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Discovering Addiction

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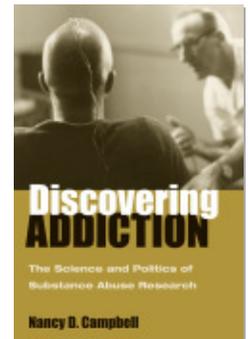
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CHAPTER 4

“The Man with the Syringe”: Pain and Pleasure in the Experimental Situation

Quoting Sigmund Freud’s claim “Behind every psychoanalyst stands the man with the syringe,”¹ psychiatrist Nathan S. Kline added, “At long last, the drugs of which Freud spoke are being found to put into the syringe” (1956, 81; Healy 2002, 105–7). Newly minted psychopharmacologists worked hand in hand with the pharmaceutical industry to expand the pharmacopeia in the second half of the twentieth century (Hertzman and Feltner 1997, 6). Tranquilizers promised transcendence in the popular press of the late 1950s (Gerard 1957). A flush of optimism linked advances in psychopharmacology to beliefs in progress, freedom, democracy, and mental health.² Beliefs in the potential contributions of pharmaceutical drugs to cold war prosperity and the well-being of democratic citizens brought about the culture of a pill for every ill. Popular texts on neuroscience and psychopharmacology became best sellers—glossing over addiction researchers’ preoccupations with the downsides of such drugs.

Addiction was always the skeleton in the closet of “the man with the syringe.” Consigned to the public sector, the study of addiction took place against the backdrop of industrial innovation in the area of pain and analgesia. Abraham Wikler wrote: “We are looking for ‘good’ analgesics—those which relieve pain in a variety of clinical conditions in such doses as do not impair other important functions to a significant degree. In other words, we are searching for drugs which have a certain ‘pattern’ of effects on patients with pain” (1952b, 227). Because the ARC was bent on elucidating the basic metabolic and neurological mechanisms of addiction, it was marginalized in industry and academia due to its singular focus when a radical cultural separation

was drawn between problem-solving pharmaceutical drugs and problem-causing illicit drugs. Inscribed within popular and political culture, this division also took hold in scientific communities. To circumvent being tarred an illegitimate science and to rehabilitate their patients' image, addiction researchers changed the name of their enterprise. The ARC did not drop the term *addiction* from its name, but by the early 1950s, leadership was urging the World Health Organization to refer to "drug dependence" rather than "addiction." The WHO did so in the 1960s, and in 1965, the NRC Committee on Drug Addiction and Narcotics (CDAN) changed its name to the Committee on Problems of Drug Dependence. The discursive shift reflected an emerging scientific consensus that aimed to destigmatize "addiction" and to abandon it as a relic of past misattributions of physiological phenomena to weak moral character or vice.

Such attempts coincided with a new regulatory consensus expressed in the 1962 Kefauver-Harris amendments to the Food, Drug, and Cosmetic Act (1938). The 1962 amendments, which came about in response to thalidomide, still govern requirements that pharmaceutical companies present substantial evidence of product safety, efficacy, and effectiveness for specific conditions named in the application to market a new legal drug. The vagueness of effectiveness standards propelled an initially reluctant FDA to take a more prominent role in clinical trials (Hertzman and Feltner 1997, 83–84). The 1962 amendments transformed testing from the use of small, carefully preselected samples to large, randomized controlled trials with minimal selection criteria (Rasmussen 2003, 456). Documenting informed consent became standard in clinical trials: the law mandated that "the person involved has legal capacity to give consent, is so situated as to be able to exercise free power of choice, and is provided with a fair explanation of all material information concerning the administration of the investigational drug, or his possible use as a control, as to enable him to make an understanding decision as to his willingness to receive said investigational drug" (*Federal Register* 31 [August 30, 1966]: 11415). Although these new provisions did not substantially change business as usual at the ARC (because studies done there already met the new requirements), the changed regulatory climate led industry to expand in-house research capacity and cultivate ties with academic units. Despite knowing some products might prove addictive, industry introduced many a new wonder drug as "nonaddictive." Following the introduction of the major tranquilizer chlorpromazine and the minor tranquilizer Miltown in the mid-1950s, this was an era of pharmacological optimism about what drugs could do for society. Cautionary notes concerning addiction were trumped by the belief that drugs would solve not only clinical but social problems.

Psychoactive drugs were touted as harbingers of a new era. Far from confining pharmacological optimism to solving problems of addiction, intractable pain, or chronic mental illness, psycho- and neuropharmacologists attended not just to troubled individuals but to the mundane pathologies of “normal” humans. Understanding everyday life as a series of biochemically directed behaviors was the context for the expansion of pharmaceutical markets.³ Popular writing about psychopharmacology conveyed a utopian sense that the “toxic side of mental processes” would yield to collective assault. Echoing Aldous Huxley’s *The Doors of Perception* (1954), Kline’s fervent belief psychopharmacology would open a new door was widely shared—except among those who knew addiction best. They were adamantly opposed to the popular position that psychoactive drugs opened the doors of perception. However, they did believe that useful knowledge could be gained from studying the effects of psychoactive drugs. What doors did such studies unlock?

THE FRONTIER OF THE MIND: THE GENRE CONVENTIONS OF POPULAR NEUROSCIENCE AND PSYCHOPHARMACOLOGY

Aldous Huxley published *The Doors of Perception* and *Heaven and Hell* (1955) to advocate democratic access to mind-altering substances. He was often the sole nonscientist addressing scientific congresses, such as the 1955 annual meeting of the American Psychiatric Association or the 1956 meeting of the New York Academy of Science (Huxley 1977, 61). Huxley urged readers of *Esquire*, *Playboy*, and the *Saturday Evening Post* to exchange “old bad habits for new and less harmful ones,” condemning alcohol for causing accidents and tobacco for making “soil sterile and lungs cancerous.” He realized that prohibition was ineffective against the “near, felt fact of a craving, here and now, for release and sedation, for a drink or a smoke” (1954, 64). Rather than advocating hedonism, he promoted using drugs other than alcohol and tobacco for relieving poverty, monotony, pain, and limitation (1954, 67). His ideas had distinctly cold war overtones—he urged Americans to keep pace with the Russians’ pharmacological enhancements of intelligence and energy.⁴

Popular texts heralded advances on the neuropharmacological frontier by offering accessible accounts of neuroscience. For example, the best-selling paperback *Drugs and the Mind* (1957), authored by biochemist Robert S. De Ropp, was a lyrical speculative fiction about the potential uses of drugs as tools for mind expansion and as routes to knowledge and self-mastery. Although he acknowledged some dangers of using drugs to offset the increasingly tense, unstable, fast-moving, and explosive aspects of midcentury culture, De Ropp

believed that well-balanced individuals were unlikely to become addicts in the coming chemopsychiatric era (32). Warning against random or disorganized drug “trips,” he interpreted popular interest in mind-affecting drugs as a signal that science and society had reached a state of maturity. According to De Ropp, only immature individuals who used drugs to escape reality risked addiction, and thus the criminalization of sick or weak individuals would be consigned to the “barbaric” past.

Drugs and the Mind emphasized the positive use of drugs to affect identity, health, and social relations. It differentiated modern drug experiences from those of the “primitive” past through associations with psychopharmacological and neurological research. *Drugs and the Mind* evoked such associations for “nonscientific” audiences by centering the brain as a cultural actor in the drama of drug use. It lyrically described the blood-brain barrier, mosaics of nerve impulses, and brain-borne sensations that overrode deleterious effects, such as enslavement. De Ropp’s text made “forbidden” knowledge accessible so readers could judge for themselves “whether chemical agents offer real or imitation happiness, genuine peace or mere numbing” (286). Those who achieved adequate self-mastery could avoid becoming “playthings” of chemicals. As a popular science writer, De Ropp attributed a powerful sense of agency to drugs, but he maintained that the strong could resist their power, and he felt sure that new drugs would be invented for the weak, who were “plagued by inward conflicts and unresolved tensions” (157). As a genre, popular pharmacology cast drugs in the utopian light of scientific rationalism: the new frontier lay within the mind.

In *Drugs and the Mind*, psychopharmacological drugs appeared as modern weapons against the “barbaric” practices of the past; drugs appeared as technologies of the self that could overcome the negative effects of human self-consciousness—fear, guilt, shame, anxiety, mental illness, and depression. Yet Nathan Kline’s forward to *Drugs and the Mind* warned against erring too far in the use of “happiness pills.”

The picture of the snarling, vicious, and dangerous monkey transformed by a few milligrams of a chemical into a friendly, “tranquil,” and “happy” animal fascinates me in an horrendous way. Such a creature is a pleasure to have around the lab, but he would not last ten minutes in his native jungle. Similarly, mankind is perfectly capable of tranquilizing himself into oblivion. (De Ropp 1957, ix)

In this formulation, self-mastery provided a wedge against addiction, allowing benefits to accrue without incurring the downside of addiction. This discourse

represented a marked change from the early 1950s representations of drug use as a sinister subversion of democracy.

The disruptions of World War II had loomed large in the early 1950s. Social experience with returning morphine-addicted veterans had converged in the earlier era with fears of rising crime among ungovernable juvenile delinquents. Nelson Algren's *The Man with the Golden Arm* (1951) showed the maladaptive side of addiction.⁵ In that book, Frankie, the "man with the golden arm," is a Polish World War II veteran living in an urban milieu of poverty, crime, irregular employment, gambling, and racial mixing. For him, morphine deadens the "projected image of one's own pain when that pain has become too great to be borne" (74). He describes how the figure of the "monkey on your back" embodies a powerful habit against which addicts are powerless: "You let the habit feed you first 'n one mornin' you wake up 'n you're feedin' the habit" (78). Algren wrote:

Through the streaked and spotted glass a monkey with a jaunty green fedora on his head returned [Frankie's] gaze. Bent in a sort of crouching cunning there on the other side of the pane, it gave Frankie the look which womenish men employ in sharing an obscenity with their own kind. Frankie felt himself struggle to waken, for the monkey was tucking the covers about his feet, still wearing that same lascivious yet somehow tender look. Felt the unclean touch of its paw and saw its lips shyly seeking his own with Sparrow's pointed face. To kiss and be kissed . . . (382)

Addiction was often depicted through the figure of the monkey, a racialized, homoerotic, and sexualized figure that appeared in popular and psychiatric discourse (Haraway 1989, 153).⁶ For instance, Robert Chessick reported a patient who had been "depressed for a long time and felt that 'the monkey on my back' was her mother. She felt that shooting the drug meant feeding the monkey, her mother" (1960, 121). Clinicians believed the metaphor itself presented treatment barriers: "The typical individual . . . conceives of his addiction as essentially ego-alien—'a monkey on his back.' With repeated experiences of failure in efforts to rid themselves of the habit, some unknown proportion of cases come to a realization that the habit really reflects some aspect of themselves and not something externally imposed" (Chein 1958, 149). Reinterpreting addiction as a relationship with the self, rather than possession by an "ego-alien" other, was considered a precondition for successful treatment.

Although professional arenas did not display the same ideological maneuvers apparent in popular portrayals that divide the "modern" subjects of psychopharmacology from "primitive" addicts, the split between biological psy-

chiatry and psychoanalytic or psychodynamic psychiatry was acrimonious. Disciplinary conflicts, conceptual and epistemological issues, and methodological disputes underpinned the configuration of the midcentury drug sciences as they do any problem-centered scientific endeavor. Often perceived as repeatedly failing to make good on ambitious promises, psychiatry and pharmacology are both divided between somatic and mental theories of mind and between biochemistry and behavior. These antagonisms have resulted in protracted social conflicts over the “intense interpretability” (Micale and Porter 1994) not only of psychiatry’s past but of the history of pharmacology. Psychoanalysis played an ironic role in the 1950s, when the scientific dismissal of psychoanalytic claims was occurring just as psychoanalysis diffused through the culture, especially through the medium of popular film. Psychopharmacologists aligned themselves with the experimental practices of psychologists and behaviorists, rather than the more interpretive and narrative practices of psychoanalysts.

When psychopharmacologists begin textbook overviews, they often survey the historical dimensions of their enterprise. They represent modern psychopharmacology as an objective, biologically oriented behavioral science and date the dawn of psychopharmacology as a distinct endeavor to the discovery of particular drugs or effects. For example, they might claim that lithium in the late 1940s or chlorpromazine in the early 1950s illustrated the proof of concept for psychopharmacology. They might draw attention to the ways in which meprobamate, mass-marketed as a minor tranquilizer under the names *Miltown* and *Equanil*, ushered in middle-class enthusiasm for pharmaceuticals in the late 1950s (Spiegel 1989; M. Smith 1991; Tone forthcoming).⁷ Psychopharmacologists writing this way rarely mention illicit drug use or credit addiction researchers with contributing to the field’s general principles (for exceptions, see Greenshaw and Dourish 1987; Pickens 1977). They more often delimit drug dependence as beyond their purview—which is strange given that many consider the ARC “probably *the* most advanced human psychopharmacological studies unit in the world at that time.”⁸

Textbook histories distinguish modern pharmacology from “protopharmacology” practiced by “great static cultures of antiquity” and “indigenous peoples everywhere” (Leake 1975, 30, 55). Such preambles contrast modern drug use to the crude empiricism of “primitive peoples” using premodern pharmacological agents. Yet pharmacologists often turn to the practices of witches or shamans to depict their science as one of the world’s oldest codifications of knowledge. The field of ethnopharmacology is engaged in a

"salvage paradigm" to preserve indigenous knowledge (Efron, Holmstedt, and Kline 1967; La Barre 1975). This anthropological cousin of psychopharmacology emerged with the explorations of New World hallucinogens by mycologist Gordon Wasson, botanist Richard Evans Schultes, and cultural anthropologist Weston La Barre (Rudgley 2003). The ethnopharmacological enterprise is pervaded by claims to universalism and a primitivizing rhetoric that literally appropriates indigenous knowledge practices (Siegel 1989; Rudgley 1993; Weil 1972).⁹ By contrast to this fascination with premodern ingestion of "essential substances," modern pharmacologists represent themselves as a "mongrel breed" that promises to "extend man's understanding of himself and his ability to control and direct behavior by chemical means" (Claridge 1970, 246–47). The science of modern pharmacology is deeply bound up with the dreams of behavioral control that flourish in appeals to scientific modernity.

A few historians evaluate pharmacology's success or failure to meet goals of prediction and control by using as a yardstick the behavioral improvements that supposedly led to a reduced number of institutionalized mental patients (an assumption that ignores the dismantling of the welfare state that began in the 1940s, prior to chlorpromazine's introduction: see Clark and del Guidice 1978; Castel, Castel, and Lovell 1982). Observers attributed a revolutionary effect to pharmacology, consigning psychoanalysis to the status of a baffled custodian of the appalling conditions of "snake pits,"¹⁰ as in the following remarks about differences between the pre- and postdrug eras.

Each year the population in mental hospitals increased, since patients continued to be admitted but very few were discharged. Typically, patient living areas were crowded and poorly furnished. Schizophrenic patients with paranoid delusions crouched in corners, living in constant fear. Catatonic patients might maintain the same rigid posture for prolonged periods, developing swollen legs and pressure sores. Hallucinating patients would pace the floor, talking to their voices and apparently unaware of their environment. Violent patients might attack staff members or other patients for reasons known only to themselves, leading to hostility and suspicion on both sides.¹¹

The preceding passage associates the era of psychoanalysis with uncontrolled squalor in inhumane institutions, a sadly unscientific state of affairs that contrasts to the clean, controlled conditions gained through the application of modern psychopharmacological technology.

Pharmacology takes place in an ambivalent zone between an evil empire of poisons and a Promethean landscape of panaceas. "Happiness pills" were a riper target—with higher social premiums and more chance of profit—than

solving the problems of drug addicts. Addiction has long been the evil twin of culturally sanctioned drug use, be it ceremonial or medicinal. For much of the twentieth century, there was a distance between the cultural momentum of pharmacological optimism and the slow progress faced by clinicians who worked directly with drug users. Users were cast as unruly subjects with intractable problems; hence pharmacology is structured around addicts as repressed subjects and objects of knowledge, as some internalist histories acknowledge (Barchas et al. 1977; Leake 1975). At times, the study of addiction is considered a source of knowledge about brains and bodies that is generalizable beyond the ranks of addicts. Joining historians who reveal the actual practices involved in human experimentation,¹² the rest of this chapter asks: To whom were drugs useful experimental tools? To whom were drug addicts useful bodies and reliable subjects? By whom were they ignored as unreliable subjects? The remainder of this chapter concerns how scientists secured and laid claim to these useful bodies—or disclaimed them as useless bodies.

“MAN AS THE ESSENTIAL FINAL TEST SITE”:

HENRY K. BEECHER AND THE HARVARD
ANESTHESIOLOGY LABORATORY

Oddly, the most prestigious node of the addiction research network coordinated by CDAN did not deal with addicts at all. Decorated World War II veteran Henry K. Beecher, director of Harvard Medical School’s Anesthesiology Laboratory at Massachusetts General Hospital, set the standard for randomized, placebo-controlled clinical trials of analgesic drugs in the late 1940s and early 1950s (Meldrum 1994).¹³ Most good analgesics are addictive: users build up physiological tolerance to such drugs as morphine, heroin, methadone, other opiates, choral hydrate, amphetamines, barbiturates, and sedative-hypnotics and suffer withdrawal when they stop using them.¹⁴ Addicted bodies can thus serve as bioassays for determining the “addiction potential” of a drug. But Beecher, who tested all these drugs and more, considered addicts unreliable subjects. Despite modeling their clinical research on the laboratory logics of the ARC, the Harvard group preferred the populations of human subjects to which they had access—terminally ill patients, postoperative pain patients, and Harvard college students.

Remembered as the “father of informed consent,” Beecher is famed for blowing the whistle on the widespread lack of informed consent in clinical research. Beecher was a flamboyant character with something of the gadfly

about him. He obscured his Midwestern, working-class origins by changing his name from "Unangst" to "Beecher" when he moved to Boston to attend Harvard Medical School in 1928 (Harkness 1999, 465). After completing his anesthesiology residency, he won a chair at Harvard just as the United States entered World War II. During the war, he conducted research on the handling of battlefield wounds and other injuries in heavy combat zones. Two decades later, he set the stage for a new regime governing clinical research in the United States when he presented a paper titled "Ethics and the Explosion of Human Experimentation" to a science journalism symposium organized by the Upjohn pharmaceutical company at the Brook Lodge Conference Center in Kalamazoo, Michigan, in March 1965 (Harkness 2003, 240n44). In the following year, the *New England Journal of Medicine* published a revised version, "Ethics and Clinical Research," and the popular press propelled the debate beyond the professional enclave at which Beecher took aim.

Historians have been at a loss to explain why Beecher became preoccupied with the ethics of clinical research. He first took an activist role in exposing clinical practices in 1954, when he and D. P. Todd coauthored an article attributing a high mortality rate (3.7 deaths per ten thousand anesthetics) to anesthesia itself.¹⁵ However, a retrospective interview by his onetime research assistant depicted Beecher as almost cavalier toward his experimental subjects in the 1950s—as more concerned with producing results than with his subjects' degree of informed consent (Lasagna 1994, 13–14). Although Beecher wrote a short book about the ethics of human experimentation (1959a), his scientific work merely mentioned that ethics were "too little pondered and too little discussed" (1959b, 59). As a historical figure, he has been constructed as an iconic embodiment of ethicality, in stark contrast to the ARC researchers, who were pilloried for experimenting on human beings. The Harvard Anesthesiology Laboratory and the ARC encode two symbolic extremes on the spectrum ranging from ethical to unethical human experimentation.

From 1947 until the mid-1960s, Beecher worked at the hub of the addiction research enterprise. Both the Harvard Anesthesiology Laboratory and the ARC belonged to overlapping pain and addiction research networks. Both research sites relied on similar laboratory logics and research practices, experimenting on human subjects with similar levels of compassion and curiosity. The rest of this chapter explores interactions between the Harvard and Lexington groups as well as CDAN, the committee that funded them both. The task of the Harvard group was to study analgesics and cough suppressants that had been tested on postaddicts at Lexington by replicating the ARC's experimental

designs in never-addicted subjects. The Harvard group organized large-scale, randomized, placebo-controlled trials and relied on statistical methods.¹⁶ Looking closely at how the Harvard group navigated practical problems of research design goes farther toward explaining Beecher's changed orientation toward ethics and his performance of ethicality than moral or psychobiographical characterizations ever could. His preoccupation with ethics was spawned not simply by his "outsider" origins or "contrarian" impulses but by a set of interactions across the separate but overlapping microsocal worlds that comprised the pain and addiction research enterprise. Understanding these interactions requires answering the following questions: What laboratory logics did Beecher practice in the decade prior to his well-known exposé on abuses of human subjects in the United States? How did they inform the ethical ideals he later espoused? To what extent did the clinical logics of the Harvard Anesthesiology Laboratory diverge from the laboratory logics of the ARC? How did researchers decide experimentation on humans should be conducted in the United States after the Nuremberg Code (1949)?

As a physician turned researcher, Beecher was untrained as a pharmacologist. At first, he was unfamiliar with the centralized coordination that I have described in the previous two chapters of this book, but his participation on the committee reinforced his sense that "the crucial study of new techniques and agents must be carried out in man." Beecher explained:

The extraordinary skill of the organic chemist and the biologist working together in identifying active agents in natural products and the chemist's progress in creating new and promising compounds which ultimately must be tried out in man, all throw an exceptionally heavy load on the experimentalist. Man as the essential final test site has come into adequate prominence only in recent decades. The current development of human biochemistry, human physiology, and human pharmacology has made it plain that man is the "animal of necessity" here. (1959a, 9)¹⁷

The preceding quotation indicates how Beecher generally thought science should work and is an apt description of how CDAN triangulated between laboratories in different social and geographic locations.

Unlike CDAN, the Harvard Anesthesiology Laboratory privileged actual clinical settings as research sites. Like the Lexington group, the Harvard group was interdisciplinary, comprised of pharmacologist Louis Lasagna, internist Jane Denton, anesthesia resident Arthur Keats, John von Felsinger, and—an extremely important resource for developing clinical trial methodology—statistician Charles Frederick Mosteller.¹⁸ Their experimental model of the ran-

domized, controlled clinical trial ultimately won acceptance from the medical and scientific elite (Meldrum 1994, 267–372). The Beecher group's experimental design took advantage of access to large numbers of naive—but fully informed and voluntarily consenting—subjects. If meaningful data was to be produced on drug-induced mood changes, Beecher believed it was going to come from aggregated response patterns corroborated by large numbers of subjects and carefully constructed control groups. The Harvard group also did pioneering work on the placebo effect, for which Beecher and Lasagna are remembered now that randomized, placebo-controlled clinical trials have become the “gold standard of objectivity in scientific medicine”; its “epistemological status as an objective scientific method” overshadows the randomized clinical trial's socially constructed character (Meldrum 1994, 373). The “objective” status of randomized clinical trials obscures the fact that subjective responses and meaning attribution comprise part of the data set on which trials rest. During the formative moments described in the present chapter, however, the meaning and significance of pain and drugs that relieve it was much debated.

The instruments Beecher's group developed to quantify subjective responses to drugs resembled those of the ARC, yet work at the two sites proceeded differently and garnered completely different public receptions. ARC studies involved small numbers of subjects and were confined to the obscure pages of pharmacology journals, whereas the large-scale trial designs by Beecher and Denton received immediate public acclaim and a great deal of attention in the medical press. The American Medical Association's Council on Pharmacy and Chemistry, whose Therapeutic Trials Committee promoted adoption of clinical trial methodology, praised Denton and Beecher for making “a distinct advance in the methods available for quantitative evaluation of the therapeutic efficacy” of analgesic and narcotic drugs (Van Winkle 1949). Historian Noemi Tousignant explains:

The Council's support associated Beecher's work to a movement of therapeutic reform to instil specific values, and techniques—particularly those of the randomized clinical trial—in American drug testing. This movement has been described as a current of elite activism for the promotion of a “rational therapeutics” that would be dictated by the norms of scientific evidence and medical professionalism, and protected against the excessive commercial aspirations of the pharmaceutical industry. . . . [T]he AMA's primary interest was in Beecher's methodological innovations rather than in the precise potency of these new analgesics. (2006, chap. 3, 17)

The Harvard group's methodology helped stamp randomized clinical trials with the highest epistemological status for certifying objectivity. The clinical trial model advanced by Beecher's group was based on a set of criticisms that Beecher leveled against contending approaches.

Experimental Limits and the Emergence of Clinical Trials

Deeply critical of behaviorism and techniques for producing experimental pain, Beecher was an eloquent critic of the laboratory's limitations. He reinforced his critique by drawing on a colorful origin myth from his World War II days, when his curiosity about subjective responses to pain and pain relief was piqued. Lasagna recounted of Beecher:

He made the observation during the war on the Anzio beachhead that soldiers suffering from wounds at least as grievous as those suffered by civilians seemed not to demand as much in the way of analgesic medication as did the civilian patients with whom he had had experience prior to the war, and he concluded that this was because there was a neurophysiological component to pain and then an emotional response to the stimuli being perceived which allowed the meaning of pain, if you will, to get into the act. (Healy 2002, 136)

Beecher believed that the meaning of a wound could change an injured person's felt need for narcotics: "Great wounds with great significance and presumably great reaction are made painless by small doses of morphine, whereas fleeting experimental pains with no serious significance are not blocked by morphine. The difference here in the two situations would seem to be in difference of significance of the two wounds. Morphine acts on the significant pain, not the other" (Beecher 1959b, 164). Beecher concluded that if meaning could modify response, then emotions, attitudes, and other psychological influences could also block pain or heighten it (Beecher 1959b, 150).

Thus did an event that took place far from the controlled setting of the laboratory become the basis for Beecher's critique of experimental pain and methods used to measure it. On the Anzio beachhead, badly wounded soldiers who should have been in great pain were instead euphoric at the prospect of being removed from the battlefield (Beecher 1959b, 165). Beecher explained: "It seems from this that the reaction, or processing, component can dominate the pain experience. It is more potent than the noxious stimuli in determining the presence or absence of suffering. The total situation has, of course, great influence on the reaction that develops in it" (1959b, 164). In a subsequent study of surgical patients, Beecher found that comparable wounds were experienced as

depressing, calamitous events. He determined that outside the wartime context, pain was experienced as more severe, and the corresponding need for pain relief was perceived to be higher (1959b, 164–65). The cultural authority that Beecher gained from this seminal wartime event placed him in a position to argue that “true operationism” embraced subjective factors instead of banishing them from experimental settings (1959b, 157).

Incorporating the subjective brought new problems of experimental design and ethics into focus. These problems were exacerbated by behavioral approaches, which Beecher disdained for mistakenly assuming that “for a given stimulus there must be a given response.” Beecher used the Anzio incident to argue that the relationship between stimulus and response was far from simple due to the “interposition of conditioning, of the processing component, of the psychic reaction.” He explained that some drugs had unexpected effects depending on the “personality make-up and mental state of the individual involved.” Consider, he wrote, the sad drunk and the happy drunk, or the narcotics addict for whom morphine was “euphoretic” versus an inexperienced nonaddict for whom the same drug proved unpleasant or “dysphoric” (1959b, x). From Beecher’s perspective, drugs were so “strongly laden with meaning and importance” that they changed the “drug-person relationship” (Beecher 1959b, 339). While the laboratory logics of Lexington and Michigan attempted to disqualify meaning, the Harvard group set out to create a science of significance by quantifying subjective effects.

According to Beecher, the value of experimental pain was sharply limited in contrast to “pathological pain” (1959b, 43–46, 114). The most prominent laboratory research aimed at isolating “pure” sensations of pain from reactions to it was a Cornell University Medical College group that consisted of physicist turned physiologist James D. Hardy, neurologist Harold G. Wolff, and research associate Helen Goodell. Best known for their central theoretical claim about “pain thresholds,” the Cornell group embarked on experimental pain research in the early 1940s. They invented several methods to produce pain and techniques to measure it; among the latter was an apparatus they called the “dolorimeter.”¹⁹ Beecher was critical of Hardy, Wolff, and Goodell, because he felt their methods failed to eliminate bias and learning effects and because they insisted that pain thresholds were uniform enough to be measured. In contrast, clinicians found that variation between individuals was a pronounced practical problem in clinical settings.

The Harvard group was also skeptical of the “dol scale,” a pain intensity scale that the Cornell group advanced on the basis of units called “just notice-

able differences” (Beecher 1959b, 21–22; Meldrum 1994, 283). The dol scale was supposed to enable comparisons between different subjects and stimuli, thus standardizing evaluations of analgesic effectiveness. Not only was Beecher unconvinced that it did so with any validity, but he held that it was erroneous to assume that an elevated pain threshold correlated with the intensity of analgesic action. Critical of the entire basis on which Hardy, Wolff, and Goodell proposed to measure pain and analgesic action, Beecher became committed to quantitative approaches as the best route to making objective claims on the basis of data on subjective effects.

Beecher severely criticized self-experimentation data, castigating an early double-blind study comparing opiate alkaloids that is typically credited with originating the scientific investigation of the behavioral effects of drugs. Of this study, conducted by David I. Macht, N. B. Herman, and C. S. Levy at Johns Hopkins University (1916), Beecher wrote:

[S]ince only the three authors were used as subjects and, considering the time required to test the six opium alkaloids studied, they must have become before long sophisticated subjects well able to differentiate between the aura of the narcotics used and a placebo. These facts plus their vested interest in the outcome lead to a less than “crucial corroboration” of their method. Unfortunately, their error in this regard is a common one, indeed, one that threatens much work in this field. The only safeguards known to the writer, and it must be agreed that these are only relatively reassuring, are to minimize the problem by using fresh subjects for only a relatively few observations, to use subjects who know nothing of the purpose of the experiments or the parameters at issue and who care nothing about the outcome. (1959b, 117)

Similarly, Beecher rebuked the Cornell group for using themselves and close associates as subjects. The Cornell group’s practice was well known. For instance, Abraham Wikler of the ARC collaborated with the Cornell group on the only self-administration study in which he participated. In that study, the experimenters and three “volunteer subjects” from Lexington self-administered more than two dozen compounds, including morphine, aspirin, alcohol, barbiturates, codeine, placebos, and unknowns, two or three hours after breakfast, then measured their effects on perception thresholds governing response to touch, vibration, smell, and hearing (Wikler, Goodell, and Wolff 1945). Beecher believed that the Cornell group took inadequate precautions to eliminate bias and suggestion (1959b, 115–18). His growing familiarity with the logic of double-blind, placebo-controlled clinical trials led him to fervently oppose the long-accepted practice of self-administration.

For Beecher, using oneself or one’s colleagues or students as experimental

subjects was problematic not from an ethical standpoint but from a practical one. Believing that drug-experienced subjects differed from inexperienced subjects, Beecher felt that knowledgeable subjects picked up on a narcotic "aura" that enabled them to identify drug effects (1959b, 53). He argued that no subject who once experienced a narcotic could forget it, so subjects could easily surmise whether they had been given drug or placebo. He thus deemed knowledgeable subjects unreliable, in the sense that their knowledge could invalidate results. Beecher argued that knowing too much was also a problem from the experimenter's perspective, for a "knowing operator's" tone of voice or inflection might heighten subjects' suggestibility to drug influences (1959b, 148).

Self-administration studies conflated the experimenter's role with the subject's role, a situation viewed by Beecher as dangerous because experimenters knew too much and were too deeply invested in outcomes. He disapprovingly quoted Carl C. Pfeiffer, chair of pharmacology at the University of Illinois, who stated that no volunteer should be used who was not "at least . . . a graduate student . . . who has investigated for himself the nature and possible dangers of the drug involved" (Carl C. Pfeiffer to Dr. Stormont, secretary of the Council on Pharmacy and Chemistry, Committee on Research, American Medical Association, September 18, 1951, quoted in Beecher 1959a, 17). In a 1957 personal communication to Beecher, Pfeiffer admitted that he no longer abided by that rule and that he was using Atlanta Penitentiary prisoners as experimental subjects (Beecher 1959a, 17). But one of Pfeiffer's graduate students, Edward F. Domino, has confirmed that self-administration was common in graduate pharmacology departments at the time (personal communication with the author, 2006). Beecher believed knowledgeable subjects skewed results because the "essential unknowns" were impossible to maintain with drug-wise subjects (1959b, 54); they simply could not be kept in the state of ignorance that he viewed as necessary for good science.

Highly trained subjects come to have a vested interest in the outcome, whether scientific or pecuniary (continuance as paid subjects) or egoistic (personal attention); the failure to eliminate their bias can have devastating results. To be sure, learning on the part of the subject is always a hazard to be watched for and minimized with proper controls, but the hazard is far greater with the experienced group. (1959b, 146)

Beecher maintained that experienced subjects knew too much about drugs and might use their knowledge base to ascertain their role in clinical trials and skew results.

Although he considered postaddicts too knowledgeable, Beecher also real-

ized that clinical researchers faced the problem of getting valid observational information from sick and postoperative patients. He also considered the “casual observations of busy doctors or ward nurses” to be “without value,” because clinicians could easily confuse drug side effects with common afflictions, such as nausea and vomiting (1959b, 58–59). Beecher argued that even techniques designed to overcome validity problems—“double unknowns,” placebo controls, randomization, correlated data, and mathematical validation of differences—could not always overcome observer bias (1959b, 59). Although the Harvard group was set up to observe around the clock, documenting the clinical experience of variation in drug effects, individual response, and variations in individual experiences over time required subjects to be in almost continuous contact with researchers. As Beecher knew, this kind of proximity and casual interchange about drug effects was next to impossible to achieve in a hospital ward or with ambulatory college students. Therefore Beecher and Lasagna performed some of their studies at the ARC and tried to mimic the laboratory logics of Lexington by setting up similar experimental situations in dissimilar material, social, and institutional conditions. Clinical trials were the Harvard group’s solution to these dilemmas. They worked on new experimental logics and statistical methodologies that relied on large sample sizes, access to naive subjects, elimination of observer bias, and disqualification of knowledgeable subjects.

Clinical trials took shape in response to an implicit critique of the laboratory logics and practices of the experienced drug researchers at the ARC, who had access to nothing but knowledgeable, drug-experienced subjects. They could not muster more than a handful of “normal” subjects for control groups and had to use themselves and their coworkers. The researchers at the ARC considered drug-wise subjects the most reliable and ethical route to knowledge about drug effects. They could not conform to Beecher’s high-turnover solution to these problems, which was to use experimental subjects only for short periods of time and “turn to fresh subjects before the old ones become drug-wise” (1959b, 146). The Harvard group could afford to adopt this practice, whereas the Lexington group could not. None of its subjects were naive.

SUBJECTS WHO KNEW TOO MUCH: THE MEANING OF “EUPHORIA” IN EXPERIMENTAL READDICTION

Tensions between the ARC and the Harvard Anesthesiology Laboratory personnel were evident at the eleventh postwar CDAN meeting, held in Lexington

on January 9–10, 1953. After touring the ARC research ward, the committee held a spirited debate during discussion of a pilot study by Beecher and Lasagna titled "Euphoria: A Study of Drug-Induced Mood Changes in Man." There was such disagreement over the term *euphoria* that the landmark study was later published in the *Journal of the American Medical Association* as "Drug-Induced Mood Changes in Man" (Lasagna, Von Felsinger, and Beecher 1955). Responding to the pilot data, Abraham Wikler said:

By an odd coincidence we have been concerned with the problem of euphoria for many years. Our first definite conclusion is that the term "euphoria" means very different things to different people, to the same person at different times, and also to groups of individuals after administration of different drugs. . . . To interpret what euphoria means is no easy task but we feel we can interpret what the individual means by euphoria by observing how he behaves verbally and non-verbally, by recording his statements and his behavior in a given setting. (Committee on Drug Addiction and Narcotics 1953, 378)

Wikler admitted that behavior and subjective effects could only be the subject of science if they were predictable and that they would become "predictable only if the situation is clearly delineated" (Committee on Drug Addiction and Narcotics 1953, 378). Whether the feelings of unusual well-being designated by such a diffuse and nonspecific term as *euphoria* were experienced by subjects thus depended on how the experimental situation was structured.

Only if they produced euphoria did ARC researchers believe they could accurately measure the abuse liability of an opiate-like drug or learn anything about how addiction worked. Their goal was not to determine low, therapeutically effective doses but to predict whether the drug was liable to abuse. Determining that required getting subjects high, which meant administering "doses in the addict range" (Committee on Drug Addiction and Narcotics 1953, 382). Because their knowing subjects had considerable experiential knowledge of the "addict range," the ARC researchers set up experimental situations to mimic natural addiction. Only these, they thought, would tell them very much of what they wanted to know. ARC researchers justified the use of high experimental doses on the following grounds: "Addicts do not use small therapeutic doses. They increase the dosage of a drug to the limit of their tolerance, so that if the conditions of natural addiction are to be stimulated, high doses must be used experimentally in evaluating the liability of addiction to new drugs" (Isbell, Wikler, et al. 1948, 391). Operationalizing euphoria raised the very basic question of why some individuals experienced it and others did not. What did it mean that terminally ill, postoperative pain patients and "normal" controls did

not experience euphoria whereas postaddicts invariably did so? More important for the kind of work being done at the ARC, did that difference invalidate results of studies on postaddicts?

Looking closely at the Harvard group's study, which was conducted at the ARC and Massachusetts General Hospital, reveals that it followed the contours of a pilot study of nine "young, intelligent, healthy male volunteer subjects" (presumably Harvard students). Experiments were repeated on twenty additional male college students; thirty chronically ill, old, hospitalized patients who were "surrounded by dying" (Beecher 1959b, 323); and thirty post-addict prisoners at Lexington. Although each group of subjects responded differently to heroin, morphine, and amphetamines, responses were similar within the group. So-called normal volunteers (the college students) found amphetamine a "more potent euphoretic" than heroin or morphine, which they experienced as unpleasant or inert. Surprised that amphetamine invoked intense euphoria, investigators who found that it relieved pain in the chronically ill suggested that there was a "real place for amphetamine as a euphoretic in the treatment of the hopelessly ill" (Beecher 1959b, 335).

In the Harvard study, postaddicts differed from both the chronically ill group and normal controls in that the former reported stimulation and "improved mentation" after opiates but found amphetamine's effects unpleasant and prolonged (Von Felsinger, Lasagna, and Beecher 1955, 1016). Unlike normal volunteers, they did not report unpleasant side effects of opiates, such as nausea, vomiting, and mental dullness. However, postaddicts indicated that they had once experienced such unpleasant effects when first using narcotics. The question before CDAN was whether such variations formed a pattern that could be explained. The Harvard group appealed to Beecher's concept of the drug-person relationship (1959b, 339), which was based on data generated in this study. The study correlated personality factors and typical versus atypical drug responses: "For example, the most frequent responses to amphetamine were euphoria and alertness; to heroin and morphine, dysphoria and sedation. These reactions were thus called typical. The opposite responses for each drug were labeled atypical" (Von Felsinger, Lasagna, and Beecher 1955, 1113). The Harvard group concluded that the atypical responders who became euphoric on heroin or morphine and dysphoric on stimulants were the least balanced subjects: "Our group with atypical reactions resembled addicts in their preference for opiates; this group was made up of the more maladjusted subjects, a finding in keeping with theories as to the importance of personality deviations in the genesis of drug addiction" (Von Felsinger, Lasagna, and Beecher 1955, 1119).

Ultimately, the Harvard investigators suggested that "differential personality dynamics, primarily in terms of the balance of mature, socially oriented controls over impulsive, egocentric emotionality, were found to be correlated with the type of drug reaction" (Von Felsinger, Lasagna, and Beecher 1955, 1119). The Harvard group found postaddicts atypical and unsuitable for study because data generated by them could not be generalized. This position had nothing to do with ethics. In fact, Beecher agreed with the Lexington group that "ethical considerations dictate the use of post-addicts in assessing the development of tolerance and physical dependence" (1959b, 340). He drew the same line the ARC did between readdicting a onetime addict and addicting someone who had never experienced addiction. However, he warned that conclusions based on results generated through the use of former addicts might lead to underestimates of the potential hazards posed by new analgesics. For this reason, Beecher was often at odds with pharmaceutical industry representatives, whose economic interests were at stake and who therefore minimized the dangers of releasing drugs onto the market in the era before thalidomide. The skeptical pharmaceutical industry representatives of CDAN treated the Harvard group critically and sought to dismiss its work on the grounds that its methods were too subjective. The pharmaceutical representatives thought such large-scale quantitative studies as Beecher's obscured their actual subjective basis, whereas the small-scale studies of the ARC were more objective.

Drug control decisions by the U.S. government, the World Health Organization, and the United Nations were made on the basis of data produced by the ARC that was sent on to the U.S. surgeon general and the international governing bodies. The positions just related informed the drug policy-making process and global drug control regimes of the mid-twentieth century. According to Beecher, both the Lexington and Harvard groups agreed that "you have to examine drugs and drug reactions under the conditions where they are going to be used" (Committee on Drug Addiction and Narcotics 1953, 381). They agreed that drug effects varied by situation: "It is obvious that the subjective effects of drugs, no less than the objective effects, are dependent on the situation in which the drug is administered. It is also likely that the production of a given mental state, even in the same situation, will not prove equally pleasant to all persons" (Beecher 1959b, 322). Furthermore, they agreed that drug effects differed according to the subject's degree of experience with the drug or drugs like it. The "pharmacological sophisticates" of Lexington, as Beecher called them, consistently rated morphine's effects more positively than did drug-naive subjects. What, then, was the value of assessments of analgesia or abuse

potential conducted in so-called postaddicts? How valid were comparisons between addicts and nonaddicts? Could any institutional experimental setting be compared to social situations where individuals self-administered drugs?

Disagreement arose between the two research groups because Beecher maintained that a “hint of a difference” led institutionalized postaddicts to experience euphoria when morphine was administered. He could not specify what this difference was, but he believed it to invalidate results of studies in postaddicts (Committee on Drug Addiction and Narcotics 1953, 381). By contrast, ARC researchers saw similarities between those who had been addicted and those who had not. They argued that just about anyone could become addicted, given exposure to the right drug under the right conditions. They set about persuading others that extrapolations from postaddicts to nonaddicts were valid. One difference was especially apparent to the Harvard group because it had implications for research design. Drug-naïve subjects did not know how to talk about drugs, so Beecher’s team had to “help subjects verbalize their responses” by supplying semantic opposites from which they could select (1959b, 333). By contrast, drug-experienced subjects possessed a rich vernacular vocabulary for expressing the inner states induced by drug experiences and a “long-standing and complex drug-person relationship that does not exist in non-addicts” (Beecher 1959b, 339). This “drug-person relationship” enabled these subjects to convey their innermost sensations with accuracy and gave them a comparative standard by which to measure drug effects. Only with great care could the meanings that former addicts attributed to drugs be disentangled from the effects they experienced in studies. This practical problem contributed to Beecher’s wariness about using former addicts far more than did the underrecognized ethical problems posed by experimental readdiction.

Experimental readdiction would now be considered ethically problematic but did not pose an ethical dilemma in the research culture of the time. Ethical guidelines for clinical research were uncertain during the 1950s, despite the Nuremberg Code (1949). Indeed, as the next chapter demonstrates, Beecher lobbied against basing governance of clinical research on the Nuremberg Code, confirming Lasagna’s (1994) insistence that Beecher had shown little interest in the ethics of human experimentation when they worked together in the mid-1950s. Certainly, Beecher’s publications were quite typical of the time in not reflecting on ethical issues.²⁰ Beecher did amass a thick file of press coverage on the Nuremberg Medical Trial, most likely because he considered the Nuremberg Code too rigid and was actively seeking alternatives.

By contrast to the Harvard group, the publications emanating from the

ARC exhibited an awareness of research ethics as early as the late 1940s, a discursive practice the larger biomedical research community did not adopt until much later. Although it is difficult to ascertain the level of awareness of the Nuremberg trials among researchers at the ARC, Wikler was himself a Yiddish speaker who remained the linchpin of a family that was directly affected by the Holocaust. His lifelong interest in Judaica led others to portray him as a Talmudic scholar. Not only was he surely aware of the Nuremberg trials, but his writings often anticipated potential criticisms of the participation of human subjects in natural experiments that mimicked the conditions of addiction. The next two chapters of the present book delve further into the indigenous ethical situation at Lexington. This chapter points to the interpretation that it was not ethics but research design that motivated Beecher's arguments against using postaddicts as research subjects, on the grounds that they knew too much about drugs and had formed unusual drug-person relationships.

Following from the laboratory logics on which their research practices built, ARC researchers believed, conversely, that it was only ethical to use postaddicts. They argued that only postaddicts could provide truly informed perspectives on the subjective effects of drugs or compare morphine's effects to those of the new synthetic opiates with any validity (Isbell, Wikler, et al. 1948, 390)—that only they experienced euphoria in ways that yielded predictive information that could prevent the release of drugs liable to be "abused." Still, addiction researchers quibbled with the use of the term *euphoria* as a framing device, because the term did not lend itself to precise definition or measurement. Researchers at Lexington found the concept of euphoria both fruitful and maddening as they sought to replicate "getting high" in a laboratory setting within a prison-hospital.

Euphoria was hard to define because of the counterintuitive variety of its clinical manifestations. Isbell, for example, recounts giving thirty milligrams of morphine to a nontolerant morphine addict "who turns pale, gags, and heaves": "[A]sk him how he feels and he is fine, wonderful. You ask him, 'You are vomiting and all this, but you are fine?' and he replies, 'Yes, it's such a good sick.' Now is that euphoria, or isn't it?" (Committee on Drug Addiction and Narcotics 1953, 382). The difficulty of quantifying euphoria could be compounded by altering the experimental situation. Drug effects would be altered if subjects were anxious, paranoid, or ill at ease. Wikler urged investigators designing an experimental setting to ask themselves, "Under what conditions are these [drugs] administered, to whom, and what for? Let's recognize the fact that the action of a drug depends upon the particular experimental condition

under which it is studied” (Committee on Drug Addiction and Narcotics 1953, 379). In mimicking natural addiction, ARC researchers sought to reproduce the subjective effects that accompanied drug administration, despite the difficulty of operationalizing them in the laboratory.

The Problem of Euphoria: Operationalizing the Concept

Laboratory life at the ARC was structured around “operationalism,” a concept drawn from Harvard physicist Percy W. Bridgman, who Wikler admired.²¹ Bridgman distinguished between “public science” and “private science.” The latter involved nonoperational terms, such as *mind, body, forces, tensions, psychic energies, conversion, or somatization* (Wikler 1952c, 95). Although conducted in incommunicable terms, private science offered an intuitive basis on which to build “public science” (Wikler 1952c, 96). Taking the operational view was integral to remodeling psychiatry as a descriptive and predictive public science. This scientific effort raised epistemological questions of the kind posed by Wikler: “How do they know when they know that they have understood the phenomena, to put it another way? And I insist that this answer must be given in terms of public operations, so that others may know how they know, when they know.” Wikler’s commitment to operationalism stemmed from his belief that public science should make its methods evident “so that others may know how they know, when they know.” Far from seeing scientism as impoverished philosophy, Wikler believed that freedom and self-mastery depended on studying the “reconstruction of necessity through man’s ingenious scientific activities.” This philosophy was infused throughout the ARC’s reconstruction of the physiological, neurological, and psychological experience of necessity that drove subjects’ everyday lives. Wikler explained that the laboratory logics of Lexington recognized addicts were not “merely automatons” but individuals who experienced “necessities” differently than others (Wikler 1964, 188).²²

Seeking to unmask the primary needs that drove his subjects, Wikler turned away from “mentalistic” intuitions, ideations, and insights, which he relegated to the realm of private science. He argued that these would have to be operationalized if addiction research was to achieve the status of a public science.²³ Drugs offered psychiatry tools to accomplish this move, but Wikler believed there were therapeutic limits on how far such investigations could or should go (1952c, 97). Predictive public science would always be limited. Wikler modestly suggested: “[L]imited goals are [the only ones] to which any scientist can possibly aspire. We must be able to give up our time-hallowed but useless quest for ‘ultimate realities’ in exchange for limited, but useful patches

of knowledge. But even a patch-work quilt may be beautiful as well as warm" (1952c, 98).

Limited, partial perspectives were circumscribed further by the thorny problem that the "so-called properties of the bodies revealed by our measurements are in fact primarily the reflex of our measuring methods and not concrete facts *in rebus Naturae*" (Wikler 1952c, 90). ARC researchers were committed to multiple frames of reference because the phenomena they studied did not yield to any one approach. They based their explanations solely on what could be reproduced in the laboratory through, as Wikler described, a modest "demonstration of correlations that are useful for particular purposes, and which can be summarized in terms of operational constructs in a variety of frames of reference, each appropriate to the type of technic used in observation." Wikler continued:

Thus, there are not one, but several kinds of psychological, physiological, biochemical, and anatomical frames of reference, and their number and areas of usefulness vary as new techniques are developed. Furthermore, these frames of reference are not reducible one to the other, for the particular experimental arrangements that define one type of operation usually preclude those that define another. (1952c, 91)

Wikler emphasized that terms had to be defined operationally, a formidable task for a psychiatry that commonly deployed such terms as *excitation*, *depression*, *inhibition*, *release*, *energy*, *homeostasis*, or *levels of integration* (1952c, 91). To Wikler's way of thinking, these terms were useless if they were not linked to observable changes (1952c, 95). Rather than rely on narrative constructions, the ARC sought to manipulate the situation in order to block or produce observable drug effects. Contrary to the Harvard group's constant questioning, Isbell cautioned against asking too much of its subjects: "There is no better way to antidote the effects of analgesic drugs, subjective and objective, than to make measurements and ask questions at stated intervals" (Committee on Drug Addiction and Narcotics 1953, 381). ARC researchers felt that continuous questioning offset potential understanding.

In Henry Beecher's view, the Lexington group tipped too far toward operationalizing everything. He portrayed their use of electroencephalograms as "elaborate" but useless. He criticized the ARC's adoption of animal reflex techniques developed in pharmaceutical houses to assess analgesic activity separately from addiction liability (Wikler 1950). When adapted to human beings, particularly postaddicts, these techniques proved so highly variable that the

ARC was forced to innovate. While Beecher recognized the usefulness of animal reflex tests for predicting analgesia (1959b, 93–94), he thought they relayed nothing about subjective responses (1959b, 57). He believed that more useful information could be generated if the “co-operative statement of the subject” could simply be read properly and interpreted as data (1959b, 158). The problem lay in figuring out how to render subjective responses into objective data without pushing operationalism to the point of diminishing the significance of meaning, the very thing that Beecher thought was most important.

True operationism embraces the use of questions and answers, and the Harvard group’s techniques, for example, are operational. Extreme operationists have gone so far as to deny that one can depend upon what the subject says about his pain. To the writer this is a kind of nihilism. If this extreme view is accepted, then even when dealing with man one would have to depend upon [physiological] reactions to pain. (1959b, 158)

For Beecher, it was the mind—not the brain—that subjective responses to drugs revealed. His purpose was not so much to gain knowledge about drugs and their effects but to achieve a basic understanding of human behavior by controlling for sensation, feeling, or mood, so as to isolate the psychic reaction or reaction component.

Despite differences, Beecher and Wikler enjoyed a scientific camaraderie, as Beecher admired the Lexington group’s attempt to operationalize “anxiety associated with the anticipation of pain” or the condition of “giving a damn about pain” (1959b, 8).²⁴ “Our hypothesis,” wrote Wikler in a letter to Beecher, “is that how much one ‘gives a damn’ about pain can be inferred from observation of the extent to which signals heralding nociceptive stimuli *which the subject cannot escape or avoid*, disrupt previously learned responses that are ‘adaptive.’ After all, is that not actually the basis on which we proceed in assessing ‘clinical’ pain for purposes of deciding whether or not to intervene?” (quoted in Beecher 1959b, 7–8). Although Wikler joked that he could not yet refute Beecher’s conclusion that “[p]ain cannot be satisfactorily defined, except as any man defines it introspectively for himself,” Beecher’s rejoinder indicated that he thought that if anyone could define pain objectively, it would be the Lexington group. This repartee lay close to the heart of their differences: Could pain be objectively defined, experimentally produced, or scientifically understood without taking into account meaning, personality, or experience? What about the modulation or absence of pain due to the opiates, whether experienced as “euphoria” or relief? Was addiction a path to understanding pain, or was it a

dead end? Was "euphoria" a route to understanding addiction, or was it a meaningless effect? If experimental setting, previous events in the life history, personality differences, or level of social experience with a drug could change how a drug affected a subject, what scientific method could possibly yield the kind of data that spoke to these questions? Methodological and epistemological questions underlay the structural tensions involved in coordinating research conducted under very different material and institutional conditions.

Structural Tensions: Coordinating Industry, Government, and Academia

After Beecher and Lasagna presented the results of their study on euphoria, pharmaceutical industry representatives complained to the CDAN leadership behind closed doors, arguing that Beecher's work was "too non-objective" and disparaging it as tangential to the committee's goals (Committee on Drug Addiction and Narcotics 1953, 387). Stating that Beecher's work was precisely what the committee had in mind, Eddy defended continued "support of fundamental studies within its field of interest, which no one firm would feel justified in initiating or supporting, yet which would add materially to our understanding of analgesia and addiction, and would, therefore, be of interest and profit to all" (Committee on Drug Addiction and Narcotics 1953, 387). Because Beecher's funding was more contingent on results than that of Seevers or the ARC, questions such as these struck at the material basis of the Harvard group and Beecher's scientific credibility. Industry representatives found his work on subjective effects too bound up with the messy world of meaning and the mire of mood and argued that it could not count as the objective science they needed to take their drugs to market. In partial defense against these criticisms, the besieged Harvard group invented the crossover trial design and double-blind method for which they are known. Instead of banishing subjective effects for the sake of objectivity, the group deployed statistical methods to render credible claims about them.

These contentious interactions point to structural problems inherent in trying to accomplish basic research through an NRC committee. Industry wanted a drug-testing service from which it could gain a stamp of approval for drugs going onto the market; the ARC wanted to concentrate on basic research rather than applied product testing; and CDAN wanted a coordinated and successful search for a nonaddicting analgesic by whatever route necessary. Far from being an instrument of the pharmaceutical industry or a subsidiary regulatory agency, the committee's autonomy gave it an independent evaluative capacity and a source of oversight. Committee chair Isaac Starr commented:

It would be easy for our program to degenerate into a simple matter of clinical testing. I have little doubt that we could get plenty of support from various drug houses for such a program and I hope none of them have had in the back of their mind that that is what is eventually going to come of it. We are interested in fundamental research in a way that the drug houses ought to be interested because in the long run, what they make money on is dependent on it. (Committee on Drug Addiction and Narcotics 1953, 388)

He argued that the committee should not become the handmaiden of industry: “If we can’t sell this broader program to industry then we ought to let the program drop. We have no intention of setting ourselves up simply as a drug testing service” (Committee on Drug Addiction and Narcotics 1953, 392). The committee remained committed to basic research and wary of close associations with industry—while cultivating the interests of industrial actors in order to channel resources toward the search for a nonaddictive analgesic.

Arguing that investigators should not have direct ties to pharmaceutical companies, Beecher was convinced that investigators’ attitudes could unconsciously influence subjects and results (1959b, 43). He also believed that companies should bear the costs associated with investigating the safety and efficacy of drugs they developed.

Costly and tedious as the methods and controls are when based upon sound practice, they are far less costly and certainly give answers in far shorter time than when drugs are distributed widely and used without any discernible controls. Also, in the method of wide distribution, the public bears the cost; in the sounder approach, the pharmaceutical industry pays. It does not seem unreasonable that the industry bear the cost of such evaluations. (1959b, 43–44)

Although pharmaceutical companies made minimal contributions to CDAN, they did so reluctantly. Indeed, new drugs were released through physicians without controlled trials or the “masses of data that might have protected them from error” (Beecher 1959b, 44). Well before the sedative thalidomide provided a clear-cut example of underscrutiny and a catalyst for a new regime,²⁵ Beecher argued that lack of a systematic drug review process led to skewed results, casual findings, and misinformation, all of which were inadequate safeguards to public health. The 1953 CDAN meeting exemplified tensions between drug researchers and the pharmaceutical industry representatives, who had attended in full force so as to get a look inside Lexington, where so many of their drugs had been tested (Committee on Drug Addiction and Narcotics 1953, 388).²⁶ To better acquaint their guests with their laboratory logics and research subjects, the ARC turned to film.

ANIMATING EXPERIMENTATION: THE FILMIC
RECORD AT LEXINGTON

Films made at the ARC were screened at CDAN meetings to better acquaint attendees with the outcomes of the methods pursued there. A film made by Wikler followed the progress of a single human subject through tolerance to and withdrawal from morphine. One made by Isbell, *Abstinence from Alcohol*, showed three human subjects undergoing abrupt withdrawal after consuming between four hundred and five hundred milliliters of 95 percent ethyl alcohol daily for three months. One suffered seven grand mal seizures; the second, evident delirium tremens; and the third, mild hallucinations with insight. Of this film, Isbell noted, "The data suggest that abstinence may be one of the precipitating factors in 'rum fits' and *delirium tremens*" (Committee on Drug Addiction and Narcotics 1953, 385). The Lexington group established that alcoholics could experience symptoms of abstinence while still drinking and helped create the scientific consensus that alcohol produced physical dependency (Isbell et al. 1955). Similarly, Isbell made a film in the late 1940s on barbiturates, as part of a six-subject study to determine whether seizures and convulsions were due to intoxication or withdrawal. At the time, no one knew what caused these severe effects, although clinical reports attesting to them and delirium tremens were widely known. To a greater degree than scientific papers could, these amateur films—made on a sixteen-millimeter camera owned by a staff member—captured aspects of the ARC that would otherwise remain invisible.

A number of conclusions can be drawn about the making of such movies. There was little reflection at the ARC about how such films might look to audiences beyond the research community. Like the "monkey movies" described in chapter 2, these data films were made for insiders. Viewing them helps indicate boundaries between interpretive communities. For instance the subject of Wikler's film *Natural and Induced Abstinence in Chronic "Spinal" Man* was a frequent patient at Lexington whose spinal cord had previously been transected by syphilitic meningo-myelitis. The study was made to validate "inferences [for human beings] previously made on the basis of observations in chronic spinal dogs" (Committee on Drug Addiction and Narcotics 1953, 385). The film participated in the laboratory logic of mimicry—a human subject was found who could replicate the conditions of the experimental animals. Much ARC data was based on animal studies, and questions remained about their validity for making claims about humans. The film was part of the process of convincing CDAN members that animal models could be extrapolated to humans. Meant to persuade those within the addiction research network that

such comparisons were valid, the films signaled something very different to those outside it.

The films present martyrlike representations of human subjects undergoing profound physiological crises. Clearly, the prisoner participants filmed were aware of what was happening to them even in the throes of suffering. They had experienced withdrawal many times off camera. For the Lexington group, filming patients going through abstinence was a way to record data—a method Wikler had used previously as a successful diagnostic technique in his quest to isolate underlying organic disturbances. However, the films cannot be seen simply as data films: in the barbiturate film, Harris Isbell was portrayed soothing a patient by stroking his arm and supporting a heavily intoxicated patient walking down the hall. Far from being staged, these attitudes of compassion were what Isbell was particularly known for at the institution. When the clinical side of the Lexington Hospital had difficulty with patients, Isbell was called over from the research unit. Patients arrived at Lexington in a variety of states—still on street drugs, beginning to suffer abstinence, or in the full throes of withdrawal—and detoxification often depended on recognizing what they were on and gradually tapering them off (Conan Kornetsky, personal communication with the author, July 28, 2006). This was something that Isbell had a reputation for doing with compassion and competence.

Within the closed world of addiction research, the films conveyed the “clinical manifestations of drug addiction,” as a medical education film made by splicing the research films together decades after they were made was titled.²⁷ To many outside the social worlds of substance abuse research this film seems callous at best, inhumane at worst. It attests to the use of prisoner patients’ bodies as inscription devices to record and make evident the pain of withdrawal. It is impossible to watch the visceral effects of withdrawal without attributing aspects of martyrdom to these lone figures engaged in their own “experiment perilous” (Fox 1959/1998). As Donna J. Haraway explains, the film medium “concern[s] the distancing of observations, the structuring of vision”; vision is “mediated by writing technologies”; and the body “becomes an inscription device” (1989, 117–18, citing Latour and Woolgar 1979, 43–54). Indeed, the bodies of the subjects depicted in these films exhibit unrestrained agitation, convulsions, vomiting, and the undisguisable anguish of withdrawal. They relentlessly, realistically inscribe drug withdrawal in ways rarely seen except through the sentimentalizing lens of melodrama.

These films are compelling documents of the physiological processes of drug addiction. Contextualizing them requires understanding the composition

and educative goals of CDAN. Many committee members never saw an addict except when they toured the Lexington facility, whereas ARC researchers were in daily contact with addicted persons. The films provided the researchers with a vehicle to humanize their subjects and persuade clinicians that the natural course of alcoholism, addiction, tolerance, and withdrawal was a physiological process, not a psychological one or an indication of moral weakness. The films graphically narrated and illustrated this process, having effects on viewers similar to the effects of the monkey movies. The films sought to register the scientific status of addiction and underline the validity of studies on postaddicts. They captured and conveyed the essential humanity of the subjects, rather than avoiding, denying, or otherwise dehumanizing them. To my knowledge, the films are no longer shown to medical students, pharmaceutical representatives, or anyone else. They counter the pharmacological optimism expressed in the popular texts analyzed at the beginning of this chapter, and they attest to the limits of euphoria by staging addiction as its problematic outcome.

One study on the history of human experimentation claims, "Through medical experimentation, *useless* bodies were rendered *useful* by being made *usable* in the national project of regeneration, thus gaining a utility they were believed otherwise to lack" (Goodman, McElligott, and Marks 2003, 12). What precisely was the use value of addicted minds and bodies, of their experiences of euphoria or dysphoria? To which scientific communities was the contested term *euphoria* useful? Could valid conclusions be extrapolated from addicts to nonaddicts, from prisoners to nonprisoners, from drug-wise subjects to the drug-naïve? The Harvard research group assumed that conclusions generated by studies of former addicts would not be broadly useful; the Lexington group operated on the opposite assumption. Interactions between the two groups were charged but respectful—mediated by CDAN and directed toward the overarching goal of identifying less-dangerous drugs.

Patterns of interaction between committee members indicate that researchers at the ARC occupied the highest rung of the hierarchy of credibility. The Harvard researchers posed almost naïve questions about heroin, with which they had little experience. When Beecher and Lasagna asked about geographical variations in drug preferences, Isbell indicated that addicts from the Eastern Seaboard preferred heroin whereas Southerners preferred morphine or Dilaudid. Questioned as to why heroin was "more dangerous than morphine," Isbell answered: "It takes less [heroin]; euphoria appears more rapidly; therefore euphoria is more impressive to the individual. Morphine creeps up on you; the effect of heroin is sudden" (Committee on Drug Addiction and Nar-

cotics 1953, 383). Wikler answered that heroin's "physical-dependence-producing liability" was greater because of the "race to raise the dose fast enough and give the injections often enough so that abstinence signs do not develop between one dose and the next." He concluded, "If physical dependence is in any way related to addiction, I think this greater physical dependence liability makes heroin the more dangerous" (Committee on Drug Addiction and Narcotics 1953, 384).

Heroin was the drug of choice for prisoner patients at Lexington throughout its existence as a narcotics hospital. The ARC grappled with nonintegrated approaches to addiction and analgesia, which were artifacts of the opposition between nonmedical use of heroin and medical use of morphine. CDAN worked to cross this divide but could not overcome the cultural construction of heroin as a dangerous and unnecessary drug about which physicians knew little. Accounting for the enduring strength of the preference for heroin preoccupied researchers at the ARC, who believed that if they could figure out why heroin was so attractive, they would know something generalizable about addiction. They were prescient in this view—although opiate receptors had been hypothesized to exist, they were not visualized until the early 1970s. The preoccupation with heroin, which fully occupies the opiate receptors so that no other drug can compete, was shared by addicts, researchers, and policy makers. The ARC understood there was something special about heroin addicts, and the scientific pursuit of how exactly to discover what the difference was proved central to its work. Key questions remained to be resolved: What natural and social processes did heroin displace? Why did heroin addicts lose appetite and desire for other forms of gratification—namely, food and sex? If heroin was the key, what would studying it unlock?