammation) and the subjective symptoms reported (like fatigue and headache) are common in people who have never had Lyme disease. Second, the ELISA and Western blot tests show no evidence of persistent infection. Third, controlled treatment trials show no response to antibiotic therapy. And fourth, certain animal studies show no active infection and there's a "lack of precedent for the use of long-term antibiotic treatment in other spirochetal infections."[38] The other side has responses to each of these claims, which I will summarize in the next few paragraphs.

First, the claim by Steere and others that there are no objective clinical signs present in chronic Lyme disease (like the rash or inflammation) speaks to debates over the definition of Lyme disease. The most recent controversy over the definition came in October 2006 when the Infectious Diseases Society of American (IDSA) updated its treatment guidelines for Lyme disease.[39] These guidelines are more restrictive than earlier ones from 2001 and require either an erythema migrans or positive laboratory tests for diagnosis. But the other side counters that since according to the CDC up to 20% of patients never develop the rash, this objective criterion will miss a lot of cases. The IDSA panel also argued that those symptoms claimed by chronic Lyme disease sufferers are just as present in the general "healthy" population: "the presence of

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[38] Ibid., 1428.

[39] Wormser, Gary P. et al. "The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America." *Clinical Infectious Diseases,* 43 (2006): 1089–1134.

arthralgia, myalgia, fatigue, and other subjective symptoms after treatment for Lyme disease must be evaluated in the context of 'background' complaints in a significant portion of individuals."[40] This takes us back to Steere's original defining of the disease in 1977. Steere knew that these subjective symptoms were too general to be usable in diagnosis. These are symptoms that are not only present in all sorts of diseases, but are also present in the general population. There are all sorts of reasons for feeling fatigue. Fatigue *can* be caused by infectious disease or cancer treatments, but it is also the effect of a busy and stressful life. But the fact that these symptoms are too subjective to be standardized across the population does not mean that they are not important in the clinical diagnosis of specific individuals. Steere and others say that chronic Lyme disease does not meet the definition of Lyme disease. The other side argues that they are using the wrong definition.

The second main point of debate concerns laboratory tests. Stricker argues that "current commercial Lyme serologic tests are not sensitive enough for diagnosis, especially during the later stages of disease."[41] The pro-chronic Lyme disease side argues that by requiring an erythema migrans or positive laboratory tests for Lyme disease diagnosis, the disease definition has been made so narrow that cases that should be included are left out.[42] Laboratory tests are one part of objective clinical criteria, but there is great debate over the accuracy of these tests and evidence that there are at least some false positive and false negatives. So, a patient who falls into the 20-percent group that never exhibits an erythema migrans and then also falls into the false negative

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[40] Ibid., 1115.
[41] Stricker, Raphael. "Counterpoint: Long-Term Antibiotic Therapy Improves Persistent Symptoms Associated with Lyme Disease." *Clinical Infectious Disease*, 45;2 (2007): 149-157, 150.
[42] See Feder et al.

group, will be completely missed until her physician deviates from the IDSA guidelines and pays close attention to the subjective symptoms and geographical history.

For all the debate about diagnosis, however, the most contentious debates about chronic Lyme disease concern antibiotic treatment. Throughout the 1990s debates in the medical literature were becoming more and more heated. Clinicians were claiming anecdotal evidence of treatment success, which they believed pointed to the existence of chronic Lyme disease, while researchers like Steere were arguing that anecdotal "bedside" evidence simply could not stand up to scientific scrutiny. Steere and his allies had scientific backing for their claims. During this period, the NIH funded three controlled treatment trials focused on chronic Lyme disease.

The first two studies, which were reported in *The New England Journal of Medicine* in July 2001, found that aggressive and prolonged treatment with antibiotics does nothing to alleviate the symptoms associated with chronic Lyme disease.[43] The trials were halted after a planned interim analysis when the data suggested no difference in efficacy between intravenous and oral antibiotics and placebo. One trial enrolled patients who were seropositive for IgG antibodies to *Borrelia burgdorferi* at time of enrollment and the other enrolled patients who were seronegative at time of enrollment. In both trials, patients had to have well-documented, previously treated Lyme disease. Patients in both studies received intravenous antibiotics for 30 days and then oral antibiotics for 60 days or matching placebo. These studies support Dr. Steere's

[43] See Klempner, Mark S. et al. "Two Controlled Trials of Antibiotic Treatment in Patients with Persistent Symptoms and a History of Lyme Disease." *New England Journal of Medicine,* 345 (2001): 85-92.

recommendation that patients be treated symptomatically, rather than with prolonged courses of antibiotics.[44]

However, these empirical findings have not changed the resolve of patients who claim to have chronic Lyme disease and the physicians who treat them. For example, Dr. Same L. Donta of Boston University Medical Center, who has treated hundreds of patients with long-term antibiotics, suggests that the antibiotics were not given long enough. He also says that if he were designing the trial, he would have chosen different antibiotics. He believes that it is possible that these studies only show that *this* particular treatment does not work.[45] The failure of one treatment certainly does not predict the failure of similar treatments.

The responses from patients and sympathetic physicians to these studies illustrate the central role of the vector of medical taxonomy and disagreements about medical authority. One group is saying, "Look, we did the studies and there is no evidence for the efficacy of treatment patients with long-term antibiotics. If these people actually had chronic Lyme disease, then those in the therapy arm of the experiment would have improved. They did not improve, so the case is closed; this confirms what we have been saying all along." The other side is saying, "You are over-generalizing from these two studies. Given the highly rigorous entry criteria for the studies and the relatively short course of antibiotics (in my practice some patients have to be on antibiotics for months before we see improvement), all you have done is prove that this particular treatment course does not work. It is scientifically suspect to

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[44] Ibid.
[45] Kolata, Gina. "Lyme Disease is Hard to Catch and Easy to Halt, Study Finds." *New York Times,* 13 June 2001.

generalize from these two studies to all patients who appear to suffer from lingering effects of Lyme disease." The two sides look at the same studies and draw very different conclusions.

A third NIH treatment study on chronic Lyme disease**,** reported in *Neurology,* in 2008 shows that the two sides have not changed much in the last few years. Brian Fallon, a neuropsychiatrist who heads the Lyme and Tick-Borne Diseases Research Center at Columbia University, and others looked at antibiotic treatment for people with cognitive impairment.[46] Study participants had to be well documented Lyme disease patients who had been previously treated with at least three weeks of intravenous antibiotics. All participants had to have the classic neurocognitive signs of Lyme disease, including losses in short-term memory and verbal fluency as well as "marked levels of fatigue, pain, and impaired physical functioning."[47] The study protocol dictated that those receiving treatment (as opposed to placebo) receive a longer-term regimen of ten weeks of antibiotics. There was also a third arm of healthy volunteers. The results showed short-term cognitive improvement for patients with post-treatment Lyme encephalopathy, but the patients relapsed once the antibiotic was discontinued.

An editorial appearing in the same issue of *Neurology* illustrates the unyielding debate. John Halperin calls for an end to the controversy over chronic Lyme disease.[48] He summarizes the findings of Fallon et al. and concludes that "Treatment resulted in no sustained benefit."[49] Yet Halperin makes no mention of the fact that there was, in

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[46] See Fallon, Brian et al. "A Randomized, Placebo-Controlled Trial of Repeated IV Antibiotic Therapy for Lyme Encephalopathy." *Neurology,* 70 (2008): 992-1003.
[47] Ibid., 992.
[48] "Prolonged Lyme Disease Treatment: Enough is Enough." *Neurology,* 70 (2008): 986-987.
[49] Ibid., 986.

fact, short-term benefit. This is the part of the result that is so significant to chronic Lyme disease advocates. To have a short-term benefit is very different from having absolutely no benefit. To advocates, the *Neurology* study in no way shows that "enough is enough." If anything, it shows the importance of developing treatment strategies that will provide sustained benefit.

The debates in the medical literature and between doctors over chronic Lyme disease are genuine. But there is a sense in which the notion of chronic Lyme disease is parasitic on acute Lyme disease, which is a much more well-recognized entity. Once acute Lyme disease was discovered and named, and the CDC started tracking cases, the disease quickly burst into public consciousness. Ordinary Americans who had never heard of Lyme disease only a few years previously, and who did not live in an area in which they were very likely to get it, quickly became frightened by what they perceived as an emerging threat. As early as 1993 an article in *Science* described the concerns that suburban and rural dwellers were becoming hysterical about the dangers of Lyme disease.[50] Health departments and researchers responded by underscoring the disease's straightforward diagnosis and treatment.

But at the same time, a growing group of patients and physicians were arguing that concerns about chronic Lyme disease were not being taken seriously. The stakes were high—people believed that they were suffering the debilitating effects of an infectious disease and their doctors believed that long-term antibiotic treatments worked. The patients believed they knew what they needed —they needed the

[50] See Barbour, A.G. and D. Fish. "The Biological and Social Phenomenon of Lyme Disease." *Science*, 260 (1993): 210-216.

recognition and credibility that comes with medical diagnosis and most importantly, they needed the relief that comes from proper treatments. Like the Morgellons sufferers who felt they were not being taken seriously, chronic Lyme disease patients turned to their political representatives to put pressure on the CDC. Yet the efforts of chronic Lyme disease patients have proven far more successful. Chronic Lyme disease patients argue that researchers, public health officials, and insurance and HMO executives are all standing between them and proper diagnosis and treatment, and they have marshaled considerable social and political power in their efforts to get what they want.

Social and Legislative Power

Federal and State Legislation

A number of patient groups have petitioned Congress for help in raising awareness of Lyme disease, as well as protecting physicians who treat chronic Lyme disease and defending insurance coverage. A number of bills have been introduced in the last few years, and while none of them have made it out of their respective committees, the very fact that these debates have made it to this level is extraordinary. The language which appears in these proposed Bills illustrates how successful the Lyme disease activists have been in marshaling political power.

In 2001 Representatives first introduced Lyme disease bills to the House: H.R. 1254 "Lyme Disease Initiative of 2001"[51] and H.R. 2118 "Lyme and Infectious Disease Information and Fairness in Treatment (LIFT) Act."[52] This language reflects the influence of Lyme activists, with a focus on concerns about under-diagnosis and under-

[51] H.R. 1254, (2001): 1-17.
[52] H.R. 2118, (2001): 1-12.

treatment. In H.R. 1254 Congress finds that "Due to scientific uncertainties about the diagnosis of acute and chronic Lyme disease, and the proper course and length of treatment, many patients have encountered difficulties in obtaining needed insurance coverage for Lyme disease."[53] H.R. 2118 echoes this sentiment: "Patients with Lyme disease are increasingly having difficulty obtaining diagnosis and treatment for the disease, and being restored to health. Because of differences in medical and scientific opinion, clinicians fear retaliation from insurance companies and medical licensure boards based on their diagnosis and treatment of patients."[54]

On January 31, 2007 Representative Christopher Smith of New Jersey, along with thirteen other house members introduced H.R. 741, "Lyme and Tick-Borne Disease Prevention, Education, and Research Act of 2007."[55] This bill never made it out of committee, but several striking things about it reflect the deep divide of the "Lyme Wars." The bill's stated purpose is "To provide for the expansion of Federal efforts concerning the prevention, education, treatment, and research activities related to Lyme and other tick-borne diseases, including the establishment of a Tick-Borne Diseases Advisory Committee."[56] This sounds innocent enough, but the text of the Bill includes statements with which many Lyme disease researchers would disagree. For example, the first finding in Sec. 2 states, "Lyme disease is a common but frequently misunderstood illness that, if not caught early and treated properly, can cause serious health problems."[57] The claim that it is "frequently misunderstood" is controversial, of

[53] H.R. 1254, 3.
[54] H.R. 2118, 3-4.
[55] H.R. 741, (2007): 1-12.
[56] Ibid., 1.
[57] Ibid., 2.

course. And number six states, "Studies indicate that the actual number of tick-borne disease cases are approximately ten times the amount reported."[58] This is another matter of much debate, but its inclusion illustrates that the Lyme activists are making legislative inroads. The language of the bill seems to take for granted that there is legitimate uncertainty in the medical literature about Lyme disease, while researchers like Steere would reject this assumption.

Much of the wording of the bill seems aimed to making sure that a broad understanding of Lyme disease is used. One of the Committee's duties is to "ensure that a broad spectrum of scientific viewpoints are represented in public health policy decisions and that information disseminated to the public and physicians is balanced."[59] This stated mission is reflected in the make-up of the Committee membership. Voting members are supposed to include scientists who represent a variety of viewpoints as well as patient representatives. The requirement that "In appointing members…the Secretary shall ensure that such members, as a group, represent a *diversity of scientific perspectives* relevant to the duties of the Committee"[60] (emphasis added) is remarkable precisely because it reflects the views of the Lyme activists.

The bill also calls for a coordinated effort at the Federal level. One section calls for surveillance and reporting activities "to evaluate the feasibility and developing a reporting system for the collection of data on physician-diagnosed cases of Lyme disease that do not meet the surveillance criteria of the Centers for Disease Control and

[58] Ibid., 3.
[59] Ibid., 4.
[60] Ibid., 5.

Prevention in order to more accurately gauge disease incidence."[61] And the final section calls for reports that contain "a scientifically qualified assessment of Lyme and other tick-borne diseases, including both acute and chronic instances, related to the broad spectrum of empirical evidence of treating physicians, as well as published peer reviewed data, that shall include recommendations for addressing research gaps in diagnosis and treatment of Lyme and other tick-borne diseases and an evaluation of treatment guidelines and their utilization."[62] All of this is worth noting if only because it mirrors so closely the views of Lyme activists. In fact, the legislation reads as if it was written by Lyme activists themselves.

Although Lyme-related legislation has not yet passed in Congress, the proposals are fascinating because they are the result of constituents petitioning their representatives. It is not unusual for Congress to look into issues surrounding illness. The hearings schedule for the Senate Committee on Health, Education, Labor, and Pensions for the first half of 2008 includes investigations into childhood obesity, cancer, and food allergies. But the most recently proposed Lyme legislation is unusual in that it clearly advocates a "broad" definition of Lyme disease and advocates for representation by competing authorities. This is a huge mark of success for Lyme activists.

Activists are also having success at the state level. For example, in June 2004, Rhode Island became the only state to require by law that insurance companies "shall provide coverage for diagnostic testing and long-term antibiotic treatment of chronic Lyme disease when determined to be medically necessary and ordered by a

[61] Ibid., 9.
[62] Ibid., 12.

physician."[63] This legislation was enacted to protect so-called "Lyme Literate Medical Doctors."

State Medical Boards

The actions of some state medical boards reflect a backlash. Some doctors have reacted to the activism of chronic Lyme disease advocates by trying to force their physician allies to conform to standard practice. Over the last two decades, several state medical boards have investigated physicians who diagnose and aggressively treat chronic Lyme disease with long-term antibiotics.[64] For example, Dr. Joseph Burrascano, a physician on Long Island, is a well known chronic Lyme disease advocate who has been investigated in New York by the State Office of Professional Medical Conduct.[65] In 1993 Dr. Burrascano informed the Senate discussion that he has successfully treated chronic Lyme patients with long-term antibiotics and criticized researchers and physicians who downplay the severity of chronic Lyme disease. He is also the author of guidelines followed by many physicians who treat chronic Lyme disease. His patients and supporters have come to his aid, donating money for his legal defense and spilling "into the corridors of the New York State Capital to lobby politicians to stop the state's investigation."[66] A letter sent to the NY State medical

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[63] Rhode Island General Assembly. "An Act Relating to Health and Safety—Lyme Disease and Treatment." Chapter 04-035. (2004) Exacted 8 June 2004.
[64] See Whitmire, Tim. "N.C. Doctor Faces Board Discipline Over Lyme Disease Treatments." *Associated Press*. 15 April 2006. The Lyme Disease Association, Inc. a patient advocacy group reports that New York, Rhode Island, Texas, Michigan, Connecticut, and California have all conducted investigations into "Lyme Literate Physicians." (see http://www.lymediseaseassociation.org/LegHowTo.html, accessed 25 October 2008).
[65] See Weintraub 223-227 and Noble, Holcomb. "Lyme Doctors Rally Behind a Colleague Under Inquiry." *New York Times*, 10 November 2000.
[66] Grann

board said, "I regard Allen Steere…as the antichrist…I owe what is left of my life to Dr. Joseph Burrascano."[67]

On April 22, 2002 Dr. Burrascano was exonerated on most of the 39 charges that the medical board brought against him. The board found some isolated problems related to record keeping, but nothing that warranted taking his medical license. The board also concluded that Dr. Burrascano should be allowed to continue to treat Lyme patients according to his own clinical judgment.[68]

An excerpt from the decision demonstrates the role of medical and scientific uncertainty in this debate:

> "The Hearing Committee recognizes the existence of the current debate within the medical community over issues concerning management of patients with recurrent or long term Lyme disease. This appears to be a highly polarized and politicized conflict, as was demonstrated to this committee by expert testimony from both sides, each supported by numerous medical journal articles, and each emphatic that the opposite position was clearly incorrect… What clearly did emerge however was that the Respondent's approach, while certainly a minority viewpoint, is one that is shared by many other physicians. We recognize that the practice of medicine may not always be an exact science, 'issued guidelines' are not regulatory, and patient care is frequently individualized."[69]

In the end, the Committee supported the authority of Burrascano to treat chronic Lyme disease patients, and its decision has been replicated in other states such as Michigan. In cases across the country, chronic Lyme disease patients have rallied to the side of their physicians to defend them from state medical boards. To many patients, it

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[67] Ibid.
[68] State of New York Department of Health. Board Order Regarding Joseph James Burrascano Jr., MD. 25 April 2002. Accessed 25 October 2008. Available from http://w3.health.state.ny.us/opmc/factions.nsf/58220a7f9eeaafab85256b180058c032/7f57f08d61de929c85256a4a0047c6da?OpenDocument.
[69] Ibid.

is preposterous that state medical boards, charged with protecting patients from harm, would actually go after the very doctors that are providing them relief**.**

Financial Interests

Investigations into physicians have been fueled by concerns about the role of money in debates over chronic Lyme disease. Part of this comes from private insurance companies and HMOs. Providers are not obligated to pay for treatments that fall outside standard medical practice. But with chronic Lyme disease, a central part of the debate is disagreement about what the standard medical treatment should be. It is in the interests of health insurers to adopt a narrow definition of Lyme disease; this will cut down on the number of claims they have to pay. But the advocates argue that health insurers are just hiding behind this argument in order to reduce their costs, and that this is unfair to the patients. Kenneth Liegner, a critical care physician in New York who treats patients with chronic Lyme disease, blames both insurance companies *and* physicians. "The doctors consulting for insurance companies are often the same ones who deny the existence of chronic Lyme disease in treatment guidelines and the same ones whose patients wind up in my office, misdiagnosed, mistreated, and horrendously sick year after year after year."[70] Liegner thinks that the doctors who deny chronic Lyme disease have a conflict of interest because they are also getting paid consulting fees by the insurance industry.

Weintraub argues that the money trail leads directly to managed care. The role of managed care in shaping the debate over chronic Lyme Disease can be seen in a controversy over school funding in New Jersey in the early 1990s. In 1992 the CDC

[70] Weintraub, 140.

conducted a small study to determine the financial impact on school districts of students with Lyme disease. They studied nine school districts within two contiguous New Jersey counties and found that Lyme disease significantly raised a district's home instruction budget. For example, the Jackson School District in Ocean County had more than 170 children with Lyme disease receiving home instruction. The Wall Township district had 54 Lyme students receiving home instruction, raising the home instruction budget 88 percent. The families surveyed were spending as much as $100,000 on medical care for a single child with chronic Lyme disease.[71]

The CDC study revealed a huge economic force working against chronic Lyme disease patients. By August 1992, major insurers in endemic areas had imposed a limit of twenty-eight days on intravenous antibiotics.[72] This represented a significant change from the 1980s, when the standards used by insurers for a diagnosis of Lyme disease were vague. But as insurers began to face a wide variety of economic concerns in the 1990s, Lyme disease increasingly became "red-flagged" as a draining expense. Many patients have come to believe that insurance companies reject their claims for coverage not based on science, but based on protecting their own bottom line.

However, concerns about the role of financial interests have also appeared on the other side. Some doctors are profiting handsomely by treating chronic Lyme disease. Since many insurers do not cover long-term antibiotic treatment, some "Lyme Literate Medical Doctors" have dispensed with dealing with insurance companies entirely. For example, Dr. Bernard Raxlen, a psychiatrist practicing in Manhattan whose entire practice is devoted to chronic Lyme disease and co-infections, is very

[71] Ibid., 192-193.
[72] Ibid., 298-299.

explicit about the financial burdens of seeking his treatment. He does not accept insurance and expects full payment at every visit. He even lists his rates on his web site: $900 for the initial appointment, $500 for the second, and $350 for subsequent appointments. A phone consult will cost $150-225, and diagnostic test results, which "can only be interpreted by Dr. Raxlen", can vary from $500-2,500.[73]

It is clear that there are powerful financial interests on each side of the debate. Some clinicians profit by treating chronic Lyme disease, while insurers profit by denying treatment. But these financial battles are important not simply for individual patients, but because they are often the primary impetus for larger political debates. Financial disputes have driven the debate over chronic Lyme disease into the offices of state legislators and state licensing boards.

Legal Investigations: Anti-Trust Investigation into IDSA Guidelines

An even more remarkable story has played out during 2007 and 2008 in Connecticut, where Richard Blumenthal, the state Attorney General, launched an investigation into the Infectious Disease Society of America (IDSA) practice guidelines to determine if they violate antitrust laws. The rationale behind the investigation is that these guidelines may harm patients by limiting their insurance coverage. According to Blumenthal, the IDSA guidelines limit options to patients and their physicians because insurance companies will use them to deny coverage.[74]

This kind of investigation into a professional society's treatment guidelines is entirely without precedent and illustrates just how much power Lyme activists have

[73] All information obtained from Dr. Raxlen's website "Lyme Resource Medical." Accessed 25 October 2008. Available from http://www.lymeresourcemedical.com/.
[74] See Warner, Susan. "State Official Subpoenas Infectious Disease Group." *The Scientist*, 7 February 2007. Accessed 25 October 2008. Available from http://www.the-scientist.com/news/display/49605/.

gained. A letter from the President of IDSA was published in the summer 2007 edition of *IDSA News* defending the guidelines: "The debate on how best to treat Lyme disease is a scientific one, and we believe it is best resolved scientifically. Unfortunately, those who are unhappy with our scientific conclusions have made it political. In some states, advocates have pressured the legislature to endorse long-term antibiotic therapy despite the evidence. In Connecticut, they have found a sympathetic ally in the attorney general, who has initiated this investigation."[75]

The anti-trust charges against the IDSA failed. However, in May 2008, Blumenthal announced that his antitrust investigation "uncovered serious flaws in the IDSA process for writing its 2006 Lyme disease guidelines and the IDSA has agreed to reassess them with the assistance of an outside arbiter."[76] The main problem was that IDSA violated its own policies in producing the guidelines. The process used in appointing the 2006 panel was not as transparent as IDSA rules required. Blumenthal concluded that this process allowed the panel chairmen to hand-pick panel members that were like-minded. This represented a conflict of interest – not a financial conflict, but an ideological conflict in how the panel members were chosen.

In an agreement between the Attorney General's Office and the IDSA, it was agreed that the IDSA will create a new panel of eight to twelve members, none of whom served on the 2006 guidelines panel, to review the guidelines. The IDSA "must

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[75] "From the President: IDSA Stands Up for Lyme Disease Guidelines." *IDSA News,* 17 (2007).
[76] Connecticut Attorney General's Office. Press Release: "Attorney General's Investigation Reveals Flawed Lyme Disease Guideline Process, IDSA Agrees To Reassess Guidelines, Install Independent Arbiter." 1 May 2008. Accessed 25 October 2008. Available from http://www.ct.gov/AG/cwp/view.asp?a=2795&q=414284.

conduct an open application process and consider all applicants."[77] Blumenthal and IDSA agreed to appoint Howard Brody, an ethicist and family physician, as ombudsman to ensure that the panel is free of conflicts of interest. The review panel will conduct an open scientific hearing and will hear presentations from interested parties. Once the panel has conducted its review and held its hearing, it will go back and review whether the information collected supports the recommendations made in 2006. At least 75 percent of the panel must support a recommendation, otherwise it will be revised.[78]

The general perception is that this agreement and the review process will not produce any significant changes, especially since only 75 percent support is needed. Since Blumenthal's more serious antitrust charges were not upheld, this agreement was a way for both the Attorney General and IDSA to save face. A recent editorial in IDSA's journal indicates that the organizations legal costs had exceeded $250,000 and that the settlement was a way for the organization to move forward while minimizing the financial effects.[79] The IDSA president, Donald M. Poretz says that he shares concerns with others that politics is potentially intruding into the scientific process and he "believe[s] that an agreement that brings this discussion back into a medical and scientific forum (rather than a courtroom) is the best outcome."[80] Blumenthal's investigation ended with a whimper, rather than a bang, but it is remarkable that it even happened in the first place.

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[77] Ibid.
[78] Ibid.
[79] Klein, Jerome O. "Danger Ahead: Politics Intrude in Infectious Diseases Society of America Guideline for Lyme Disease." *Clinical Infectious Diseases*, 47 (2008): 1197-1199.
[80] Poretz, Donald M. "Clarification of the Agreement between the Infectious Diseases Society of America and the Attorney General of Connecticut." *Clinical Infectious Diseases*, 47 (2008): 1200.

How has Chronic Lyme Disease Changed the Practice of Medicine?

Whether or not the IDSA guidelines change significantly, it is clear that chronic Lyme disease advocates have successfully deployed their political power to shape medical treatment. They have taken on professional societies; they have battled insurance companies; they have had bills introduced to Congress; they have made the reputations of individual physicians. Lyme disease advocates have taken their initial success in helping discover acute Lyme disease and pushed it to an entirely new level. In 2001 Dr. Alan Steere told a reporter, "Doctors can't say what they think anymore. If you quote me as saying these things, I'm as good as dead."[81] What does it mean when the discoverer of Lyme disease is greeted at public speaking engagements with patients holding signs reading, "How many more will you kill?" and "Steer clear of Steere!"[82]?

As with Morgellons disease, the activism of Lyme disease patients has been fueled by a gap between their subjective, individual experience and the generalizable explanations provided by "scientific" medicine. They believe their suffering is physical; their physicians suggest it may be psychological. They believe the cause of their illness is an infection; the literature suggests otherwise. They believe that antibiotics can treat their disease; the studies suggest that, at least in the long term, antibiotics do not work. Thirty years ago, patients would have had little recourse but to accept what they were told. But the authority of physicians is not what it was thirty years ago, and as a consequence, patients have begun to take matters into their own hands.

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[81] Grann
[82] Ibid.

In some ways, this tension between individual experience and generalizable research parallels a larger debate in medicine today over evidence-based medicine (EBM). In 1992 the Evidence-Based Medicine Working Group, based primarily at McMaster University in Ontario, Canada announced "a new paradigm" of medical practice.[83] At first the goal of evidence-based medicine (EBM) was to teach medical students and physicians to search and critically evaluate the medical literature in order to answer clinical questions. But over the last fifteen years it has become primarily associated with the production of secondary sources that digest and summarize the medical literature for clinicians. EBM is a large and influential movement. Groups like the National Guidelines Clearinghouse in the United States and the international Cochrane Collaboration use the evidence hierarchy of EBM to produce practice guidelines and summaries that influence clinical practice around the world. EBM also influences research funding and publication decisions. It has also prompted a larger movement of evidence-based practice which is now shaping decisions in nursing, dentistry, and outside of healthcare in places like education.[84]

On the face of it, EBM might seem uncontroversial. Many EBM advocates argue that the movement is simply making explicit something that was always implicit in medicine – basing treatment decisions on scientific evidence. But EBM has also attracted a tremendous amount of criticism and resentment. Many clinicians argue that practice guidelines are too rigidly focused on generalizable data and make no room for

[83] Borgerson, Kirstin and Robyn Blumm. "Evidence-Based Medicine." *Perspectives in Biology and Medicine*, 48;4 (2005): 1475-176.
[84] Ibid.

individual variation.[85] Others argue that EBM does not capture the role of the relationship between individual doctors and patients. Some critics say EBM downplays social and cultural differences at the expense of aggregate data.[86] Much of this criticism is based on the idea that EBM misses something essential about individual experience.

It is also notable that the rise of EBM has taken place at a time when the authority and power of physicians has declined. In the 1970s, physicians saw their authority being challenged by patients, who, in parallel with the consumer rights movement, began demanding more control over their own medical decisions. In the 1980s, physicians saw their authority take yet another blow, as corporate-style medicine began to replace solo, fee-for-service practices. By the 1990s, EBM-backed practice guidelines enforced by managed care and insurance companies had, to many physicians, come to feel like yet another attack on their personal clinical judgment.

While EBM described a new paradigm for clinical medicine, the story of chronic Lyme disease describes a competing paradigm. Chronic Lyme disease activists have deployed a "folkway" methodology to acquire medical power that includes not just social, political, and legal forces, but also medical forces, such as alliances with physicians and the production of research and peer reviewed publications. Like critics of EBM, who argue that EBM misses out on the individual experiences of patients and the individualized clinical judgments of physicians, chronic Lyme disease activists

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[85] See Upshur, Ross E.G. "Looking for Rules in a World of Exceptions: Reflections on Evidence-Based Practice." *Perspectives in Biology and Medicine,* 48;4 (2005): 477-489.

[86] See Lambert, Helen, Elisa J. Gordon, and Elizabeth A. Bogdan-Lovis. "Introduction: Gift Horse or Trojan Horse? Social Science Perspectives on Evidence-Based Health Care." *Social Science and Medicine,* 62 (2006): 2613-2620. De Vries, Raymond and Trudo Lemmens. "The Social and Cultural Shaping of Medical Evidence: Case Studies from Pharmaceutical Research and Obstetric Science." *Social Science and Medicine,* 62 (2006): 2694-2706. Goldenberg, Maya J. "On Evidence and Evidence-Based Medicine: Lessons from the Philosophy of Science." *Social Science and Medicine,* 62 (2006): 2621-2632.

argue that their subjective, individual experiences are being ignored by researchers like Steere. Conversely, for those same researchers and public health officials who are skeptical about chronic Lyme disease, the methodology of chronic Lyme disease advocates illustrates why the methodology of EBM is so important. In their view, patients can have all sorts of mistaken beliefs about their experiences (just look at Morgellons disease), but medical authority can sort out these beliefs by systematically relying on the aggregation of empirical evidence.

The next chapter moves away from examining the influence of patients on medical practice to looking at their influence on medical research. There are important parallels between the two, but in many ways the ethical stakes are higher in the research context. Understanding the role of patient activism is central to understanding changes in research ethics, but understanding the role of other forces like pharmaceutical companies and the FDA in shaping patient activism is just as important.

CHAPTER THREE

Research Ethics

Abstract

Beginning in the 1980s with the emergence of HIV/AIDS, patients began to engage in political activism to shape medical research. The traditional way of thinking about the protection of human research subjects had been framed by historical abuses like the Tuskegee Syphilis Study. The idea was that subjects need to be protected from overzealous researchers treating subjects as a means to their own ends. AIDS activists turned this model on its head, arguing that research is not a burden to subjects, but rather a great benefit. In the context of the AIDS crisis in the early 1980s, with no available treatments, activists saw participation in research as their only possible chance to receive medical treatment. This resulted in a shift in research ethics and regulation. In the 1990s the research landscape shifted again, as clinical trials moved from academic health centers to contract research organizations (CROs) and private testing sites. This shift transferred power from academic researchers to the private sector. Patient advocacy groups began to form alliances with the pharmaceutical industry, because they saw industry as promoting their interests. In this chapter I trace these power shifts (to patients and to private research) in the light of the recent legal case *Abigail Alliance et al. v. von Eschenbach et al.* and the ethics of risk. The Abigail Alliance case can be seen as a direct descendent of HIV/AIDS patient activism. However, much less attention has been paid to the privatization of research, and this has led to shortcomings in research ethics and regulation.

Introduction

Abigail Burroughs was diagnosed with squamous cell carcinoma in her neck and lungs in 1999 at the age of nineteen.[1] This type of cancer is rare in someone so young; it is usually diagnosed in older men with a history of smoking and alcohol use. Her doctors tried all standard therapies for her cancer, but the therapies failed. Abigail's oncologist at Johns Hopkins University thought that the drug Erbitux (cetuximab) had a

[1] See Kovach, Sue. "The Abigail Alliance: Motivated by Tragic Circumstances, Families Battle an Uncaring Bureaucracy." *Life Extension*, (2007): 25-30. Abigail Alliance. "The Abigail Story." Accessed 25 October 2008. Available from http://abigail-alliance.org/story.htm.

significant chance of helping her. Erbitux had showed a good response in early trials, but Abigail was ineligible for the clinical trial because she did not meet the enrollment criteria. Erbitux was being tested in patients who had squamous cell carcinoma located in the colon. Abigail and her physicians appealed to the FDA (U.S. Food and Drug Administration) for compassionate use, a provision that allows access to experimental drugs for patients who do not meet enrollment criteria but for whom a treating physician believes the drug may provide benefit. The request was denied.[2]

Abigail died in March 2001 at the age of twenty-one. Erbitux was later approved by the FDA and is available today. In November 2001 Abigail's father, Frank Burroughs, founded the "Abigail Alliance for Better Access to Developmental Drugs." The main mission of the Abigail Alliance is "To help cancer patients and others with life threatening illness" but its focus is on expanding access and compassionate use programs for people with a terminal illness who have exhausted conventional treatment options. They are working to make sure that anyone in a situation like that of Abigail will have access to their own Erbitux.[3]

In 2002 with the Washington Legal Foundation (WLF),[4] the Abigail Alliance formally petitioned the FDA through a "citizen petition" to allow terminally ill patients

[2] Ibid.
[3] See Abigail Alliance. Accessed 25 October 2008. Available from http://abigail-alliance.org.
[4] WLF is a public interest law firm with a libertarian orientation.

access to experimental drugs that had been approved for phase II clinical trials.[5] The petition was denied. In July 2003 WLF and the Abigail Alliance sued the FDA.[6]

The lawsuit argues that the FDA violates the constitutional rights of terminally ill patients when it denies them access to potentially beneficial experimental drugs. It argues that FDA regulations violate patients' rights to privacy and liberty and sentence them to die without due process. The Abigail Alliance contends that patients who do not qualify to participate in a specific research trial have a right to access the experimental drug if the drug has passed phase I testing and the patient has no other options. The Alliance draws the line between phase I and phase II because if a drug has passed phase I then it has been proven to be at least minimally safe.[7] The Alliance is not asking for free drugs, and it emphasizes that patients must be willing to accept all responsibility for adverse events.[8]

The Alliance argues that under FDA regulations a majority of patients with life threatening illnesses do not have access to promising new therapies during the years of testing and review required by the FDA. These therapies are unavailable even though there is evidence of safety and even though patients have no alternative treatment. The

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[5] Citizen Petition of the Abigail Alliance and the Washington Legal Foundation to the Food and Drug Administration, U.S. Dept. of Health and Human Services. "In re Tier 1 Initial Approval Program to Expedite the Availability of Lifesaving Drugs." 11 June 2003. Accessed 25 October 2008. Available from http://www.fda.gov/ohrms/dockets/dailys/03/Jun03/061703/03p-0274-cp00001-01-vol1.pdf

[6] The original lawsuit was named *Abigail Alliance et al. v. McClellan et al.* The name changed with changes in the FDA commissioner. Its most recent name is *Abigail Alliance et al. v. von Eschenbach et al.*

[7] More on the phases and how trials work later in this chapter.

[8] Case documents are available from WLF. Accessed 25 October 2008. Available from http://www.wlf.org/Litigating/casedetail.asp?detail=266. See also Jacobson, Peter D. and Wendy E. Parmet. "A New Era of Unapproved Drugs: The Case of *Abigail Alliance v Von Eschenbach*." *JAMA*, 297 (2007): 205-208. Dresser, Rebecca. "Investigational Drugs and the Constitution." *Hastings Center Report*, 36 (2006): 9-10. Robertson, John A. "Controversial Medical Treatment and the Right to Health Care." *Hastings Center Report*, 36 (2006): 15-20. Caplan, Arthur. "Is it Sound Public Policy to Let the Terminally Ill Access Experimental Medical Innovations?" *American Journal of Bioethics*, 7;6 (2007): 1-3.

Alliance contends that the FDA's expanded access and compassionate use programs are insufficiently sized and help only a small number of patients. The argument that the FDA violates Constitutional rights to privacy and liberty is based on the premise that the FDA interferes with the right of patients to choose appropriate treatment. By taking away a possible treatment option, the FDA violates the Fifth Amendment against the deprivation of life without due process.

In May 2006 a panel of the U.S. Court of Appeals for the District of Columbia Circuit ruled in favor of the Alliance and WLF. In a 2-1 decision the court ruled that terminally ill patients have a "fundamental right" protected by the Constitution to access experimental drugs that have not been fully approved by the FDA. In August 2007 the *en banc* appeals court reversed that decision 8-2 concluding that there is no such fundamental right. The WLF appealed to the U.S. Supreme Court and in January 2008 the court announced (without comment) that it would not hear the appeal.[9]

While the Federal Courts rejected the Alliance's legal arguments, the moral arguments put forward by the Abigail Alliance point to significant issues in research ethics. Historically, the purpose of research ethics and regulation has been to protect patients from harm. Yet according to the Abigail Alliance lawsuit, research regulators were actually harming patients by denying them experimental drugs. How did we reach a point where patients are actually suing the FDA for too much protection? To answer this question, I will need to examine two major power shifts in research ethics. The first is a shift of power from physicians and researchers to patients. This shift has been well-documented and is similar to the power shift discussed in the previous chapter. The

[9] See WLF.

second shift of power, which has received far less recognition, has been from academic researchers to private physicians and research companies. These two shifts are critical for an understanding of the Abigail Alliance case and how patient activism has shaped research ethics. Perhaps more importantly, they point to significant areas where research ethics has fallen short of its mission.

First Power Shift: HIV/AIDS Patient Activism and Rewriting the Rules of Research

On March 24, 1987 New York ACT UP's (AIDS Coalition to Unleash Power) first demonstration took place at the New York Stock Exchange. Protestors criticized the high price of AZT (the first FDA approved HIV/AIDS drug) and the FDA's long drug approval process.[10] The next day the FDA announced a two-year reduction in the approval process. Formed in 1987, ACT-UP was the most vocal and militant AIDS activist group, but it was only one among many. On October 11, 1988 ACT UP joined ACT NOW protestors and shut down FDA headquarters chanting, "Test drugs, not people" and protesting what they called the government's inadequate response to the AIDS epidemic.[11]

At the heart of the AIDS activist movement was a sense that time was running out. First reported by the CDC in 1981, what came to be known as AIDS remained a mystery for several years. The first blood test to identify AIDS was not available until 1985, and the first experimental drug trials for AZT did not start until 1985. By then,

[10] See ACT UP New York. "First Demonstration Flyer." Accessed 25 October 2008. Available from http://www.actupny.org/documents/1stFlyer.html.
[11] Epstein, Steven. *Impure Science: AIDS, Activism, and the Politics of Knowledge*. Berkeley: University of California Press, 1996, 222-223.

over 25,000 people had died of AIDS in the United States alone.[12] AIDS patients were desperate for treatment, yet the process of developing and approving new drugs seemed painfully slow. Once a drug made it to the clinical trial phase, strict eligibility criteria were used to determine which patients could enroll. Often these trials were limited to white males, and protocols frequently required participants to refrain from taking other medications and seeking alternative therapies. At the height of the AIDS epidemic in the US, physicians were faced with patients imploring them for access to clinical trials; many of these patients saw research participation as their only chance for survival. Some AIDS patients, convinced that clinical trials were their only alternative to death, argued that their grave prognosis meant that they should be allowed to take greater risks with their health.[13]

The first clinical trials for AZT, then a promising new therapy for HIV/AIDS, were announced in 1985 with great fanfare.[14] But ACT UP soon began to protest limited enrollments in the AZT trials with slogans like "Clinical trials are health care too!" As Robert Wachter observed at the time, ACT UP used a novel mix of public protest and private deal-making. He wrote, "The activists' unprecedented modus operandi is a study in contrasts: street theater and intimidation on the one hand, detailed position papers and painstaking negotiation on the other."[15]

More than twenty five years after the beginning of the AIDS epidemic, AIDS/HIV activism is used as a model of success by other patient groups, largely

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[12] See Sepkowitz, Kent A. "AIDS—The First 20 Years." *New England Journal of Medicine*, 344 (2001): 1764-1772.
[13] See Epstein, Chapter 5.
[14] Ibid., 192.
[15] Wachter RM. "AIDs, Activism, and the Politics of Health. *New England Journal of Medicine*. 326 (1992): 128-133, 128.

because its methods worked so well.[16] The protests and lobbying by AIDS/HIV activists brought about specific, concrete results. For example, on February 2, 1989 ACT UP protested the FDA's new protocols for the drug DHPG (gancyclovir). The new protocols excluded many current DHPG users access to the drug. In response to the protests, the FDA made DHPG available under "compassionate use" and promised to reconsider the protocols.[17] Today, hundreds of patient advocacy groups work to promote awareness of specific diseases; they employ lobbyists and public relations firms to advance their cause; and they are routinely given a voice on the committees that make decisions about clinical trials and drug approval.[18] In many cases, these groups simply aim to secure research dollars by achieving a more visible public profile. But many want to go further. Like the early AIDS activists, these advocacy groups want to influence the way that medical research itself is shaped and conducted.

It is now widely agreed that HIV/AIDS activism changed the face of pharmaceutical research. HIV/AIDS advocates, along with breast cancer advocates, were among the first in the U.S. to demand changes regarding patient participation in how research is conducted and to demand greater access to clinical trials.[19] Largely as a result of HIV/AIDS activism, patients in the United States have benefited from

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[16] See Dresser, Rebecca. *When Science Offers Salvation: Patient Advocacy and Research Ethics*. New York: Oxford University Press, 2001, 165-167.
[17] ACT Up New York. "FDA Action Handbook." Accessed 25 October 2008. Available from http://www.actupny.org/documents/FDAhandbook5.html.
[18] See Collyar, Deborah. "How Have Patient Advocates in the United States Benefited Cancer Research?" *Nature Reviews Cancer,* 5 (2005): 73-78. Terry, Sharon F. et al. "Advocacy Groups as Research Organizations: The PXE International Example." *Nature Reviews Genetics*, 8 (2007): 157-164. Brower, Vicki. "The Squeaky Wheel Gets the Grease." *EMBO Reports*, 6 (2005): 1014-1017. Morreim, E. Haavi. "By Any Other Name: The Many Iterations of 'Patient Advocate'." *IRB: Ethics and Human Research*, 26 (2004): 1-8.
[19] Dresser (2001), 23.

increased access to clinical trials, quicker drug approval times, and more compassionate use programs.

In particular, the efforts of HIV/AIDS activists led to four major FDA policy changes to promote expanded access to clinical trials and investigational drugs. The first was the Treatment Investigational New Drug (IND) program which was adopted in 1987. The IND Program allowed pharmaceutical companies to provide study drugs to patients who did not meet formal entry criteria for participation in clinical trials.[20] In 1988, the FDA agreed to adopt new regulations to expedite drug development. (At the time, it typically took ten years for a new drug to be approved.) In 1992, the FDA instituted a "parallel track" mechanism for access to investigational drugs. The parallel track mechanism made investigational drugs targeted at HIV/AIDS available earlier in the investigational process as long as safety-testing showed there were no obvious risks. Also in 1992, the FDA instituted an accelerated approval rule which allowed it to rely on so-called "surrogate endpoint data" in approving new drugs for serious diseases.[21]

In addition to these concrete policy changes, HIV/AIDS activists were instrumental in producing two broad changes in social attitudes regarding medical research. The first, as Steve Epstein has written in his book *Impure Science*, concerns a direct challenge to scientific expertise. Epstein argues that the politicization of AIDS in the 1980s and 1990s produced a new conception of scientific knowledge. AIDS activism generated new conceptions of scientific practice, new knowledge claims, and a new and diverse set of AIDS experts. For Epstein, these new conceptions of scientific knowledge emerged out of what he calls "credibility struggles." Epstein describes

[20] Ibid., 48.
[21] Ibid., 48-50.

credibility as "the capacity of claims-makers to enroll supporters behind their arguments, legitimate those arguments as authoritative knowledge, and present themselves as the sort of people who can voice the truth."[22] As Epstein writes, the AIDS activist movement may not have been the first to put forward lay people who could speak credibly about scientific knowledge, but it was the first social movement to transform disease victims into "activist experts."

This transformation was fueled partly by distrust of the scientific establishment. As a marginalized group, the gay men behind the AIDS activist movement of the 1980s had good reason to be suspicious of established authorities. In fact, they were often blamed for the spread of the disease. But as Epstein points out, their distrust of scientific experts in particular was mirrored by a larger sense of ambivalence in the culture as a whole towards the institutions of science and their technological products. According to Epstein, what was distinctive about the AIDS movement was the way it transformed this distrust into a different form of scientific authority based on the experience of patients. As he puts it, the AIDS movement "was more than just a 'disease constituency' pressuring the government for more funding, but it is in fact an alternative basis of expertise."[23]

The other broad change in social attitudes produced by the AIDS movement was a dramatic re-conception of the purpose of research ethics and regulation. The history of research ethics is often described as a series of reactions to scandals, such as the Tuskegee Syphilis Study and studies at the Jewish Chronic Disease Hospital. In the syphilis study investigators in rural Alabama withheld effective treatment for syphilis

[22] Epstein, 3.
[23] Ibid., 8.

without the knowledge or consent of nearly four hundred African-American participants.[24] The study went on for nearly forty years without any intervention. In 1963 studies at the Jewish Chronic Disease Hospital in New York City were conducted to learn about the human transplant rejection process. Live liver cancer cells were injected into patients hospitalized with various chronic health conditions. Earlier studies showed that healthy people will immediately reject implanted cancer cells and the investigators wanted to determine if this would be true for ill people. But subjects were never told that they would be injected with live cancer cells because the researchers thought that this information would unnecessarily frighten them.[25]

A key ethical principle emerging from these and other scandals is that people need to be protected from the harms of unethical research.[26] Indeed, this principle is implicit in the very term "human research subject protection." As a regulatory matter in the U.S., this duty to protect subjects falls mainly to the FDA and local Institutional Review Boards, which oversee strict, complicated guidelines dictating the conduct of clinical trials.[27]

Beginning in the 1980s, however, as AIDS activists demanded changes at the FDA, there was a shift in the primary focus of research ethics from protection to access.[28] Ethicists and regulators began to argue that medical research should not always be seen as something potentially harmful from which patients needed to be

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[24] See Jones, James H. *Bad Blood: The Tuskegee Syphilis Experiment.* New York, Free Press, 1993.
[25] See Faden, Ruth R., Tom L. Beauchamp, and Nancy M. P. King. *A History and Theory of Informed Consent.* New York: Oxford University Press, 1986, 161-162.
[26] See National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. Bethesda, MD: Department of Health, Education, and Welfare, 1978.
[27] Faden et al.
[28] See Mastroianni, Anna and Jeffrey Kahn. "Swinging on the Pendulum: Shifting Views of Justice in Human Subjects Research." *Hastings Center Report*, 31 (2001): 21-28.

protected, but that it could also be a positive good, to which patients can legitimately demand inclusion. This shift turned the fundamental impetus behind research ethics on its head. If access to clinical trials is viewed as a *good*, and subjects want to be enrolled in the potentially risky studies from which regulators believe they should be protected, then the ethical calculus involving the ethics of the trial becomes much more complex. Research is often described as a balance between potential risks and benefits, but the appropriate balance between risks and benefits is often a matter of fierce disagreement. If an ill patient with a bleak prognosis is willing to take unusually high risks by enrolling in a clinical trial, is it the duty of ethicists and regulators to say no?

Since the 1970s, the period that saw the patients' rights movement and the "birth of bioethics",[29] we have seen a general shift in ethical values away from paternalism and towards more patient autonomy. Few are willing to argue that this is a bad thing. Patients have become empowered to make decisions for themselves with the help of experts who can provide information and guidance. Some critics may argue that the case of chronic Lyme disease shows the harmful effects of patients becoming too empowered: individuals who reject medical expertise that conflicts with their own idiosyncratic beliefs about their illness. But in the HIV/AIDS context of the 1980s, the idea of patients or research subjects having too much power would have been laughable. There was a great urgency to the threat of HIV/AIDS: gay men were already marginalized, and AIDS patients did not trust the medical establishment to act in their best interests.

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[29] See Stevens, M. L. Tina. *Bioethics in America: Origins and Cultural Politics.* Baltimore: Johns Hopkins University Press, 2000. Jonsen, Albert R. *The Birth of Bioethics.* New York: Oxford University Press, 2003.

AIDS activism changed the focus of ethicists and regulators away from the risks of research and towards its benefits. The potential benefits of research operate at two levels. First, there may be therapeutic benefits to specific individuals enrolled in clinical trials. If an individual receives the agent being tested and his or her condition improves, then the specific individual has benefited from enrollment. Second, there may be benefits to larger groups, owing to the results produced by a trial. If a gay man takes part in a clinical trial that helps produce a new treatment for AIDS, then he has arguably helped benefit the community of gay men as a whole.

This change in focus has resulted in a larger shift in the populations that are recruited for clinical trials. For many years, the standard patient group for medical research has been white men. Researchers wanted a sample group as homogenous as possible in order to increase certainty that the clinical outcomes of the trials are the result of the agent being tested, and not because of natural variations among subjects. This is especially important if the sample size is small. The problem is that it is not always clear that the results of such trials are generalizable to other populations. For example, women and members of some ethnic groups seem to metabolize certain drugs at different rates. Are trials of drugs tested on white men applicable to them? Nor it is clear that data from trials on adults can be applied safely to children. If white men are the standard subjects, this also might mean that the agents being tested are being studied and eventually marketed largely for the benefit of white men.[30]

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[30] See DeBruin, Debra. "Justice and the Inclusion of Women in Clinical Studies: An Argument for Further Reform." *Kennedy Institute of Ethics Journal,* 4;2 (1994): 117-146. Kahn, Jeffrey P., Anna C. Mastroianni, and Jeremy Sugarman, eds. *Beyond Consent: Seeking Justice in Research*. New York: Oxford University Press, 1998.

This recognition has led to additional policies at the federal level mandating that research increasingly focus on previously marginalized groups.[31] Federal guidelines now mandate greater inclusion of women and minorities in clinical trials, and patient groups now have greater voices in shaping the research done on their illnesses. The rationale behind these changes is that access to the benefits of research is matter of justice, especially when the research is publicly funded. But this shift of power has also raised significant questions about the conditions under which it is ethically acceptable for people to participate in risky experimental research. If the purpose of research regulations is to protect people from the ethical violations of studies like those at Tuskegee and the Jewish Chronic Disease Hospital, how should regulators respond when patients like the early AIDS activists or Abigail Burroughs *want* to take a potentially risky experimental drug?

The Ethics of Risk in Clinical Trials

Most, but not all research in the United States that uses human subjects is covered by federal regulations meant to ensure the ethical conduct of research and protection of human subjects. All research conducted at an institution that receives federal funding must be approved by an Institutional Review Board (IRB), even those research projects that are not directly publicly funded. Also, the FDA will approve a drug for public use only if its clinical trials have followed federal regulations. This

[31] See "NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research." 2001. Accessed 25 October 2008. Available from http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html. "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects." 6 March 1998. Accessed 25 October 2008. Available from http://grants.nih.gov/grants/guide/notice-files/not98-024.html.

stipulation is supposed to guarantee that private companies, such as pharmaceutical companies, whose aim is to have their drugs approved for public use, will follow the federal regulations.[32]

A clinical trial is a type of study meant to move an agent from the lab bench to the bedside. It marks the first testing of an agent in human subjects. All other scientific research (for example, in other animal models) should be completed before a clinical trial begins. These procedures are meant to protect human subjects by ensuring that a new agent is given to humans only after all available evidence suggests that it will be safe.

The FDA requires four phases of clinical trials, each phase using an increasingly larger group of subjects. The agent tested must meet certain criteria before passage to the next phase. Phase I uses a small group of subjects to assess the safety of an experimental drug or treatment. The group is usually made up of healthy subjects (although in some cases, such as cancer trials, it is made up of patients.) Once minimal safety has been demonstrated, the trial moves into phase II where the drug or treatment is tested in a larger group for effectiveness. Once there is preliminary evidence of effectiveness, the trial moves into phase III where much larger groups of subjects are enrolled for longer periods of time. Phase IV comes after the drug or treatment has been approved for public use, and is used mainly for detecting side-effects in a much larger population.[33]

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[32] See U.S. Department of Health and Human Services. "Basic HHS Policy for Protection of Human Research Subjects." *Title 45 Code of Federal Regulations*. June 2005, known as the "Common Rule."
[33] See NIH, "Clinical Trials." Accessed 25 October 2008. Available from www.clinicaltrials.gov. These categories are being revised, but there has been no announcement yet.

Federal regulations, codified in the "Common Rule," set out certain requirements that must be met before approving research involving human subjects. This includes minimizing risks to subjects, but it also refers to striking a balance between risk and benefit. Risks are supposed to be reasonable in relation to anticipated benefits.[34] The benefits that can be considered include both benefits to the individual subject and benefits to society. In evaluating risk, only risk to the individual may be considered.

For most later-stage clinical trials, patients enroll largely because they expect some therapeutic benefit. Often these are patients who are unsatisfied with standard therapy. These patients want to try something new and they are willing to take part in a trial, even though the drug is still investigational, because they stand to benefit personally. While these patients are taking some risk, they are protected by the principle of clinical equipoise, which is designed to keep sick subjects from having their treatment compromised in a clinical trial. For the requirements of clinical equipoise to be met, there must be genuine disagreement or uncertainty among expert clinicians about the preferred treatment for the condition being studied. According to the principle of clinical equipoise, it is unethical to knowingly enroll patients in a trial where they will receive substandard care.[35] These patients may be taking risks, but those risks are balanced by the possibility of therapeutic benefit, and if the trial has been designed according to clinical equipoise that will be a fair trade-off, and their care will not be compromised.

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[34] See Common Rule 46.111(a)(2).
[35] See Freedman, Benjamin. "Equipoise and the Ethics of Clinical Research. *New England Journal of Medicine*, 317 (1987): 141-145.

But phase I trials present a unique problem, since the trials are not designed to provide subjects with any therapeutic benefit. All phase I trials will involve some level of risk (just as all treatments involve risk) and there is much debate over how to balance risk and benefit in these trials. These trials are meant to establish safety—is it safe for humans to take this drug and at what doses? Of course, the researchers hope that there will be some evidence of effectiveness, but phase I trials are not designed to measure efficacy. And because the number of subjects is small, any evidence of effectiveness is generally not statistically significant. Phase I studies are usually conducted in a small number of healthy volunteers (20-80) and typically last a few days to a few weeks. In order to determine the safe dosage of a new drug, researchers gradually increase the dosage taken by subjects in order to determine the maximum tolerated dosage. Subjects are closely monitored, often in a clinical setting, so that researchers can document the effects of the drug.[36]

The benefits to healthy volunteers participating in phase I trials are unclear.[37] There are no obvious medical benefits besides a free physical exam. Trial volunteers often receive payment for their participation,[38] but the FDA is very explicit in stipulating that financial compensation should not be included in the benefit assessment; instead it is a "recruitment incentive."[39] While some people may enjoy some sort of psychological benefit from acting altruistically, this benefit seems very dubious. It appears that the only meaningful way to understand benefits in phase I trials using

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[36] See NIH, "Clinical Trials"
[37] See Shamoo, Adil E. and David B. Resnik. "Strategies to Minimize Risks and Exploitation in Phase One Trials on Healthy Subjects." *American Journal of Bioethics*. 6 (2006): W1-W13.
[38] See Elliott, Carl. "Guinea-Pigging." *New Yorker*, 7 January 2008.
[39] Many have argued that this distinction does not make sense.

healthy volunteers is to consider the benefits to society. In order for a trial to be ethically justified, these expected benefits must be considerable, and the risk to the individual must be minimized.

Certain things built into the design of a study can help minimize risk. For example, before phase I trials are begun there must be evidence that everything short of human testing has been done to assess the safety of the agent being tested. The study design should require small incremental increases as dosage is tested, rather than starting at a very high dose that may immediately induce toxicity in the subject. Developing careful inclusion and exclusion criteria can also minimize risk. For example, testing the drug on healthy subjects helps minimize the chance that an underlying medical condition will exacerbate the side effects of the agent being tested. Another important way that risks are minimized is through close monitoring throughout a trial and dropping the subject at the earliest signs of harm.[40]

The question of how to balance risk and benefit changes when phase I trials use patients as their subjects. Researchers do not test cancer drugs on healthy volunteers because the drugs are so toxic.[41] The patients enrolled in phase I trials for cancer drugs are the sickest patients for whom all standard therapies have failed. Yet even here, of course, phase I trials are not designed to test the efficacy of a drug. They are designed to test toxicity, side-effects, and dosage. While it is possible that some patients might benefit, very few of them actually do. In this context, how should we balance risk and benefit when the potential benefits are so limited and the potential toxicity (risk) is so

[40] See Shamoo and Resnick.
[41] The same is true for most HIV/AIDS drugs although there are some that enroll healthy volunteers.

great? There is evidence that patients will be willing to participate in phase I trials even if the risks are great.

Many patients enrolled in research studies mistakenly believe that the purpose of the study is to treat their illness. The psychiatrist and ethicist Paul Appelbaum has famously called this mistaken belief the "therapeutic misconception."[42] Many cancer patients believe that they may directly benefit from participating in a phase I trial, even if told otherwise. For example, a study by Christopher Daugherty et al. found that 85 percent of 27 oncology patients in phase 1 trials said they participated in the trial because they expected some possible therapeutic benefit.[43] [44] A more recent empirical study by Agrawal and others surveyed 163 oncology patients participating in phase I trials.[45] A majority of patients seem to understand the purpose and risks of research. 90 percent of those interviewed said that they would participate in a trial even if the experimental drug caused serious side effects, including a 10 percent chance of death. Seventy-five percent reported moderate or severe pressure to participate in a trial because their cancer was spreading, but this pressure seemed to mostly come from their own desire to fight their cancer. Only seven-percent reported feeling pressure from investigators and nine-percent felt pressure from their families.[46]

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[42] See Appelbaum, Paul S. et al. "False Hopes and Best Data: Consent to Research and the Therapeutic Misconception." *Hastings Center Report,* 17 (1987): 20-24.
[43] Daugherty, Christopher et al. "Perceptions of Cancer Patients and Their Physicians Involved in Phase I Trials." *Journal of Clinical Oncology*. 13 (1995) 1062-1072.
[44] This study has been challenged by Manish Agrawal and Ezekiel Emanuel who argue that this result gets misinterpreted as meaning that the patients did not understand. It is possible that patients understand that there is a low chance of them benefiting directly, but still hope that they will benefit. See Agrawal and Emanuel. "Ethics of Phase 1 Oncology Studies: Reexamining the Arguments and Data." *JAMA*, 290 (2003): 1075-1082.
[45] Agrawal, Manish et al. "Patients' Decision-Making Process Regarding Participation in Phase I Oncology Research." *Journal of Clinical Oncology,* 24 (2006): 4479-4483.
[46] Ibid.

These studies suggest a larger ethical issue in clinical research. Ethicists have generally conceded that competent adults may enroll in trials with a certain amount of risk out of a desire to help others. Insofar as these trials lead to effective treatments, society as a whole will benefit from these patients' altruism. Yet many patients who enroll in clinical trials are vulnerable because of their illnesses, especially those with very poor prognoses. A sense of desperation may lead these patients to take part in risky trials where there is little chance of any therapeutic benefit. There is a thin line between the altruistic patient who enrolls in a trial to help other people and the desperate patient who enrolls in a risky trial out of an unrealistic hope for a cure. How do ethicists and regulators ensure that researchers do not exploit that desperation?

In the past, ethicists and regulators have attempted to design guidelines and procedures to prevent researchers from taking advantage of very sick patients. Those procedures were designed largely for researchers in academic settings. Beginning in the early 1990s, however, pharmaceutical research became much more commercialized, moving from partnerships with academia to private contractors. And as clinical research has become more commercialized, some ethicists have begun to question whether these ethical guidelines are sufficient to protect patients from exploitation. Yet as the pharmaceutical industry understood, patients themselves often see clinical research as their best hope for the future.

Second Power Shift: Academic Research to CROs and Private Physicians and Pharma Befriends Patient Activism

In 1990, Gerry Mossinghoff, president of the Pharmaceutical Research and Manufacturers of America (PhRMA), the pharmaceutical industry trade group, set up a new organization called the Healthcare Quality Alliance. The purpose of the Healthcare Quality Alliance, which was housed in PhRMA headquarters, was to coordinate and support a wide range of new and traditional patient organizations, including the American Diabetes Association and the American Cancer Society.[47] The Alliance looked for areas where PhRMA's interests allied with the interests of patient advocacy groups. At first the Alliance focused on lobbying Congress to increase spending on basic medical research at the NIH, using patient groups and individuals to make the case to members of Congress. But the Alliance soon moved into more specific efforts that were directly beneficial for the drug industry. As Greg Critser puts it, "At bottom, the alliance became a way to put a human face on any pharmaceutical demand – and if the demand happened to further pharma goals, so much the better."[48]

The Alliance began pressing its members to take a more active role in the drug approval process. Patient advocates began testifying at FDA advisory committee meetings on behalf of pharmaceutical companies. Mossingoff also encouraged pharmaceutical companies to invite patient groups to their plants, in order to build trust. As a result, when a pharmaceutical company expected to have trouble getting a drug approved by the FDA, they could approach patient groups and brief them about what

[47] Critser, Greg. *Generation Rx: How Prescription Drugs are Altering American Lives, Minds, and Bodies.* New York: Mariner Books, 2005, 26-27.
[48] Ibid., 27.

they should say in an advisory committee meeting.[49] The Alliance underwrote compilations of the latest medical information and breakthroughs and then sent patients and physicians to the Hill to share these "education opportunities for members of Congress."[50] Joe Isaacs, a staffer at the National Health Council who worked closely with the PhRMA says, "We basically created the disease-of-the-month club."[51]

Putting a human face on pharmaceutical demands was highly effective for both parties. Patient groups were getting attention and felt like they were making progress in producing more drugs for their particular conditions. For the pharmaceutical industry, the Alliance almost immediately produced a financial pay-off. For example, when Medicare threatened to not pay for expensive new beta-blocking drugs, patients went to Capital Hill to protest. Medicare decided to cover the drugs.

As patient advocacy groups were seeing their political influence rise, however, academic medical researchers were seeing their own power starting to wane. The 1990s were a time of extraordinary profits for the pharmaceutical industry; for much of the decade, the pharmaceutical industry was the single most profitable industry in the world.[52] But it was also a period in which pharmaceutical companies began to abandon universities as sites for clinical trials, preferring instead to partner with researchers and companies in the private sector, such as Contract Research Organizations (CROs).[53]

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[49] Ibid., 28.
[50] Ibid.
[51] Ibid., 27.
[52] See Public Citizen. "2002 Drug Industry Profits: Hefty Pharmaceutical Profit Margins Dwarf Other Industries." 2003. Accessed 25 October 2008. Available from http://www.citizen.org/documents/Pharma_Report.pdf
[53] See Shuchman, Miriam. "Commercializing Clinical Trials—Risks and Benefits of the CRO Boom." *New England Journal of Medicine*, 357 (2007): 1365-1368. Petryna, Adriana. "Clinical Trials Offshored: On Private Sector Science and Public Health." *BioSocieties*, 2 (2007): 21-40.

This shift represented a significant reversal. In the 1980s academic research had experienced a boom, spurred by changes in federal laws. The *Bayh-Dole Act* and the *Stevenson-Wydler Technology Innovation Act*, both enacted in 1980, allowed patenting and technology transfer by universities. This meant that universities and individual researchers could profit from their discoveries. As a result, universities were given a huge incentive to partner with pharmaceutical companies. The companies were eager to tap into the expertise of academic researchers, and perhaps even more importantly, into the pool of potential research subjects located in academic health centers.[54]

By the early 1990s, however, pharmaceutical companies had begun to find this partnership to be inefficient. Clinical trials were becoming more complex; university bureaucracies were slow and cumbersome; and it was getting more difficult to recruit research subjects. As a consequence, pharmaceutical companies began to move their clinical trials away from academic health centers to CROs and private testing sites. Today four out of every five clinical trials are performed in the private sector. According to the Tufts Center for the Study of Drug Development, ten of the largest CROS enrolled more than 640,000 subjects in clinical trials in 2004.[55] CROs provide approximately 40 percent of the personnel engaged in drug development[56] and in 2003 CROs played a substantial role in 64 percent of phase I, II, and III clinical trials.[57] In

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[54] See Bouchard, Ron A. and Trudo Lemmens. "Privatizing Biomedical Research—A 'Third Way'." *Nature Biotechnology* 26 (2008): 31-36.
[55] Shuchman, 1365.
[56] Petryna, 26.
[57] Shuchman, 1365.

1993 the drug industry spent $1.6 billion on contract research; by 2006, the figure had grown to $15 billion.

For the pharmaceutical industry, the rationale behind the move to the private sectors was simple: CROs and other private research services offer increased speed and efficiency. They are also less expensive, partly because of the difference in pay scales between CROs and academia.[58] According to Shuchman, these differences are directly reflected in their employees. Researchers in the pharmaceutical industry and academia tend to be more educated, better skilled, and older than CRO employees.[59] CROs move faster because they break each part of a study into discrete steps and emphasize speed in each step. The Tufts study also found that projects with a greater use of CROs finished closer to their projected completion date than studies that relied less on CROs.[60]

Adriana Petryna, an anthropologist studying clinical trials in the U.S. and abroad, argues that one of the main explanations of the shift to private contract research is that today's research demands larger pools of human subjects. The sheer number of clinical trials has increased in part because of the success of "me-too drugs" which have become a huge source for profits. But the number of trials has increased also because some categories of drugs, like anti-hypertensives for high blood pressure and statins for high cholesterol, are quickly expanding. Another contributing factor is that regulatory demands in the U.S. demand larger groups for testing long-term safety**.** The inability of academic health centers to recruit sufficient numbers of patients quickly has increased contract research, but it has also sent more trials outside the U.S. Sometimes studies

[58] Shuchman, 1367.
[59] Ibid.
[60] Ibid.

where recruiters are having a hard time attracting a sufficient number of subjects will actually change locations part-way into a trial.[61] For one study cited by Petryna, it had taken a year for 50 investigative sites in Western Europe to recruit sufficient numbers of rheumatoid arthritis patients. Once the study moved, five central-European sites were able to recruit the same number of subjects in just two months.[62]

The increased use of CROs by pharmaceutical companies was just one part of the move away from academia. In the early 1990s, pharmaceutical companies and CROs also began to prefer working with physicians in private medical practices and primary care centers over physicians working at academic health centers.[63] Once again, financial concerns played a central role. For pharmaceutical companies and CROs it was less expensive and easier to work with private physicians. There was far less red tape in private practices than in academic health centers. But private physicians were also highly motivated to participate in research for financial reasons. In the era of managed care, Petryna suggests**,** physicians were eager to turn their practices into investigative sites because it helped them recoup their shrinking profits.[64]

While it is clear that patient advocacy groups saw their political power grow by partnering with the pharmaceutical industry, it is less clear whether the partnership has actually benefited patients. The 1990s and early 2000s may have been the era of the blockbuster drug, but it was also an era that saw record numbers of drugs later withdrawn from the market, because of dangers they represented for patients. In 1997 the FDA removed the drug fen-phen (a combination of fenfluramine and phentermine)

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[61] These mid-trial shifts are called "rescue studies." Petryna, 25.
[62] Ibid., 34.
[63] Ibid., 33.
[64] Ibid.

after a study at the Mayo Clinic showed that thirty percent of patients taking fen-phen developed heart valve disease.[65] Vioxx was one of the most commonly used prescription drugs in America when a link to heart disease led regulators to pull it from the market in 2004.[66]

The shift of power from academic researchers to private research companies has also generated concerns about scientific integrity. Some critics have argued that CROs have a conflict of interest.[67] Because CROs are paid in full by pharmaceutical companies, and hope to have more contracts with companies in the future, they may have a financial incentive to cut corners at the expense of the quality of the research. This concern is exacerbated by the fact that CRO employees are typically not as well trained as academic staff. In addition, the ethical oversight of clinical trials conducted CROs is typically performed by for-profit IRBs, which are paid by the CROs and pharmaceutical companies themselves.[68]

The private drug-testing system also relies heavily on private physicians to conduct trials. There is no substantive research on this, but the nature of the relationship between industry and an academic researcher is likely to be different than the relationship between industry and a private physician. Private physicians are much

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[65] See Boodman, Sandra. "Diet Drug Danger; Rare Side Effects Raise Concern for Millions of Americans Who Have Turned to Pills to Lose Weight." *Washington Post*, 15 July 1997. In the year before it was withdrawn, over 18 million prescriptions had been written. Subsequent court proceedings have demonstrated that American Home Products knew about the potential dangers of the combination and downplayed risks in order to promote profits.

[66] Vioxx averaged $2.5 billion in sales each year. It is estimated that Vioxx caused as many as 138,000 heart attacks and 55,000 deaths in the United States. See Johnson, Carrie. "Merck Agrees to Blanket Settlement on Vioxx." *Washington Post* 10 November 2007.

[67] See Lenzer, Jeanne. "Truly Independent Research?" *BMJ* 337 (2008): 602-606.

[68] For more on for-profit IRBs see Lemmens, Trudo and Benjamin Freedman. "Ethics Review for Sale?" Conflict of Interest and Commercial Research Review Boards." *The Milbank Quarterly*, 78;4 (2000): 547-584.

more like subcontractors, doing whatever the drug company or CRO tells them to do. They also have a financial stake in recruiting subjects quickly. Perhaps most importantly, because private physicians are untrained as academic researchers and unlikely to be as motivated by concerns about their academic reputation, it is not clear how reliable they are as investigators.

The problems of relying on private physicians for drug testing became evident in the case of Ketek (telithromycin), an antibiotic developed by Aventis (now Sanofi Aventis).[69] In March 2000 Aventis submitted its first application to the FDA to sell Ketek, an antibiotic used to treat respiratory infections, in the U.S. In June 2001 the FDA declined to approve the drug, citing insufficient evidence of safety. Liver damage is a common concern with antibiotics, and in order to receive FDA approval Sanofi-Aventis needed more proof that such a risk was small. At the request of the FDA, Sanofi-Aventis conducted a new study which they contracted out to the CRO Pharmaceutical Product Development Inc. (PPD). Starting in October 2001 this study, study 3014, enrolled more than 24,000 people at various sites in the United States. The study was supposed to enroll patients with respiratory infections, and participants were given either Ketek or Augmentin (amoxicillin clavulanate), a widely used antibiotic. PPD contracted with primary care physicians to conduct the study. Physicians could receive $450 for each patient they enrolled: $100 at the time a patient signed up, $150 when they submitted results and another $150 when all the questions were resolved.[70]

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[69] Mathews, Anna Wilde. "Infected Data: Fraud, Errors Taint Key Study of Widely Used Sanofi Drug; Despite Some Faked Results, FDA Approves Antibiotic." *Wall Street Journal*, 1 May 2006.
[70] Ibid.

However, FDA inspectors discovered that two of the top-recruiting private physicians used by PPD to enroll patients seriously violated the integrity of the study. Dr. Maria "Anne" Kirkman Campbell in Gadsden, Alabama enrolled the most patients in the study (407 total). However, an FDA investigation found that many of the patients she reportedly enrolled were completely fictitious. She made up patients and created fake laboratory reports, all of which were sent to PPD. Dr. Campbell is now in federal prison after pleading guilty to defrauding Aventis and others. Dr. Egisto Salerno, who enrolled the third most patients in study 3014, was on probation with the state medical board at the time he participated in the trial, for gross negligence and failure to keep accurate records. Shortly after the study, police responded to a domestic disturbance call at his home and found him waiving a loaded semiautomatic handgun and hiding a bag of cocaine in his underwear.[71]

Although PPD alerted Aventis to concerns about both of these study sites (and others), Aventis investigated and found no wrongdoing. However, after study 3014 was complete and the data were submitted to the FDA the agency conducted its own investigations and determined that it included so many flaws that it could not be used. The FDA still approved Ketek without relying on study 3014, based on the drug's record in Europe and other countries.[72] Yet safety concerns over Ketek still remain. In 2005 a 26-year-old construction worker died in North Carolina from liver failure after

[71] Ibid.
[72] In July 2001 Ketek was approved in Europe.

taking Ketek, and in 2006 the *Annals of Internal Medicine* reported two additional cases of liver damage in people taking Ketek.[73]

The shift to commercialized research has created a new set of motivations by physicians, CROs, and others, which patients have not quite begun to fully understand. This shift has changed some of the dynamics of patient activism, not to mention the dynamics of research ethics and regulation.[74] The number of clinical trials has increased dramatically, yet the FDA only inspects about one percent of trials. Private IRBs review these trials, but the private IRBs are paid by the trial sponsors. Patient advocacy groups claim to work on behalf of patients, but many advocacy groups have formed alliances with the pharmaceutical companies conducting the trials. In this new research environment, who will ensure the welfare of research subjects?

Conclusion

In the first shift of power described in this chapter, research subjects made alliances with academic researchers and regulators in order to claim some power for themselves. These relationships still reflected important moral dimensions in medicine. Physicians were bound by tradition and an ethical code, which reinforced their obligations to respect their patients and research subjects. In addition, the lessons of research scandals had resulted in professional and institutional safeguards aimed at protecting research subjects from harm or exploitation. The FDA is charged with protecting people from unsafe drugs, and while it has instituted significant changes

[73] Clay, KD et al. "Severe Hepatotoxicity of Telithromycin: Three Case Reports and Literature Review." *Annals of Internal Medicine.* 144 (2006): 415-420.
[74] See Evans, David et al. "Big Pharma's Shameful Secret." *Bloomberg Markets,* December 2005.

beginning in the 1980s at the behest of patient activists, the Abigail Alliance case suggests that the FDA is still unwilling to place the autonomy of patients over its duty to protect them from potential harm

However, the second shift of power, towards commercialized clinical research, has changed the shape of patient activism. Under the old system of drug research, when pharmaceutical companies partnered with academic researchers, the political power of patients was much more limited. Academic researchers had no interest in hearing from subjects, because subjects had nothing to offer them. (Subjects do not help academic researchers get NIH grants.) But once the balance of power shifted to the private sector and clinical research became a more thoroughly commercial activity, the pharmaceutical industry began to understand that patient advocacy groups could help serve their commercial aims. As a result, patient advocacy groups and pharmaceutical companies began to form strategic alliances. These were alliances of convenience for both parties, of course. Each party benefited from the other's power. In the end, however, their aims will necessarily diverge. For-profit organizations such as pharmaceutical companies and CROs generally do not see themselves as having a moral obligation to put the interests of patients over their own financial well-being. They may be happy to align with patients when it is in their interest, but will they sacrifice their overall financial interests in the name of patient care?

In 2002 the biotech company Amgen began testing a treatment for Parkinson's disease using the hormone GDNF (glial cell-line derived neurotrophic factor).[75] GDNF

[75] See Pollack, Andrew. "Many See Hope In Parkinson's Drug Pulled from Testing." *New York Times,* 26 November 2004. Wade, Nicholas. "Promising Results Are Seen in Small Parkinson's Trial." *New York Times* 8 April 2003.

was delivered directly into the brains of Parkinson's patients via a pump inserted in their abdomen. Early trials were promising, but in June 2004, Amgen announced that the treatment failed in a larger study and decided to stop clinical trials. That, in itself, was not unusual. What made the GDNF trial unique was that some of the patients enrolled in the trials did not quietly accept the results announced by Amgen. These patients had experienced relief from their Parkinson's disease while taking GDNF, and they wanted the chance to keep taking the drug once the trial was canceled. But the only way to get the drug was through Amgen. Although the FDA said that it was permissible for Amgen to continue providing patients with the drug, Amgen refused. According to *The New York Times*, "Company officials said that besides exposing patients to unnecessary risks, to let them continue treatment would only generate false hopes. It might also ultimately hinder development of improved versions of the drug."[76]

Since the FDA had approved continuing therapy, Amgen's concerns about exposing patients to unnecessary risks struck patient advocates as disingenuous. Robin Anthony Elliott, executive director of the Parkinson's Disease Foundation told the *New York Times*, "We think there is kind of a moral pact that one makes with a company in these situations that gives them the privilege of having continued access to treatment."[77] Yet what kind of "moral pact" is a for-profit corporation bound by? Whatever the relationship between Amgen investigators and research subjects is, it is not the same as a relationship between physicians and patients. The patients who enrolled in Amgen

[76] Pollack
[77] Ibid.

trials may have thought of the relationship this way, but Amgen is a corporation which answers to its shareholders.

Is the relationship between a corporation and a patient like the relationship between doctor and patient, governed by the norms of medicine, or is it more like a commercial relationship, governed by the norms of business? This question will become even more important in the next chapter, which will examine the way that patients have been used not merely to press a research agenda, but to market drugs.

CHAPTER FOUR

Social Phobia

Abstract

This chapter describes the emergence of social phobia (social anxiety disorder) in the 1980s and its explosive growth in the 1990s. Key catalysts were the *DSM-III (Diagnostic and Statistical Manual of Mental Disorders)*, the introduction of a new class of antidepressants called the SSRIs (selective serotonin reuptake inhibitors), and the marketing of drugs directly to potential consumers. Pharmaceutical companies benefited greatly from shifts within psychiatry away from psychoanalysis and towards greater focus on neuropsychiatry. The growth of social phobia, and in particular its broad definition which now includes what twenty years ago was called "shyness", and its treatment with SSRIs, illustrates what sociologists call medicalization. Medicalization is a process by which nonmedical problems become re-defined and treated as medical problems. When social anxiety disorder was introduced in the *DSM-III* in 1980, it was thought to be uncommon. By the time the FDA approved Paxil (an SSRI) in 1999 for its treatment, it was estimated that as many as one in eight people experience it sometime in their lives. Heavily promoting diseases and cures is not entirely new, but the extent to which pharmaceutical companies created new markets in the 1990s increased dramatically. A significant part of this story is how GlaxoSmithKline, the maker of Paxil (paroxetine), co-opted the power of patient advocacy groups by creating and funding its own fake patient group, which promoted awareness and treatment of social phobia.

Introduction

In 1999 bus shelters across the country were plastered with posters asking us to "Imagine Being Allergic to People." There is a picture of an attractive man, sitting alone at an outdoor café, staring into a teacup. The accompanying copy says:

> "You know what it's like to be allergic to cats, or dust, or pollen. You sneeze, you itch, you're physically ill. Now, imagine that you felt allergic to people. You blush, sweat, shake—even find it hard to breathe. That's what social anxiety disorder feels like. Over ten million Americans suffer from **social anxiety disorder**, an excessive, persistent, disabling fear of embarrassment or humiliation in social, work, or performance situations. The good news is that this disorder is treatable.

> People can overcome social anxiety disorder. So, if you feel like you're "allergic to people" talk to your doctor or other health professional."[1]

At the bottom of the posters there is a toll-free number and website listed for more information. There is also a reference to a group called the Social Anxiety Disorders Coalition, which consists of the Anxiety Disorders Association of America, the American Psychiatric Association and Freedom from Fear (FFF).

Anyone looking at this poster would likely assume that these organizations are part of some grass roots movement: sufferers of social anxiety disorder banding together to try to increase awareness of their disease. It turns out, however, that the Social Anxiety Disorder Coalition is a phony patient advocacy group created and funded by GlaxoSmithKline,[2] the maker of Paxil (paroxetine), an SSRI antidepressant and the first drug approved for the treatment of social anxiety disorder. Cohn and Wolfe, GlaxoSmithKline's public relations firm, had cobbled together this whole group themselves. As Brendan Koerner reported in an investigative report in *Mother Jones*, if a prospective social anxiety disorder sufferer called the phone number on the poster, they were connected to an office at Cohn and Wolfe.[3]

By 1999 alliances between patient advocacy groups and pharmaceutical companies were nothing new.[4] Patient groups had begun to help pharmaceutical companies humanize diseases and promote awareness as well as treatments. They were

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[1] Copy of the ad reproduced in Lane, Christopher. *Shyness: How Normal Behavior Became a Sickness.* New Haven and London: Yale University Press, 2007, 124.

[2] GlaxoSmithKline is the present name of the company that has experienced several acquisitions and mergers over the past two decades. When Paxil was approved for social anxiety disorder the company was still known as SmithKline and other names include SmithKline Beecham and GlaxoSmithKline Beecham. For consistency, throughout this chapter I will use the contemporary name to refer to the maker of Paxil.

[3] Koerner, Brendan I. "Disorders Made to Order." *Mother Jones*, 1 July 2002.

[4] See Chapter Three.

also lobbying Congress for increased funding and quicker FDA approvals. What is important about the social anxiety disorder awareness campaign is that GlaxoSmithKline skipped patient advocates altogether, using a fake patient group to market the condition-- and by implication, the drug used to treat the condition--to real patients. Patient advocacy groups had become so influential that drug companies had moved from trying to co-op their power to a complete impersonation. Today watchdog organizations have begun referring to groups such as the Social Anxiety Disorder Coalition as "Astroturf" groups, to suggest their artificial resemblance to grassroots organizations.[5]

The marketing of Paxil was a remarkable success. Within two years Paxil had become the ninth most profitable drug in America, surpassing sales of Prozac for the first time, and Cohn and Wolfe had picked up an award for the best public relations campaign of 1999.[6] The success of Paxil was all the more remarkable for the fact that the main disorder which it treated, social anxiety disorder, had been seen by psychiatrists as a very rare disorder only a decade earlier, and did not even officially exist until 1980. Today, however, many experts say that social anxiety disorder is the third most common mental disorder in the United States.[7] The story of the rise of social anxiety disorder and its treatment by antidepressants is a powerful illustration of how pharmaceutical companies have learned the lessons of patient activism and used patients to market their drugs.

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[5] See Marshall, Jessica. "Patient Groups Special: Swallowing the Best Advice?" *New Scientist*, 27 October 2006.
[6] See Koerner and Lane, 126.
[7] See Stein, Murray B. and Dan J. "Social Anxiety Disorder." *Lancet*, 371 (2008): 1115-1125.

Defining Social Phobia (Social Anxiety Disorder)[8]

It is estimated that one in eight Americans suffer from social anxiety disorder, or social phobia, at some point in their lives.[9] Social phobia is characterized by excessive anxiety and self-consciousness in everyday social situations. The disorder first appeared in the *DSM*[10] in 1980, the manual's third edition. Accounts of social phobia usually cite the importance of *DSM-III* in promoting the condition, but there is rarely any discussion of how this actually came about. In his book, *Shyness: How Normal Behavior Became a Sickness*, Christopher Lane gives the first detailed account of how social anxiety disorder came to appear in the *DSM-III*. Using access to important archives and interviews with key players, Lane argues that in fact, the production of *DSM-III* was arbitrary and unsystematic.

The *DSM-III* completely changed that way that professionals and the public think about mental health. *DSM-III* was more than just a revision of *DSM-II*; it was a complete overhaul of the manual, introducing many new mental disorders. When the process to revise the *DSM* was first begun in 1974, the field of psychiatry was suffering from an image problem. Several scandals had challenged the field's reputation. For example, in 1973, *Science* reported a sting operation where, at the direction of investigators, eight ordinary people went to twelve different hospitals, claiming to that they kept hearing voices saying "empty," "hollow," and "thud."[11] Seven of them were

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[8] The term social phobia was replaced in *DSM-IV* with social anxiety disorder. I use them both interchangeably in this chapter.

[9] Stein MB, JR Walker, and DR Forde. "Setting Diagnostic Thresholds for Social Phobia: Considerations from a Community Survey of Social Anxiety." *American Journal of Psychiatry*. 151; 3 (1994): 408-412.

[10] Produced by the American Psychiatric Association the *DSM* is currently in its fourth edition. Discussions in this chapter refer to a several different editions: *DSM-I* (1952), *DSM-II* (1968), *DSM-III* (1980), *DSM-IIIR* (1987), and *DSM-IV* (1994). *DSM-V* is expected in 2012.

[11] Lane, 40 and Rosenhan, D.L. "On Being Sane in Insane Places." *Science*, 179 (1973): 251-252.

hospitalized and diagnosed as having schizophrenia, despite the fact that they were otherwise perfectly healthy. The *Science* report was widely seen as an indication that the field was in disarray and reinforced the perception that psychiatry was unscientific and arbitrary.

The *DSM-II*, the predecessor to *DSM-III*, re-enforced these images of psychiatry. It was a thin, inexpensive book that, according to Lane was often mocked for its flaws and for being outdated.[12] The American Psychiatric Association (APA) sought to use the revision of the *DSM* to revamp the entire field, combating perceptions that psychiatry was unscientific. At the heart of this image problem was a battle between the neuropsychiatrists and the psychoanalysts. The tension between these two camps was huge, and they represented fundamental differences in understandings of how the psyche works as well as different solutions to address mental disorders. Neuropsychiatrists generally saw mental illness as a biological phenomenon, remediable by biological interventions, whereas the psychoanalytic camp believed that mental health professionals must look at emotional and cultural influences as well. The APA was home to both approaches, which set up serious conflicts and turf battles. There were concerns that these battles would end up damaging the profession.[13]

Melvin Sabshin, the medical director of the APA, thought that a new edition of the *DSM* would help end the fights and scandals: "I wanted it to rely on data rather than opinion or ideology alone [so the field would be] better prepared to deal with the vicissitudes of economic pressures."[14] His mention of economic pressures is

[12] Lane, 40.
[13] Ibid.
[14] Ibid., 40-41.

particularly interesting because it implies that making mental disorders more "scientific" is what makes them more legitimate and acceptable. Sabshin wanted a standardized classification system that would reflect the current state of knowledge. In retrospect, the idea that the *DSM-III* would resolve these turf battles seems quite naïve. Even from the start, it appeared impossible for the committee in charge of revising the manual to remain ideologically neutral. Because the two camps were in such great conflict, it was impossible from the start to produce one manual that would satisfy both sides.

Understanding this framing is important. It was not the case that there was some sort of strategic conspiracy to completely redefine our understanding of mental disorders. In fact, however, this was the practical effect. The idea behind *DSM-III* was that there were underreported mental disorders that needed to be identified, and that the *DSM* would update the understanding of mental disorders by psychiatrists as well as the public. The framers of *DSM-III* believed that by naming and identifying these underreported disorders, the manual would more accurately reflect what existed out there in the world. But this approach sides with the neuropsychiatric approach from the start, which is committed to rapid, standardized results. The divide between neuropsychiatrists and psychoanalysts guaranteed that decisions about what appeared in the new edition would be political and contentious.[15]

The project to revise the *DSM* was labeled the "APA Task Force on Nomenclature and Statistics" and Dr. Robert Spitzer was appointed to chair the effort. Dr. Spitzer is a member of The Biometrics Department of the New York State

[15] Lane, 41.

Psychiatric Institute at Columbia Presbyterian Medical Center, where he has worked for nearly forty years.[16] After graduating from medical school at NYU, Spitzer was a resident and student at the Columbia Center for Psychoanalytic Training and Research. He had tried Reichian analysis as a teenager and he found that experience helpful as he struggled with expressing his emotions. In college he wrote a paper criticizing Reich, but he was still interested in psychotherapy. However, his career had floundered. Psychoanalysis was too abstract and too theoretical. Spitzer commented in an interview a few years ago, "I was always unsure that I was being helpful, and I was uncomfortable listening and empathizing—I just didn't know what the hell to do."[17] Spitzer's own reservations reflected the growing crisis in psychiatry over reliability and validity. In 1966 Spitzer happened to share a lunch table with the chairman of the *DSM*-II task force. By the end of the meal, Spitzer was asked to serve as note-taker. He was soon promoted, and when the time came to produce *DSM-III,* Spitzer was appointed chair.

Nowadays the chairmanship of the *DSM* committee is a coveted position, but that was not true at the time. Donald Klein, a panic expert at Columbia who worked on *DSM-III* commented, "When Bob was appointed to the *DSM-III,* the job was of no consequence. In fact, one of the reasons Bob got the job was that it wasn't considered that important. The vast majority of psychiatrists, or for that matter the APA, didn't expect anything to come from it."[18] The various committees within the Task Force were supposed to reflect a variety of views and gather experts from throughout the field. In order for the revision to be successful and meet the purpose of improving psychiatry's

[16] See Lane's description of Spitzer, 6-7 and 39-46. Also Spiegel, Alix. "The Dictionary of Disorder: How One Man Revolutionized Psychiatry." *New Yorker*, 3 January 2005.
[17] Spiegel.
[18] Ibid.

reputation, there would have to be support from the whole diverse field of psychiatry. Spitzer was appointed head of the project because he had expertise in both camps. It quickly became clear, however, that he was aligned with neuropsychiatry.

When *DSM-III* was completed, it represented a huge change from *DSM-II*. The process took six years and the final results added 112 new mental disorders and disease categories.[19] For example, *DSM-II* had just one large category capturing anxiety, called "anxiety neurosis." The new edition split anxiety neurosis into seven new parts: agoraphobia, panic disorder, post-traumatic stress disorder (PTSD), obsessive compulsive disorder (OCD), generalized anxiety disorder, simply phobia, and social phobia.[20] This change as well as others significantly increased the number of mental disorders. *DSM-IIIR* lists 292 categories of mental disorders and *DSM-IV* lists over 350.[21] A third of the mental illnesses described in *DSM-III* were "discovered" by the task force. In some cases, this "discovery" was a matter of searching the medical literature and finding reports of disorders not included in *DSM-II*. In other cases, members of the various committees were themselves experts on some particular disorder and they argued for its prevalence.

The fact that so many new disorders were introduced in *DSM-III* is not itself a bad thing; perhaps psychiatry really did need to catch up with what was actually going on "out there" in the world. What is problematic, however, is that the process for coming up with these new disorders was hardly systematic and scientific. Lane's description, through interviews and examination of meeting archives, leaves the

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[19] Lane, 42.
[20] Ibid.
[21] Lane, 43.

impression that many of the new disorders simply came off the top of the heads of the committee members, especially Spitzer's. Theodore Millon, a consultant to the task force says, "There was very little systematic research, and much of the research that existed was really a hodgepodge—scattered, inconsistent and ambiguous."[22] Renee Garfinkel, an administrator at the American Psychological Association said, "The poverty of thought that went into the decision-making process was frightening" (45). These observations are quite ironic, since the purpose of the revised edition was to make the field more scientific.

Many critics accused Spitzer and his hand picked task-force of bias. Spitzer denies this, claiming that the task force was simply cataloging symptoms. *DSM-III* does not favor neuropsychiatric frameworks over psychodynamic ones. But as Lane also explains, Spitzer's claim is disingenuous. By excluding some conditions, like anxiety neurosis, that areas like psychoanalysis had recognized for decades, *DSM-III* was tipped in favor of peuropsychiatry. By leaving out terms like anxiety neurosis, the task force signaled that such ways of thinking about mental illness were outdated.[23] Spitzer claimed that the task-force's project was merely descriptive, but the proposed terms, like avoidance personality disorder and social phobia was also prescriptive.[24] Including them signaled that they were discrete illnesses which deserved to be treated. These choices also reflect the biological perspective of a neuropsychiatric framework: "to psychiatrists the word *disorder* implies a stronger biological connection than

[22] Ibid., 44-45.
[23] Lane, 46.
[24] Ibid., 56.

neurosis."[25] Grounding social phobia and other conditions in biological explanations paved the way for their growth by legitimizing them.

The inclusion of social phobia in *DSM-III* was not based on a large amount of evidence.[26] The Task Force had latched onto a report by Isaac Marks and Michael Gelder. In 1966 Marks and Gelder had published a review describing several different kinds of panic they saw in patients.[27] A small number of patients grew anxious when required to participate in social situations. Signs of their distress included fears of blushing in public, attending dances or parties, and shaking when the center of attention. Four years later Marks published a report stating, "Evidence is lacking that [social phobia] is a coherent group…We need to know more about social phobics before definitely classifying them on their own."[28] Yet, Spitzer's group took this as evidence that social phobia existed.[29]

The reshaping of "anxiety neurosis" into seven distinct disorders is just one example of ways in which *DSM-III* both expanded categories of mental disorders and introduced new ones. One move that proved instrumental in reshaping anxiety disorders was the evolution of "introverted personality disorder" into "schizoid personality disorder." According to *DSM-II,* introverted personality disorder aligns with personality disorders. But as the task force worked and expanded many of the earlier categories, there started to be a lot of overlap between disorders. So, it also

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[25] Ibid.
[26] Ibid., 71.
[27] See Marks, I.M. and M.G. Gelder. "Different Ages of Onset in Varieties of Phobia." *American Journal of Psychiatry*, 123 (1966): 218-221.
[28] Lane, 72 and Marks, I.M. "The Classification of Phobic Disorders." *British Journal of Psychiatry*, 116 (1970): 377-386.
[29] Interestingly, Marks refers to the so called pandemic of social phobia in the 1990s as an "advertising ploy" (Lane, 73).

made sense to think of introverted personality disorder as an anxiety disorder. In addition, a new illness "avoidant-personality disorder" (APD) was recommended by the Advisory Committee on Personality Disorders.[30] No one could say how it was different from social phobia and schizoid personality disorder, but that did not seem to matter. The committee essentially formed three distinct illnesses out of behavior that was essentially the same.

Later editions of *DSM* expanded the domain of social phobia still further. The original definition focused on patients with a single social anxiety, such as public speaking or eating in public. Those with multiple anxieties or general social anxiety were thought to have something else. In addition, it was not enough for a patient with social phobia to simply fear a situation; a person's anxiety must cause him or her to avoid the social situation completely. *DSM-IIIR*, published in 1987, redefined the condition to include routine embarrassment and "possible scrutiny by others." In 1994, *DSM-IV* renamed the illness "social anxiety disorder" and expanded the definition even further. In *DSM-IV* social anxiety disorder still involved excessive worry about embarrassing oneself in front of other people, but it was not limited to one activity, and it only required that anxiety *may* keep a person from that activity, such as going to school or work.

As the *DSM* was being revised, estimates of the prevalence of social phobia increased dramatically. In 1980 the *DSM-III* indicated that social phobia was a rare disorder, and the ECA study, conducted in the early 1980s, found the prevalence to be

[30] Lane, 92.

2.75% in community populations.[31] A decade later, however, the NCS study estimated the lifetime prevalence at 13.3%, making social phobia the third most common mental illness in the United States, behind depression and substance abuse. Estimates of the percentage of the population who suffer from social phobia now range up to 19%.[32]

What explains the huge change in just a decade? Did social anxiety really increase that much in the general population? Allan Horwitz argues that the increase in prevalence came about partly because of the change in the survey questions used to measure it. In early surveys, a diagnosis of social phobia simply required a "compelling desire to avoid exposure to social or performance situations," whereas later surveys required only "marked distress" in these situations.[33] Given these differences in wording, it is not at all surprising that prevalence would increase so drastically. As Horwitz notes, "Social phobias illustrate not only how community studies overestimate rates of disorder, but also how these studies can in large part *create* the disorders they supposedly measure."[34]

DSM-III was also a lucky break for pharmaceutical companies. Horwitz and Wakefield note that "There is no evidence that pharmaceutical companies had a role in developing *DSM-III* diagnostic criteria…Yet, serendipitously, the new diagnostic model was ideally suited to promoting the pharmaceutical treatment of the conditions it

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[31] Horwitz, Allen V. *Creating Mental Illness*. Chicago, University of Chicago Press, 2002, 95.
[32] Ibid.
[33] Ibid.
[34] Ibid.

delineated."[35] *DSM-III* was supposed to maintain a neutral stance toward the etiology of mental disorders, but in practice, its focus on symptoms served the pharmaceutical industry nicely.[36] If the diagnosis of a mental disorder depended solely on the behavioral symptoms of a patient, then that diagnostic category could be expanded by manipulating the criteria necessary to diagnose it. And of course, the wider a disease category can be expanded, the more drugs that can be sold to treat it.

Paxil, the SSRIs, and the Medicalization of Shyness

Over the past two decades, antidepressants such as Prozac, Zoloft, and Paxil have earned record breaking profits. These drugs have been used so widely that they have become common terms in popular culture. Yet in the 1970s and early 1980s depression was considered a rare disease, and many drug companies thought that antidepressants would be unprofitable. Eli Lilly, the maker of Prozac (fluoxetine), actually killed development of the drug seven times before allowing it to go to market.[37] When Prozac was submitted to regulators in Germany in 1984,[38] the regulators concluded, "Considering the benefit and the risk, we think this preparation totally unsuitable for the treatment of depression."[39]

The FDA approved Prozac (fluoxetine) for major depression in 1987. By 1989, annual sales had reached $350 million, which was more than the total amount that Americans had previously spent on antidepressants. By 1995 Prozac exceeded $1

[35] Horwitz, Allen V. and Jerome C. Wakefield. *The Loss of Sadness: How Psychiatry Transformed Normal Sorrow into Depressive Disorder*. New York: Oxford University Press, 2007, 182.
[36] Ibid., 179.
[37] Healy, David. *Let Them Eat Prozac*. New York and London: New York University Press, 2004, 39.
[38] Ibid., 90.
[39] Ibid.

billion annually in sales, the mark at which a drug is generally considered a "blockbuster." By 1998, it had reached $2 billion.[40] Magazine articles touted the new antidepressants as "breakthrough drugs" that would change the lives of millions. SSRIs were believed to have fewer side effects than traditional antidepressants, and some people said that the drugs made them feel better than they had ever felt before.

In *Listening to Prozac* psychiatrist Peter Kramer coined the term "cosmetic psychopharmacology" to refer to what he was seeing in some of his patients on Prozac.[41] By cosmetic psychopharmacology, Kramer was referring to drugs that not only make sick people well, but which make well patients feel "better than well." Kramer found that occasionally, Prozac produced dramatic turnarounds in patients who were not clinically depressed, but who were lonely, obsessive, sad or shy. In earlier times, these patients would not have been candidates for antidepressants, which were unpleasant to take. Yet on Prozac, according to Kramer, these patients thrived.

Prozac may have been the most popular form of cosmetic psychopharmacology, but it was by no means the first. In 1955, Wallace Laboratories had introduced Miltown (meprobamate), a "tranquilizer" and the first psychiatric drug developed and marketed for the anxiety and depression of everyday life.[42] Miltown was met with a popular frenzy, and according to the historian, Edward Shorter, "by 1956, one American in twenty was taking tranquilizers within a given month."[43] The follow-up to Miltown was Valium (diazepam), which proved even more popular. Psychiatrists embraced

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[40] Barber, Charles. *Comfortably Numb: How Psychiatry Is Medicating a Nation.* New York: Pantheon Books, 2008, xv.
[41] Kramer, Peter D. *Listening to Prozac: A Psychiatrist Explores Antidepressant Drugs and the Remaking of the Self*. New York: Penguin Books, 1993.
[42] Shorter, Edward. *A History of Psychiatry: From the Era of the Asylum to the Age of Prozac*. New York: Wiley, 1997.
[43] Shorter, 316.

Valium; it was more potent than the mild Miltown but did not sedate patients like the antipsychotics. It offered psychiatrists an effective tool for treating patients who did not suffer from serious psychotic conditions, but rather from the anxiety of ordinary life. Introduced in 1963, Valium later became the most successful drug in pharmaceutical history, until it was surpassed by Prozac.[44]

The problem with Valium and other benzodiazepines is that they are addictive. In 1975 the FDA began to heavily regulate their prescription. Yet concerns about "tranquilizers" such as Valium were as much cultural as medical. The cultural backlash was characterized by concerns that these drugs were not treating a well-defined mental disorder, but simply sedating people so that they could tolerate the stresses of everyday living. In 1980 the FDA regulations stated that "anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic."[45] By the time the *DSM-III* came out in 1980, the public enthusiasm for anti-anxiety drugs was just beginning to wane.

When pharmaceutical companies began to introduce the SSRI antidepressants in the late 1980s and early 1990s, it would have been possible to market the drugs as treatments for anxiety. However, the pharmaceutical companies worried that this would be difficult, because of the lingering concerns and memories of anxiolytics such as Valium.[46] They also anticipated that these concerns might be a barrier to FDA approval. But the description of major depressive disorder (MDD) in the *DSM-III* gave drug manufacturers the perfect alternative. As Horwitz and Wakefield suggest, "the

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[44] Ibid., 318.
[45] Ibid., 181.
[46] Horwitz and Wakfield, 182.

DSM diagnosis of MDD was more suitable than any of the various anxiety disorders for capturing the distress of persons seeking help from general physicians and outpatient psychiatrists."[47] Hence the pharmaceutical industry initially tested and marketed the SSRIs as antidepressants.

Paxil was approved by the FDA for major depressive disorder in 1992, five years after Prozac, and one year after Zoloft.[48] As the decade progressed, Paxil also received FDA approval for obsessive-compulsive disorder, panic disorder, post-traumatic stress disorder, premenstrual dysphoric disorder, generalized anxiety disorder, and of course, social phobia. (Its patent expired in 2006.) In addition to Paxil, Prozac and Zoloft, the class of SSRIs now also includes Celexa (citalopram), Lexapro (escitalopram oxalate), and Luvox (fluvoxamine maleate), as well as the chemically similar SNRIs (serotonin-norepinephrine reuptake inhibitors) such as Effexor (venlafaxine) and Cymbalta (duloxetine).[49]

In the early 1990s, Paxil had a difficult time competing with Prozac and Zoloft, which dominated the SSRI market. By the mid-1990s, the market for antidepressants was even more saturated, and GlaxoSmithKline decided that the time was right to market Paxil for anxiety. By this point the American population had become comfortable with the SSRIs, and memories of the problems of anxiolytics such as Valium had begun to recede. Picking up on the *DSM-IIIR* expanded definition of social

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[47] Ibid.
[48] See Healy, David. *The Anti-Depressant Era*. Cambridge, MA: Harvard University Press, 1997.
[49] See Barber.

phobia and the renaming in *DSM-IV* to "social anxiety disorder," GlaxoSmithKline decided to market Paxil as an anti-anxiety drug.[50]

Although Paxil was already approved as an antidepressant, GlaxoSmithKline had to provide evidence to the FDA that Paxil was also an effective treatment for anxiety. The company succeeded in 1999, just one and a half years from the time it started the approval process, and Paxil became the first drug approved by the FDA for social anxiety disorder. The "Imagine Being Allergic to People Campaign" was timed perfectly with the FDA announcement. Paxil won five patent extensions between 1998 and 2001 which brought additional profits of $1 billion for each of the five years the brand was extended.[51] [52]

Sociologists call medicalization "a process by which nonmedical problems become defined and treated as medical problems, usually in terms of illnesses or disorders."[53] In recent decades, sociologists argue, distractibility has been medicalized into attention deficit disorder, fatness has been medicalized into obesity, and sadness has been medicalized into clinical depression. The marketing of Paxil depended on a similar kind of domain expansion, reflecting what may be called the medicalization of shyness. Giving shy people a drug simply to make them more outgoing might seem to fall outside the ordinary domain of medicine. But many physicians feel more

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[50] Critser, Greg. *Generation Rx: How Prescription Drugs are Altering American Lives, Minds, and Bodies*. New York: Mariner Books, 2005, 63-64.
[51] Medawar, Charles and Anita Hardon. *Medicines Out of Control? Antidepressants and the Conspiracy of Goodwill.* Netherlands: Aksant Academic Publishers, 2004.
[52] In the years since 1999 the FDA has approved Prozac, Zoloft and Effexor for social anxiety disorder as well.
[53] Conrad, Peter. "Medicalization and Social Control." In *Perspectives in Medical Sociology*, edited by Phil Brown, 137-62. Prospect Heights, IL: Waveland Press, Inc., 1996, 137.

comfortable prescribing Paxil if it is for a recognized mental disorder such as "social anxiety disorder."

In the 1960s and 70s, sociologists working on medicalization emphasized the power of physicians and professional organizations. Medicalization was largely seen as a way of expanding professional power. But in his essay, "The Shifting Engines of Medicalization", medical sociologist Peter Conrad describes how medicalization today is being powered by different forces: managed care, of course, but also the pharmaceutical and biotechnology industries, as well as consumers themselves.[54] Today, pharmaceutical companies medicalize conditions as a way of marketing their drugs. Pfizer medicalized impotence into "erectile dysfunction" as a way of selling Viagra; Lilly medicalized menstruation into "premenstrual dysphoric disorder" as a way of selling Sarafem; and GlaxoSmithKline medicalized shyness into "social anxiety disorder" as a way of selling Paxil.

Defenders of social phobia as a genuine mental disorder, rather than simply medicalized shyness, sometimes invoke what Lane refers to as a "transhistorical" argument. These defenders argue that the symptoms of social phobia can also be seen in many other historical periods. But Lane argues that the transhistorical argument is simply not true: shyness and anxiety have meant different things throughout history. Shyness has a long history, but it has not always been connected with anxiety, and it was not used to describe humans until the seventeenth century. Before then, "shy" was used to describe an animal that was easily frightened. When the adjective "shy" started

[54] Conrad, Peter. "The Shifting Engines of Medicalization." *Journal of Health and Social Behavior,* 46 (2005): 3-14.

to be applied to humans, it usually meant something like reticent, suspicious, or untrustworthy. It was not seen as a sign of mental pathology.[55]

Anxiety, on the other hand, according to the *Oxford English Dictionary*, made its first appearance in English in Sir Thomas More's writing in 1525: "There dyed he, without grudge, without anxietie."[56] But here anxiety means worry or concern, not illness. The Greeks described the phenomenon we would call stage fright, but there is no evidence that it was considered abnormal. The association of anxiety with more extreme cases did not come until the end of the nineteenth century, when medical lexicons began calling anxiety a morbid "condition of agitation and depression [whose] …marked expression … forms a dangerous symptom in acute diseases."[57]

Another argument that is used to support the existence of the disorder is cross-cultural: social phobia is a global phenomenon. This argument is used to discount claims that social phobia is really just a reflection of contemporary American society, which values outgoing personalities, and considers deviance from that norm a disorder. In 1987, for example, Kutaiba Chaleby published a report "Social Phobia in the Saudis" based on his observations of 35 outpatients at the King Faisal Specialist Hospital in Riyadh. Chaleby claimed that these 35 patients met the *DSM-III* criteria of social phobia, writing that "the high incidence of social phobia in Saudi Arabia is the first observation worthy of discussion. Is there a genetic predisposition?"[58] However, Chaleby concedes in the paper that of those 35 patients, "only 22 (63%) actually

[55] Lane, 11-17.
[56] Ibid., 11.
[57] Ibid.
[58] Ibid., 18.

presented with social phobia."[59] This is obviously a very small sample on which to base a generalization about a whole country. Yet this is how the marketing of an illness often works. A researcher will identify a phenomenon that seems to be in the shadows, move it into the sun by publishing small studies and holding conferences, and then the disorder becomes much more prevalent.[60]

Another common comparison is often made between social phobia and Japanese-Korean *taijin kyofusho*, a disorder which has been recognized in Japan since the 19th century. But these conditions are not entirely analogous. In the West, social phobia is an anxiety disorder, but *taijin kyofusho* is closer to an extreme kind of shame, which is consistent with Japanese and Korean cultural sensibilities.[61] Social phobia concerns people who avoid particular activities and settings because they fear being personally embarrassed. *Taijin kyofusho* concerns people who withdraw from society because they fear bringing embarrassment to other people, especially their parents.

While Paxil is now just one of many treatments used for social phobia, it is often cited as a key example of how the pharmaceutical industry creates markets for its products by promoting the illness itself. Conrad notes that "GlaxoSmithKline's campaign for Paxil increased the medicalization of anxiety, implying that shyness and worrying may be medical problems, with Paxil as the proper treatment."[62] Marcia Angell writes in *The Truth about the Drug Companies* that at the time that Paxil was approved for social anxiety disorder, the product director said to her, "Every marketer's

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[59] Ibid., 17.
[60] In Chapter One we saw the potential for something similar Morgellons disease—people all around the world report the same thing, so it must be true.
[61] Lane, 17 and Elliott, Carl. *Better than Well: American Medicine Meets the American Dream*. New York and London: W.W. Norton, 2003, 71-73.
[62] Conrad, 7.

dream is to find an unidentified or unknown market and develop it. That is what we were able to do with social anxiety disorder."[63]

GlaxoSmithKline did not simply develop the market for social anxiety disorder, however; they developed it in a particular way. During the 1990s, the pharmaceutical industry learned that it could market drugs by exploiting the growing power of patients themselves.

Marketing Directly to Patients

Pharmaceutical companies have a long history of marketing their products to physicians.[64] Professional journals are filled with ads; drug reps offer doctors free samples and pens, and pharmaceutical companies sponsor all sorts of "educational" conferences in an attempt to increase prescriptions. This was so even in the 1970s, when the consumer movement was gaining huge momentum in the United States. Led in part by Ralph Nader, consumer advocates championed a consumer's right to be protected from products that were unsafe. More importantly for our purposes, they advocated the rights of consumers to be fully informed about the products there were buying. This advocacy would prepare the ground for the marketing of drugs directly to consumers twenty years later.[65]

Up until the early 1990s, pharmaceutical executives largely objected to marketing drugs directly to patients. DTC advertising seemed to go against the

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[63] Angell, Marcia. *The Truth about the Drug Companies: How They Deceive Us and What to Do About It.* New York: Random House, 2004, 88.
[64] See Hilts, Philip J. *Protecting America's Health: The FDA, Business, and One Hundred Years of Regulation.* New York: Knopf, 2003.
[65] Critser, 11-12 and 31-55.

institutional culture of both pharmaceutical companies and medicine. Many executives, whose backgrounds were often in medicine, thought that DTC advertising was vulgar and compromised the physician-patient relationship. And even the executives who favored DTC advertising were set back by two troubling events in the 1980s.[66]

In the early 1980s Eli Lilly introduced a new arthritis drug called Oraflex. There was a lot of competition among arthritis drugs, and instead of sending out information kits to medical journals, which was a standard marketing tool, Lilly's marketing department decided to send out kits to thousands of mainstream press outlets. These kits pushed the unproven notion that Oraflex actually healed tissues. The strategy initially worked, and Eli Lilly sold half a million prescriptions of Oraflex in its first fourteen weeks on the market. But soon the plan backfired, when Oraflex was found to have liver and kidney toxicity. 55 people died before Oraflex was pulled from the market in 1983. Consequently, in any discussion of loosening restrictions on DTC advertising, Oraflex became a resounding warning of the potential dangers.[67]

The other event that squelched moves to loosen restrictions on DTC advertising involved President Reagan's FDA commissioner, Dr. Arthur Hull Hayes. Hayes was a proponent of deregulation and a convert to the cause of DTC advertising. In 1982 Hayes gave a speech to the Pharmaceutical Advertising Council touting the benefits of DTC advertising. The advertising executives were highly receptive, but no one else was. In fact, Hayes was attacked from very possible quarter, including allies in Congress, his own staff, and even pharmaceutical executives. Representative John

[66] Ibid., 32.
[67] Ibid., 32-33.

Dingell, chairman of the House Subcommittee on Oversight and Investigations, accused Hayes of misinterpreting the federal code. Dingell even queried thirty-six of the top pharmaceutical executives in the country. All but five of the executives wrote lengthy letters about why DTC advertising was a horrible idea. Some called it "unprofessional" and "downright dangerous."[68] The chairman of GlaxoSmithKline, Tom Collins, warned that "advertising would have the objective of driving patients into doctors' offices seeking prescriptions. We believe that the chances of damaging doctor-patient relations and for encouraging costly competitive battles are real, while the likelihood that meaningful patient education will occur is small."[69]

The major medical societies, such as the American Medical Association, also came out against DTC advertising. Medical societies were concerned that DTC advertising would cause people to lose respect for the medical profession. As a result, Hayes was pushed out of office, and along with him, the push for DTC advertising. There were no laws specifically against DTC ads, but in 1984 the FDA imposed a moratorium on DTC advertising, requiring any advertising to include a lengthy disclosure of drug information, including side effects. In order to meet FDA regulatory requirements, advertisements would have to be quite long. In effect, this made television advertisements too expensive.[70]

Pharmaceutical executives may have been reluctant to advertise directly to consumers, but they were still eager to tap into what they saw as a huge revenue source. They accomplished this with public awareness campaigns. If an advertisement did not

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[68] Ibid., 33-35.
[69] Ibid., 35.
[70] Ibid., 36, 43.

promote the therapeutic effect of a drug, but simply made the public aware of a disease, it did not have to meet the long disclosure guidelines. The first public awareness success story was a campaign by Merrill for its allergy medication, Seldane.[71] The campaign did not name the drug, but hinted at its benefits and encouraged allergy sufferers to see their doctors for more information. The campaign was a huge success, and media outlets were thrilled with the marketing revenue.

During the 1990s, the climate for pharmaceutical marketing began to change. For one thing, marketing began to assume much greater prominence. Between 1995 and 2000, the number of marketing staff working for U.S. pharmaceutical companies increased 60%, while research staff decreased by 29%.[72] Pharmaceutical companies also began to concentrate on blockbuster drugs such as Prozac, Prilosec and Claritin. In 1991 blockbusters accounted for a mere 6% of the pharmaceutical market, but by 2001 that figure was 45%.[73] What is more, the case of Seldane had also shown marketers the power of reaching directly to consumers. Some pharmaceutical companies began to change their minds about DTC advertising.

In order for the FDA to relax its regulations governing DTC ads, however, the pharmaceutical industry needed the AMA to accept the benefits of DTC advertising. Their pitch came at the right time. Physicians were feeling disempowered by the growth of managed care, which was intrusive and constraining. Patients were growing resentful, damaging physicians' abilities to communicate with them. A marketing executive from Upjohn explained to AMA executives that their ban on DTC advertising

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[71] Ibid., 42-44.
[72] Medawar and Hardon
[73] See Henry J. Kaiser Family Foundation. "Impact of Direct-to-Consumer Advertising on Prescription Drug Spending." June 2003.

was also undermining the doctor-patient relationship. Wendy Borow-Johnson, of Upjohn, says that she "pointed out how inconsistent it was that we could be doing all these things to promote patient information and proactive patient-physician relationships and then say essentially, 'No, patients can't handle information about drug'."[74] It would be better for the doctor-patient relationship, she suggested, if patients were empowered with more medical information, which DTC advertising could provide.

In 1992 the AMA rescinded its ban on DTC advertising.[75] In 1997 the FDA rescinded the "brief summary" requirement in DTC ads.[76] Major pharmaceutical companies did a complete reversal. In 1984 American Home Products (AHP) had claimed that "DTC advertising would make [patients] extraordinarily susceptible to product promises."[77] But by 1995 the AHP chief counsel argued, "Empowering the patient as well as the physician with information increases the likelihood that someone—patient, friend, or relative of the patient, or physician—will get the dialogue started. Getting the dialogue started is key to avoiding underuse as well as overuse of prescription drugs, to proper weighing of risk factors, to consumers' understanding why and when and how to take the drugs, the whole process of intelligent and careful and proper prescribing."[78] As Critser puts it, the "consumer's right to know"—a great triumph in the 1970s—had become the corporation's right to "subtly encourage."

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[74] Critser, 45-46.
[75] Ibid., 46.
[76] Ibid., 52.
[77] Ibid., 51.
[78] Ibid.

The FDA's decision to waive the detailed summary requirement in 1997 made it possible for companies to advertise prescription drugs on television. Today DTC advertising is an enormous industry and focuses primarily on promoting the top twenty or so "blockbuster" drugs (more than $1 billion in annual sales). In 1999 the top 25 most heavily advertised drugs accounted for 77% of all mass media advertising dollars for prescription drugs.[79] In 2003 the pharmaceutical industry spent nearly $3 billion a year on DTC advertising, mostly on drugs for chronic conditions.[80] Today that figure is estimated to be close to $4 billion.

While DTC advertising is still just a relatively small percentage of promotional spending by pharmaceutical companies, it is steadily increasing.[81] Quite simply, pharmaceutical companies use DTC advertising because it works; it is highly influential in influencing both physicians and patients. A report in 2000 by the National Institute for Health Care Management found that physicians wrote 34.2% more prescriptions in 1999 than in 1998 for the 25 DTC-promoted drugs that contributed most to overall drug spending. In contrast, physicians wrote only 5.1% more prescriptions for all other prescription drugs. A 1999 survey of 1, 2000 people conducted by *Prevention* magazine and the American Pharmaceutical Association found that 31% of respondents reported talking with their physician about a drug they had seen advertised. Of those

[79] See National Institute for Health Care Management (NIHCM). "Prescription Drugs and Mass Advertising." September 2000.
[80] Critser, 53.
[81] For example, in 2001 14% of promotional spending overall went to DTC while 29% went to detailing and 55% to sampling.

people (372), 104 (or 8.7% of all respondents) asked their doctor for a drug, and 87 said their doctor complied and wrote a prescription for it.[82]

The power of patients to influence the prescriptions they are given was vividly demonstrated in an unusual study by researchers at the University of Washington. The researchers sent actors with fake symptoms to the offices of family physicians and general internists, some with instructions to ask the physicians for drugs. The actors presented as new patients with one of two conditions. Half of the actors simulated patients suffering from depression, which would warrant treatment with medication. The other half described experiencing a recent upheaval in their life and having fatigue, stress and difficulty sleeping, which would not ordinarily warrant medication. The actors did one of three things: some made no specific treatment request, others requested a prescription for antidepressants, and still others specifically requested a prescription for Paxil. According to the study, if an actor requested a prescription, the doctor was much more likely to comply, even if the patient's condition was not one that ordinarily warranted medication. When the patients asked for Paxil, 55 percent were given prescriptions. In fact, 50 percent were given a diagnosis of depression, even though their symptoms were not those of depression.[83]

This study is particularly interesting when considering an additional tool that GlaxoSmithKline has used to encourage patients to diagnose themselves with social phobia. The Social Phobia Inventory (SPIN) was developed by a group of psychiatrists

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[82] NIHCM, 3.

[83] See Kravitz, Richard L. et al. "Influence of Patients' Requests for Direct-to-Consumer Advertised Antidepressants: A Randomized Controlled Trial." *JAMA* 293 (2005): 1995-2002.

at Duke University supported by a grant from GlaxoSmithKline.[84] A link to the self-test is prominently displayed on Paxil's website.[85] The instructions remind people that only a doctor can make a diagnosis of social anxiety disorder (and more importantly, write a prescription), but clearly the purpose of the test is to encourage people to self-diagnose. SPIN consists of seventeen brief problems like, ""parties and social events scare me" and "I avoid speaking to anyone in authority." For each statement, the test taker chooses one of five options ranging from "not at all" to "extremely" that describes how much they have been bothered by these problems in the past week. If you answer "a little bit" or "not at all" the test results will tell you that your answers are not indicative of someone suffering from social anxiety disorder. But you are still encouraged to see a healthcare provider to discuss any concerns. If you answer a minimum of "somewhat" to all of the problems posed, you will score 34 out of 68 which is enough to suggest that you may be suffering from social anxiety disorder and should see your doctor. In previous chapters we saw different types of expertise claimed by patient activists. SPIN actually creates a new kind of expert in the service of marketing. This is another illustration of companies selling drugs by going over the heads of doctors and straight to the patients.

The marketing campaign for Paxil was one of the first to benefit from the relaxed regulations on advertising. GlaxoSmithKline spent more than $92 million in

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[84] Connor, Kathryn M. et al. "Psychometric Properties of the Social Phobia Inventory (SPIN)." *British Journal of Psychiatry* 176 (2000): 379-386. GlaxoSmithKline's website identifies Jonathan Davidson, one of Connor's co-authors, as the author of SPIN. Davidson discloses receiving various fees from GlaxoSmithKline.

[85] See http://www.paxilcr.com/social_anxiety_disorder/sad_take_self_test.html. Accessed 25 October 2008.

one year to market Paxil—more than Nike spent marketing its top shoes.[86] The marketing worked: Paxil quickly passed Prozac and Zoloft as the top selling antidepressant. Paxil's DTC success with Paxil also extended beyond social anxiety disorder. When Paxil was approved for the treatment of "generalized anxiety disorder" in April 2001, GlaxoSmithKline promoted this previously little-known condition with an aggressive public relations campaign including personal profiles, patient surveys meant to inform people, expert testimony, and countless newspaper articles and DTC ads on television.[87] The campaign was also able to capitalize on the emotional turmoil of the events of September 11, 2001, by increasing its ads for Paxil. Some of the ads in the weeks following 9/11 even included images of the World Trade Towers collapsing. GlaxoSmithKline spent almost twice on advertising ($16 million) in October 2001 than it had the previous October. The ads worked: in the three months following 9/11 Medicaid recipients living within three miles of the World Trade Center filed eighteen percent more claims for antidepressants.[88]

By the time Paxil was being advertised on television, GlaxoSmithKline had prepared the ground through subtler marketing to consumers. GlaxoSmithKline had positioned social anxiety disorder as a severe condition with the "Imagine Being Allergic to People" public awareness campaign. They also used the media to promote public understanding by aggressively using news releases and referring reporters to experts and sufferers who could fill out the story. Of course, these experts and "lay people" telling their stories were often paid by GlaxoSmithKline. GlaxoSmithKline

[86] Barber, 47.
[87] Ibid., 46-47.
[88] Ibid.

also used endorsements by celebrities such as football player Ricky Williams, who appeared on the *Oprah Winfrey Show* to tell a heartfelt story of his anxiety and social awkwardness. Paxil, said Williams, helped him become more like himself. Most reporters simply repeated the story line that GlaxoSmithKline was promoting.[89]

Buying Patient Advocacy

In the 1970s and 1980s patient activism was primarily about grass-roots efforts to empower patients. People with similar interests and concerns banded together to take on powerful groups like physicians, researchers, the FDA, and pharmaceutical companies. By the end of the 1990s, the nature of many patient groups looked very different. Today, patient advocacy groups often receive a significant portion of their funding directly from drug companies. In the U.S. a random sampling of patient groups with annual revenues over $100,000 found that 80% received industry funding and only two (0.8%) did not accept it.[90] These are not typically charitable donations by the companies; instead, the funding usually comes from a company's marketing or sales divisions.

Pharmaceutical companies support patient advocacy groups because they expect to benefit, of course. They hope that patient advocacy groups will advocate for increased research funding, disease awareness, quicker FDA approvals and more insurance coverage. Simply put, the companies would not be supporting patient advocacy groups if it did not serve their financial needs. An investigation by the

[89] Lane, 132-133.
[90] Mintzes, Barbara. "Should Patient Groups Accept Money from Drug Companies? No." *BMJ* 334 (2007): 935.

Philadelphia Inquirer into six patient advocacy groups found that groups receiving funding from the makers of drugs that treat the disease they advocate for tended to be slower to publicize treatment problems than breakthroughs.[91] Patient advocacy groups rarely disclose their financial ties with drug companies, in part because they are rarely required to.

The investment by pharmaceutical companies in patient advocacy groups pays off. Many proceedings in the legislative and regulatory realms require testimony from patients, and often that testimony is given by advocacy group leaders. Yet all patient advocacy groups have agendas, and the concern is that those who receive industry funding will tend to represent the agenda of industry. In a recent article in *JAMA*, Peter Lurie and others examined voting patterns at FDA Advisory Committee Meetings, and correlated those votes with funding sources as revealed in the conflict of interest disclosures.[92] They found that of 44 public session testimonies offered by patient groups, 32 acknowledged receiving funds from a company whose products were potentially affected by the hearing.[93] Laurie, of Public Citizen, told the Boston Globe that he had noticed a shift at FDA hearings, which he said "were becoming contaminated by people who didn't represent the public in any way. They represented particular moneyed interests."[94]

Some patient advocacy groups have gone even further. In the wake of the scandal over Vioxx , the Merck arthritis drug which was withdrawn from the market in

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[91] Ginsberg, Thomas. "Donations Tie Drug Firms and Nonprofits: Many Patient Groups Reveal Few, If Any, Details on Relationships with Pharmaceutical Donors." *Philadelphia Inquirer*. 28 May 2006.
[92] Lurie, Peter et al. "Financial Conflict of Interest Disclosure and Voting Patterns at Food and Drug Administration Drug Advisory Committee Meetings." *JAMA* 295 (2006): 1921-1928.
[93] Ibid., 1925.
[94] Henderson, Diedtra. "Drug Firms' Funding of Advocates Often Escapes Government Scrutiny. Many Patient Groups Depend on It, Raising Tricky Ethical Questions." *Boston Globe*. 18 March 2007.

2004, a Senate committee meeting was held to investigate whether FDA safety standards were too lax.[95] No pharmaceutical companies testified, but three witnesses representing industry-funded patient groups did. Nancy Davenport-Ennis of the National Patient Advocate Foundation warned committee members that an overemphasis on safety could delay the approval of important new treatments. Although the National Patient Advocate Foundation receives financial support from at least ten drug companies, including Pfizer, Merck and GlaxoSmithKline, Davenport-Ennis claimed that the contributions were unrestricted and did not influence the work of the group. She also said that industry funding is very common: "I don't think there is a patient-advocacy group in America that does not receive some level of funding from a pharmaceutical company."[96] Yet according to David Graham, an FDA scientist turned whistleblower over the dangers of Vioxx, the National Patient Advocate Foundation turned to hardball tactics and tried to discredit him in the days before his Congressional testimony.[97]

Sometimes the leaders of patient advocacy groups have also benefitted from their alliance with the pharmaceutical industry. In 1989 Elzora K. Brown founded the Breast Cancer Resource Committee, a patient advocacy group. Herself a victim of breast and ovarian cancer, Brown has become an important advocate for African-American women with breast cancer. She regularly testifies at FDA hearings and speaks to large groups of powerful people. But few know that she has personally profited from her advocacy. Brown has accepted major funding from pharmaceutical

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[95] U.S. Senate Committee on Finance. "FDA, Merck and Vioxx: Putting Patient Safety First?" 18 November 2004.
[96] Drinkard, Jim. "Drugmakers Go Furthest to Sway Congress." *USA Today* 25 April 2005.
[97] Ibid.

companies that produce cancer treatments. Diedtra Henderson's investigative reporting in 2007 found that from 1996 to 2004, the years for which tax records were available, Brown's organization raised about $3.4 million from mostly corporate donors, including drug companies. Brown's salary rose to $162,500 in 2002, nearly one-third of the money raised that year. She also lived and worked in a Washington D.C. townhouse rented by her group and used the Committee's credit card for her own expenses.[98]

What is significant about the alliance between the pharmaceutical industry and patient advocacy groups is not merely that industry would fund an external group as a way of marketing drugs. The pharmaceutical industry had been funding other external sources for years, such as physicians, professional medical groups and politicians. What is significant is the fact that patient advocacy groups have become so powerful that industry felt they were worth funding. GlaxoSmithKline, according to its annual Corporate Responsibility Report, now maintains an in-house "Global Advocacy Team" to coordinate its interactions with patient advocacy groups. It sponsors an annual Patient Advocacy Leadership Summit, which in 2004 was attended by 400 people from 23 countries representing 233 different patient advocacy groups. According to the report, the summit includes a forum for patient groups to learn more about GlaxoSmithKline. It also includes a range of workshops for attendees, "including sessions on media training."[99]

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[98] See Henderson.

[99] GlaxoSmithKline, "Corporate Responsibility Report 2004: Patient Advocacy." Accessed 25 October 2008. Available from http://www.gsk.com/responsibility/cr_report_2004/la_patient_advocacy.htm.

Conclusion

The rise of social phobia, and its treatment with Paxil, is a story about how patient groups have changed. In the first three chapters, we saw patients banding together in groups to pursue common goals. In this chapter, however, we have seen GlaxoSmithKline transform Paxil into a blockbuster drug by co-opting patient groups and marketing the drug directly to patients. GlaxoSmithKline may not have manufactured social phobia, but they did take advantage of changes in the *DSM* and larger cultural attitudes as a way of medicalizing shyness.

Of course, it is legitimate to ask: what exactly is the harm in medicalizing shyness? If Paxil can help shy people to become more outgoing, less inhibited, and more comfortable in their own skin, why shouldn't doctors prescribe it? The most persuasive reason comes from the side-effects of the drug. In 2004, British regulators banned the use of Paxil in patients under the age of 18 when suppressed data from GlaxoSmithKline showed that children taking Paxil were three times more likely to harm themselves or have suicidal thoughts than those taking placebos.[100] Three years earlier, a Wyoming jury had awarded over $6 million to the family of a man taking Paxil who had committed suicide after shooting his wife, daughter and granddaughter.[101] In 2005 the FDA began a comprehensive review to assess the risk of suicidal thinking or behavior in people taking antidepressants. Later that year it required labeling changes that warned of this risk and recommended close monitoring. In May 2007 the agency ordered "makers of all antidepressant medications [to] update the existing black box warning on their products' labeling to include warnings about

[100] Harris, Gardiner. "FDA Links Drugs to Being Suicidal." *New York Times* 14 September 2004.
[101] Hilts, Philip J. "Jury Awards $6.4 Million in Killings Tied to Drug." *New York Times*. 8 June 2001.

increased risks of suicidal thinking and behavior, known as suicidality, in young adults ages 18 to 24 during initial treatment (generally the first one to two months)."[102]

The concern that the SSRIs might increase the risk of suicide (and homicide) was not new. An FDA advisory committee had considered the topic as early as 1991,[103] but the committee had concluded that the drugs did not increase suicide risk, and did not recommend a black box warning.[104] It was only after other countries had placed restrictions and warnings on the SSRIs that the FDA reconsidered its 1991 decision.

Evidence of the suicide risk did not simply come from post-marketing studies. GlaxoSmithKline suppressed its own research data showing suicide risks associated with Paxil. As the *New Scientist* reported last year, litigation against GlaxoSmithKline revealed internal memos and reports suggesting that as early as 1989 the company had data from clinical trials showing an eightfold increase in suicide risk.[105] An FDA reviewer has said that if he had been aware of these data when Paxil was first up or approval, he never would have voted to approve.[106]

When the FDA initially approved Paxil, it was as a treatment for major depression. Major depression is a serious mental illness which, if left untreated, significantly increases a person's suicide risk. Given this balance, the risk of taking Paxil may well be small compared to the risk of not being treated. But most patients

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102 FDA. "FDA Proposes New Warnings About Suicidal Thinking, Behavior in Young Adults Who Take Antidepressant Medications." 2 May 2007. Accessed 25 October 2008. Available from http://www.fda.gov/bbs/topics/NEWS/2007/NEW01624.html

[103] See Elliott, Carl. "Introduction." In Carl Elliott and Tod Chambers, eds. *Prozac as a Way of Life*. Chapel Hill, University of North Carolina Press, 2004, 1-18, 13.

[104] Critics have noted that the committee included a large number of advisors who had received payments from antidepressant manufacturers. See Glenmullen, Joseph. *Prozac Backlash*. New York: Touchstone, 2000.

[105] Giles, Jim. "Did GSK Trial Data Mask Paxil Suicide Risk?" *New Scientist*, 8 February 2008.

[106] Ibid.

who take Paxil do not have major depression. The reason Paxil became so profitable for GlaxoSmithKline was the skill of the company in expanding the range of people who might be given a prescription – people who are shy, anxious, obsessive or unhappy. Since 1999 Paxil's main sales have been for anxiety disorders. What is more, GlaxoSmithKline, like the other antidepressant manufacturers, marketed the drug by expanding the range of practitioners prescribing it. No longer were psychiatrists the main prescribers of antidepressants; by the late 1990s, 70% of prescriptions for antidepressants were being written by primary care physicians, who may not be as familiar with the side-effect profile of the drug.[107] Once antidepressants are being prescribed to this broad a population of patients, who are not at any increased risk of suicide, a rare but lethal side-effect can become very dangerous.

When the FDA put a black-box warning on SSRIs, it was largely driven by patients who gave heart-wrenching stories about children on SSRIs who had committed suicide. Gail Griffith, the FDA's patient representative on the advisory committee on antidepressants and suicide, became a patient activist following the attempted suicide of her own seventeen-year-old son.[108] Griffith voted in favor of the black-box warning, but has since reversed her position. She believes that the scientific judgment of the committee was clouded by the patient activists: " "Trotting out members of the public to air emotionally devastating, personal, and anecdotal stories and having those stories sit as evidence for the committee amounts to a barrage that can't help but sway how you

[107] Elliott, 6.
[108] Rosack, Jim. "Patient Rep Reverses Position on SSRI Black-Box Warning." *Psychiatric News* 20 May 2005.

feel and how you look at the data you are seeing."[109] SSRI marketers used patients to sell their drugs and earn enormous profits for pharmaceutical companies. Ironically, in the end, this same patient power is what did them in.

[109] Ibid.

CONCLUSION

In this dissertation I have traced some of the ways that patient activism has shaped the practice of medicine over the last three decades. Patient activism has led to a variety of shifts of power, some of which correspond with larger changes in medicine. These shifts can be generally divided into two types: a shift in power from physicians to patients, and an overlapping shift in power from professional medicine to various corporate entities.

First, as I have shown here, the past thirty years have seen patients take more and more control over their own medical care. Patient groups today play a significant role in identifying new diseases, determining the course of research, and lobbying on behalf of diseases and treatments. Individual patients are empowered to make their own healthcare choices, and patients also band together to promote similar interests. Successful patient activism often includes marshaling political and social power, especially when patients want something that professional medicine does not want to give them.

Second, over this same period the pharmaceutical industry became a hugely profitable business, increasing its economic power as it produced blockbuster drugs and marketed them directly to patients. The pharmaceutical industry also became a more powerful political force, through large donations and political lobbying. During the 1990s the pharmaceutical industry began to move its research activities away from partnerships with academic health centers and into the private sector, conducting

clinical trials with CROs and for-profit testing sites, overseen by for-profit IRBs. At the same time, the organization of clinical medicine also changed. The older fee-for-service model of medical practice was replaced with a corporate model, where physicians are more specialized and practice in group settings. The influence of professional medical bodies waned, and more power is now held by corporate entities such as insurance companies, HMOs, and for-profit hospitals.

Each of the shifts that I have documented here has its own moral story, but they also point to larger trends in medicine that have important moral consequences. In concluding, I will point to four different points of tension for ethics: a shift in the locus of moral expertise, the changing physician-patient relationship, ambiguity in the goals of medicine, and the role of bioethicists as watchdogs for patients.

Medical Expertise

Accompanying the rising power of patients has been a shift in the locus of medical expertise. Forty years ago the idea that lay people could claim knowledge and expertise on a par with professionals would have been virtually unthinkable, but today we have patient groups challenging the expertise of physicians whose authority was once considered near-absolute. Patients search for detailed medical information on the Internet. They see advertisements on television that tell them which treatment is best for their condition. Patients visit their doctors armed with information and opinions about what should be done. Physicians may still hold the balance of power--patients cannot write their own prescriptions or perform their own surgeries--but physicians are no longer the unchallenged masters of medical expertise.

This shift is not just a matter of more access to the same information. As I showed in the chapter on chronic Lyme disease, a divide has opened up between two sorts of medical expertise: the evidence-based medicine of physicians, and the "folkway" methodology of patient activists. Chronic Lyme disease sufferers rely on the personal, subjective experience of illness, claiming a privileged kind of expertise based on their own experience. At the same time, physicians have moved further towards a type of expertise based on objective, generalizable, population-based, scientific studies. Much of what has been documented in this dissertation can be seen as a clash between these two types of expertise: patients saying that the scientific studies and explanations do not fit their experiences, and physicians saying that the experiences of the patients do not have scientific explanations. In some cases, like Morgellons disease, it appears that patients have made only limited headway in promoting their own understanding of the illness in question. But in others, as in the "Lyme Wars," it may turn out that the expertise of patients will continue to gain even greater traction.

As part of this shift towards the expertise of patients, more illnesses are coming to be defined by patients themselves. Morgellons disease and chronic Lyme disease are conditions whose expansion comes largely from the activity of patients. A quick look at Internet chat boards devoted to either disease shows postings reflecting grassroots movements of patients helping one another and relying on the expertise and experience of each other. A long list of contested conditions have developed in a similar fashion over the last several decades, such as fibromyalgia, chronic fatigue syndrome, repetitive strain disorder, Gulf War Syndrome, multiple chemical sensitivity, and Body Integrity Identity Disorder. As varied as these conditions are, any one of them could have been

used as a case study in this dissertation. What they have in common are patients who struggle to explain their own experiences, who have been turned away or gone untreated by mainstream medicine, and who claim personal expertise in explaining their experiences. Morgellons disease and chronic Lyme disease are not exceptional; they are indicative of larger social trends.

Physician-Patient Relationship

Over the last thirty years the physician-patient relationship has changed significantly. Physicians are less authoritarian, patients more assertive; the relationship is often now described as a partnership. The physician-patient relationship has also been altered by larger institutional changes, making it less personal and more bureaucratic. Patients are constrained by their insurance policies and have less choice about which physicians they see. Solo practices have been replaced by group practices, where a patient may see a different physician at every visit. More medical care is received in emergency rooms and urgent care centers then ever before. Patients are much less likely to see the same physician on a consistent basis. The physician-patient relationship has changed, but it is unclear what the old model has been traded for.

The old physician-patient relationship is often referred to as a "paternalistic" model, which suggests the authoritarian, benevolent relationship between parent and child. Paternalism suggests that the parent is acting in the best interests of the child, protecting her from harms that he or she may not fully understand. A young child may cry when a parent prevents him from running out into a busy street, but no one would blame the parent for upsetting the child, and the child learns to trust that the parent is

acting in his best interests. Under the old model, patients did not need to come armed with their own information, because they trusted the information their physician gave them.

The new model looks more like a business relationship, where physicians are "healthcare providers" and patients are "healthcare consumers." This new model changes the moral dimensions of the relationship. A business relationship does not involve the same level of trust as a professional relationship. Most people do not trust a mechanic or a car salesperson always to act in the customers' best interest; in the background of any encounter with a salesperson is the expectation that the salesperson will do what it takes to close the deal. Basic norms about fairness must be followed, but in a business relationship we do not expect the seller to put her own interests above those of the buyer.

Howard Brody, a philosopher and practicing physician, writes that most physicians "believe that becoming and practicing as a physician is a somewhat different matter, morally, from simply setting oneself up in business."[1] We expect physicians to put aside many of their own interests in the name of promoting their patients' interests. Some writers believe that these expectations come out of some sort of morality inherent to medicine. The profession itself reinforces this with a historical tradition that refers to the "practice of medicine." The idea here is that the practice of medicine involves something separate from the practitioners themselves. A practice is something that can

[1] Brody, Howard. *Hooked: Ethics, the Medical Profession, and the Pharmaceutical Industry.* Lanham, Maryland: Rowman and Littlefield Publishers, Inc., 2007, 23.

only be learned through extensive training and reflects inherent standards and expectations based on notions of the "good."[2]

Most people expect their physicians to follow certain ethical norms, dictated by the norms of the profession. Many of these expectations are not based on having a long term relationship with a particular physician. They are based instead on expectations about the norms, customs and institutions of medicine. I expect an emergency room physician I am meeting for the first time to keep my personal and medical information confidential. I trust that she will give me treatment that is in my best interests, not because of who I am or what insurance coverage I have, but because I am her patient.[3] The shift to a consumer model of the physician-patient relationship may erode much of this trust inherent in the older model, resulting in a model where patients will not trust any physician who disagrees with them.

In his book, *Do We Still Need Doctors?* John Lantos describes some of the changes in health care that I have taken up here, where the traditional core of medicine is crumbling.[4] The figure of the doctor, Lantos suggests, is not so much a locus of technical skill as a particular configuration of moral roles and duties. He argues that doctors are not essential to health care. Health care can easily be provided by other specialists and technicians, who may even be more efficient at their jobs. According to Lantos, imagining a world in which we have of health care but no doctors is "no more of a challenge than imagining a world in which we have shoes but no cobblers, trains

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[2] Ibid., 24.
[3] Ibid., 25.
[4] Lantos, John D. *Do We Still Need Doctors?"* New York: Routledge, 1997.

but no engineers, farms but no farmers, or drive-through banks with nothing but automatic teller machines. Something is lost but something is gained."[5]

The older paternalistic model of the physician-patient relationship may not have been ideal, but are we really better off with a consumer model? For many physician-patient interactions, perhaps a consumer model makes sense. A patient gets a sore throat, visits an urgent care center and sees an anonymous doctor who orders a strep test and then prescribes antibiotics. The encounter does not allow for much intimacy, but it is not the type of encounter where intimacy is needed, and it is probably a cost-efficient way of treating strep throat. Most people can go to the Internet and find out for themselves the standard diagnosis and treatments for strep throat and confirm that a physician acted appropriately. But when the stakes are much higher – when a patient has been diagnosed with cancer, or has a child who is gravely ill and no one knows why – it may be more important to have a doctor whose judgment the patient can trust and who will act in the best interests of the patient. This is not just a matter of limited time and intelligence. In those circumstances where life is most precarious and the outcome completely unknown, something important is lost if a patient does not respect and trust her caregivers.

According to Kalman Applbaum, an anthropologist, medical consumerism may sound empowering, but it mostly serves the interests of industry by eroding the doctor's role as expert.[6] The pharmaceutical industry co-opts the ethical dimensions of medicine in the name of consumer choice and empowerment. Applbaum writes, "For in our

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[5] Ibid., 7.
[6] Applbaum, Kalman. "Pharmaceutical Marketing and the Invention of the Medical Consumer." *PLoS Medicine*, 3;4 (2006): e189.

pursuit of a near-utopian promise of perfect health, we have, without realizing it, given corporate marketers free reign to take control of the true instruments of our freedom: objectivity in science, ethics and fairness in health care, and the privilege to endow medicine with the autonomy to fulfill its oath to work for the benefit of the sick."[7]

Goals of Medicine

Accompanying the move to a consumer model of the physician-patient relationship is an ambiguity in the goals of medicine. Traditionally, doctors have seen the goals of medicine as bound up with a patient's medical needs. With a consumer model, however, medicine has begun to shift to the goal of serving a patient's desires.

In bioethics, discussions of the goals of medicine are often attempts to set out the moral content of medicine. For example, Leon Kass defends a teleological understanding of the nature and goals of medicine.[8] He argues that health is the primary goal of medicine and that "health is a naturally given although precarious standard or norm, characterized by 'wholeness' and 'well-working,' toward which the body aspires on its own, and that the pursuit of health depends far more than we realize on cultivating habits of living that assist the body in its efforts toward wholeness."[9] A healthy human being is the *telos* of a physician's art.[10] Kass' view of health is narrow; it "is different from pleasure, happiness, civic peace and order, virtue, wisdom, and

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[7] Ibid.
[8] Kass, Leon. *Toward a More Natural Science: Biology and Human Affairs*. New York: Free Press, 1985.
[9] Ibid., 11.
[10] Ibid., 159.

truth."[11] While worthy, these goals all fall outside the goals of medicine. Thus any practice by physicians that does not aim toward the well-working of his or her patients falls outside the physician's task.

This is a conservative view of the moral nature of medicine. For Kass, giving a patient an ineffective treatment or a placebo simply to make them feel better would fall outside the goals of medicine. Kass argues that the goals of medicine are fixed and unchanging, even as new medical technologies arrive. He expresses concern that as technologies improve, the medical profession has a "clear need to articulate and delimit the physician's domain and responsibilities, to protect against expansion and contraction."[12]

In contrast, others have argued that medicine is entirely a social practice. Its goals are simply what society makes them to be. For example, Erik Parens argues that we have limited theoretical tools for dealing with concerns over how the goals of medicine fit in with the goals of society.[13] Parens asks us to imagine a group of people who resemble doctors, but who call themselves *schmocters*.[14] They do not claim to practice medicine; they call what they practice *schmedicine*. "They are expert in using new biotechnologies to enhance human capacities and traits, and they sell their expertise to willing, indeed, enthusiastic purchasers."[15] Plenty of people are eager to buy their services. If we cannot fall back on arguments based on the internal goals of

[11] Ibid., 164.
[12] Ibid., 177-178.
[13] Parens, Erik. "Is Better Always Good?" *Hastings Center Report*, 28;1 (1998): S1-S20.
[14] Parens attributes these terms to James Lindeman Nelson who attributes Saul Kripke.
[15] Ibid., S6.

medicine, as Kass does, do we have any moral grounds for objecting to what *schmocters* do?

The point Parens is making is that even if physicians could be persuaded not to provide some services on the grounds that they are enhancements, rather than treatments, or that they serve the desires of patients, rather than their medical needs, and even if insurance companies refused to reimburse their services, "there is no good reason to think that *schmocters* would be dissuaded from providing those services."[16] S*chmocters* do not care about the goals of medicine; they care about the goals of *schmedicine*. Even if every physician subscribed to Kass' narrow view of the goals of medicine, it is possible some other enterprise would pop up to fill that void.

Parens' thought experiment can help us make sense of some of the clashes documented in this dissertation. On the old model of medicine, doctors serve patients' medical needs. But with the shift of power to patients, medicine has become more about serving a patient's medical desires (schmocters). In Parens' example, if a patient desires enhancement and if he cannot get it from a doctor who practices medicine, he can simply go to a *schmocter* who practices *schmedicine*. But the same is true for patients who want antibiotics for Lyme disease or access to experimental drugs. Patients want all sorts of things that doctors think they do not need. Sometimes patients are right, as in the early HIV trial disputes, and they really do need the things they want. And sometimes physicians, as in the case of cosmetic surgery or elective induced deliveries, are willing to give patients things they do not really need.

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[16] Ibid.

One could look at the work in this dissertation and argue that it shows that medicine needs to reclaim its authority — that medicine has become too focused on the desire of patients rather than their needs, and that we should make an effort to strengthen the internal goals of medicine. But even if Kass is right and medicine is an inherently moral practice, it is entirely possible that a new kind of practice will emerge or even that medicine will evolve a different set of goals, which could serve desires rather than needs. If we fully embrace a consumerist model of medicine this seems not only plausible, but likely.

Power and Bioethics

The time period I examine in this dissertation roughly corresponds to the rise of bioethics. Although there are competing stories about the "birth of bioethics," at least one strand of bioethics has aligned itself with the growing power of patients. Bioethicists have done a great amount of work examining and challenging the traditional paternalistic model of the physician-patient relationship, often framing the ethical issues in terms of patient autonomy. In addition, the field of bioethics has begun to claim power for itself, arguing that moral expertise does not lie solely with doctors, and that scholars from other fields should have a voice in shaping the ethics of medicine. Most people have generally seen the growth of bioethics as a change for the better. But it may also have had an unexpected result, in that bioethics has created a space for the consumerist model of medicine to thrive.

The government regulates most businesses in order to protect consumers. Regulatory agencies like the Food and Drug Administration, the Environmental

Protection Agency and the Securities and Exchange Commission are meant to provide checks on corporate power. In contrast, medicine and other professions are, for the most part, self-regulating. Medicine has been trusted to regulate itself at least partly because it has been assumed that doctors can be trusted to work for the interests of patients. But if medicine is transformed into a business and patients are turned into consumers, who will be responsible for protecting the interests of patients? In many ways the patient activism documented in this dissertation came about because patients saw a need to advocate for themselves. But this seems like an enormous responsibility to place on individual patients.

Bioethicists sometimes claim to be watchdogs for patients. Yet bioethicists rarely partner with patient activists or work in watchdog organizations. In fact, like patient advocacy groups, some bioethicists have begun to collaborate with the pharmaceutical and biotechnology industries. A number of bioethics centers have sought out funding from the pharmaceutical industry, and some prominent bioethicists work as consultants and advisors to industry.[17] As with patient advocacy groups, the willingness of the pharmaceutical industry to fund and work with bioethicists can also be seen as an indicator of the growing power and influence of bioethics. But it has also called into question the role of bioethics as the patient's watchdog.

In general, however, as the field of bioethics has developed, its power has come not from the pharmaceutical industry or from patients, but from the institutions of medicine itself. Bioethicists are now located in academic health centers; they consult in hospitals; they publish in medical journals; and they receive grants from the National

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[17] See Elliott, Carl. "Pharma Buys a Conscience." *American Prospect*, 12;17 (2001).

Institutes of Health. Perhaps bioethicists are afraid of being co-opted by patients; to team up with patients could be to give up a claim to objectivity or academic rigor. But it should not be surprising if some patients themselves believe that bioethicists have been co-opted by medicine. A challenge facing bioethics will be whether it can continue to grow without compromising its scholarly detachment or sense of intellectual fairness.

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