IATROGENIC ADDICTION: THE PROBLEM, ITS DEFINITION AND HISTORY

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IT is a sad paradox that the healing arts can cause sickness and disease. From witch doctors and early Western medicine, down to the era of William Harvey or to Benjamin Rush, the posthumous "Father of American Psychiatry," we deal with a profession which for centuries routinely inflicted grievous bodily harm without qualm and, further, often at the behest of society. Physicians confidently treated battle wounds with boiling oil and infectious diseases with blistering, vomiting and purging.

Many of these treatments lasted into our century, among them calomel, or mercurous chloride, perennially popular with physicians and the public and still prescribed in the period between the two world wars. Phlebotomy or bleeding was considered legitimate almost as long. Even Sir William Osler, the most noted physician in the English-speaking world, recommended phlebotomy for selected cases of pneumonia as late as 1909.[1]

Nothing so far mentioned concerns addiction, iatrogrenic or autogenic, but I want to establish at the outset that the medical profession has a long record of treating patients with useless or harmful remedies often in clinical settings of complete mutual confidence. Iatrogenic diseases, complications and injury have been, in fact, common in the history of medicine. We may look upon addiction to certain dispensed drugs as one variation among the occasional effect of drug therapies.

During the 19th century, with the development of organic chemistry and the manufacturing pharmaceutical industry, the purity of natural substances available to physicians improved. As the composition of natural substances such as opium and coca leaves was separated into several active ingredients,

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the potency of drugs increased. Further, modes of application were improved so that these active ingredients, such as morphine, could be more effectively introduced into the body's physiology. Here the most dramatic step forward was the perfection of the hypodermic syringe.[2] By the second half of the 19th century several addicting forms of opium were available. Heroin, the last to be developed, appeared on the pharmaceutical market in 1898.[3] Cocaine's distribution in a pure form began in the 1880s.[4]

Before we had purified constituents of natural substances and methods of directly introducing them into the body's tissues, preparations of addicting medicines were widespread. Among the addicting preparations then was laudanum, an early version of a cocktail, composed of an alcoholic extract of crude opium along with flavoring. Also, there was syrup of opium, "black drop" or opium dissolved in acetic acid, and paregoric, as well as crude opium itself. Clearly, the concentration of morphine in these preparations was low. Still, addiction was possible. In the era before pharmaceutical regulations and narcotic laws, some addiction resulted from folk customs employing opium. An observer reported in 1782 that the Quaker women of Nantucket "have adopted the Asiatic custom of taking a dose of opium every morning; and so deeply rooted is it, that they would be at a loss how to live without this indulgence; they would rather be deprived of any necessity than forgo their favorite luxury."[5] Similarly, the English marsh, or fen, dwellers in East Anglia believed a daily dose of opium to be a protective against illness, particularly fevers.[6]

Addiction might also begin through a chance encounter with opium. The famous literary cases of the 19th century illustrate some of the types of involvement with the drug prior to any significant limitations on availability. The "prophet of opium," Thomas De Quincey, first took opium for pain when he was a student at Oxford. His poetic mind found revery through opium and eventually he used laudanum regularly. In 1822 his account, *The Confessions of an English Opium Eater,* captured in a popular form the excitement and esoterica of opium use with the result that he was often criticized for making the drug seem desirable to the uninitiated.[7] Samuel Taylor Coleridge similarly took opium for pain while a student at Cambridge, then later for relief from grief and even later for decaying teeth. One might speculate on the quantity of opiates consumed for dental complaints in the 19th century or for the commonplace results of poor sanitation, such as diarrhea, or for cough suppression in the century of tuberculosis. Like De Quincey, Coleridge eventually used laudanum regularly. To Coleridge it brought relief from swelling in his feet, knees and back. He started at 100

drops a day and a decade later was taking up to 20,000 drops a day. He was able to reduce his intake but never to eliminate his dependence on opium by the time of his death in 1834.[8] The experiences of both De Quincey and Coleridge are case histories of easy access to laudanum, its frequent use for everyday pains and the gradual fall into addiction which led to much misery. Often, withdrawal symptoms were seen as separate ailments for which laudanum was considered a remedy. In general, dependence to such a large degree was considered shameful and to be hidden from others, if possible.

If control of opium's public availability was weak, the role it had among a physician's multiple therapies was powerful. Consider the treatments already mentioned: blistering, purging, vomiting, bleeding, mercury compounds—not a happy prospect for a sick patient. But there was one sovereign remedy for pain, dysentery and almost whatever else ailed the patient: opium in one of its many forms.

In the *American Dispensatory,* first published in Philadelphia in 1806, near the time of De Quincey's and Coleridge's addiction, opiates were recognized as a hazard should they be used habitually. Such continued use would result in "tremors, paralysis, stupidity and general emaciation."[9] While now we would suspect such a syndrome to be more likely due to alcoholism than opiate use, nevertheless, this standard reference for American physicians noted the dangers of opium even at this early date. Balancing this warning, made incidentally within a detailed description of the drug, was a long list of uses: intermittent fevers, wounds, fractures, burns, active inflammations, dysentery, cholera, colic, tetanus, dyspepsia, hysteria, hypochondriasis, asthma, rabies, epilepsy and pain in general. One can understand the appeal that a mild and effective drug would have to physicians and patients.

Besides the enormous humanitarian value of reducing pain and fear, the drug also became a pawn in the vigorous competition for patients among health deliverers. There were more people offering health care—homeopaths, regular physicians, natural bone-setters, local wise ones and so on—than communities needed. Confusion over medical theories, the abundance of physicians and a growing objection by patients in the United States to the severe treatments meted out by regular physicians—they called it "heroic treatment"—made an opiate a very attractive remedy on all sides: it was painless, it worked, it relieved pain and worry and it made tolerable a host of ailments whose cause and proper treatment were completely unknown. Small wonder that the importation of opium into the United States started to rise early in the century and grew more rapidly than the population until the 1890s. In 1840, when importation statistics commenced, to the mid-1890s

when the per capita consumption began to level off, the amount of crude opium for each person in the United States rose from 12 grains to 52 grains.[10] One grain was a typical adult dose of crude opium.

The isolation of morphine during the first decade of the 19th century and its large scale production from crude opium thereafter certainly contributed to the increase in opium consumption. Then, in midcentury, the hypodermic syringe was developed and gradually spread into use. Curiously, although described before 1860, the hypodermic syringe did not seem to be used much in the early stages of the Civil War.[11] Therefore, 1865 can be taken as the approximate date by which Europe and America were quite familiar with the new device.

Hypodermic injectors discovered that they needed much less morphine to obtain the same analgesia by means of the oral route. This was interpreted to mean that the danger of addiction from use of hypodermic syringes was less, because less of the drug was employed. Clinical practice is a difficult arena in which to discover generalizations, and we too often see just what we expect. This must be the explanation why years of widespread hypodermic use passed before it was obvious that this route, usually subcutaneous, was, in fact, a shortcut to addiction. Warnings began to appear in English literature in 1870. But by that time hypodermic use was spreading faster than the warnings. The initiating physician commonly suggested that the patient obtain a hypodermic set and administer his own injections. To illustrate these observations, let us take a few cases from the mid-19th century. This first is from Norman Kerr. Writing of an event which took place in Britain about 1870, he states:

> A gentleman who was a martyr to unbearable attacks of sciatica of a purely neurotic origin, who had been thoughtfully treated and kept from his perilous practice by his medical attendant, went off to consult one of the greatest surgeons of that day. The patient in a day or two thereafter returned to the family physician, exhibiting the hypodermic syringe which he had been ordered by the consultant, and demonstrating the dexterity with which he could perform the operation. The unfortunate sufferer had not the slightest idea that this self-medication involved any danger.[12]

A second example, one from the United States, is provided by Dr. Alonzo Calkins in a monograph published in Philadelphia in 1871. He begins by referring to the relatively new hypodermic method.

> In this way one-third the quantity that would ordinarily be taken by the mouth suffices, i.e., the same amount exerts a triple force. This practice, as favoring the habit, appears to be less hazardous in instances, but not certainly. Eulenberg in a case of disease made 1200 injections in all, and without manifest injury appertaining. Any reliance placed on this form of use, however, for its supposed comparative security, is

> likely to prove delusive.... Dr. Sewall of New York has just reported two cases. In the first, the practice, after two months' continuance, was arrested, but not without much embarrassment; the second patient still continues on.... This gentleman, now of middle life, having suffered much from a diseased ankle, was advised (professionally) to use morphine hypodermically. The immediate effect being found most soothing and satisfactory, an indefinite continuance was suggested; and now, after a habituation for two years, the invalid is now hopelessly delivered over, an abject slave to the habit... The thigh of the affected limb is literally studded with punctures, to be counted by the score.[13]

In Germany about this time Dr. Eduard Levinstein of Berlin was performing experiments to understand better the morbid craving for morphine, *Die Morphiumsucht,* which he described in several papers. His chief study was published in 1877 and translated into English the next year. Dr. Levinstein described withdrawal symptoms in great detail. His method of treatment was abrupt withdrawal in a hospital setting, with physiological support and careful nursing care. Here is one case from 1876.

> Mrs. B.D., a physician's wife, 32 years of age, was when 24 years old and previous to her marriage, treated with injections of morphia on account of oppressiveness and mental anxiety.
>
> At the time of her first pregnancy, 8 years ago, on account of sickness and faceache, injections of morphia were again resorted to; she miscarried in the sixth month of her pregnancy. Since that time she has suffered from craving for morphia, using on the average 8 grains of morphia per day...
>
> During the past summer the patient suffered from [an intermittent fever]. For one and a half years the menstrual discharge has stopped. The symptoms brought on by the use of the drug were as follows: loss of appetite, patient at last living only on milk and raw eggs. Constipation, sleeplessness during the night, drowsiness during the day. Profuse perspiration.[14]

Like his other patients, she was treated through abrupt withdrawal. After six weeks her health returned to normal and she was discharged.

Self-addiction among physicians was, as one might expect, not uncommon. Dr. T.D. Crothers, a recognized American authority, estimated that late in the last century 8% to 10% of physicians were openly or secretly drug, chiefly morphine, habitues. In 1899 he warned, after a nine-year study involving 3,244 physicians, that at least 6% used morphine or opium regularly.[15]

The 19th century closed, then, with per capita consumption of opiates at an all-time high in the United States, many physicians self-addicted, widespread use of hypodermics by patients and no national laws controlling the availability, dispensing, prescribing or even labelling of narcotics.

If one were to look at one powerful statement of the popular attitude toward iatrogenic addiction at the end of the century, one might well exam-

ine the most important play of America's greatest playwright: Eugene O'Neill's *Long Day's Journey Into Night.* It is a drama of iatrogenic addiction. After the birth of Eugene, his mother became addicted to morphine due, the family believed, to the incompetence of the physician. I cannot help but be impressed that the core of the plot is precisely the problem we are discussing there today.

In the play Edmund—the Eugene O'Neill figure in this autobiographical drama—berates his father about the mother's addiction:

> It should never have gotten hold of her! I know damn well she's not to blame! And I know who is! You are! Your damned stinginess! If you'd spent money for a decent doctor when she was so sick after I was born, she'd never have known morphine existed! Instead you put her in the hand of a hotel quack who wouldn't admit his ignorance and took the easiest way out, not giving a damn what happened to her afterwards! All because his fee was cheap! Another one of your bargains!

And the father remonstrates: "You must try to see my side of it too, lad. How was I to know he was that kind of doctor? He had a good reputation. . . ."[16]

The bitterness, shame and anger over iatrogenic addiction portrayed in *Long Day's Journey Into Night* illustrates the popular force behind the early national narcotic law, the Harrison Act of 1914 and the powerful reaction to drug use in the United States after a century of unrestrained consumption. It also helps us to understand the reality and fear of iatrogenic addiction. The dope doctor, the "hotel quack" or even those with "a good reputation" were all a potential danger to the helpless patient.

It was a common belief that most physicians were casual in the administration of addicting drugs, and covered their administrations with a cloud of obscure terms opaque to the layman. Also, the public knew that hundreds of physicians were themselves addicted to opiates. The number of addicts in the United States became a national issue, and experts commonly asserted that a full one half of these addicts had been made so by physicians.[17] The quality of medical education had been low except in a few great medical schools. The Flexner Report on medical education which led to the closing of dozens of inadequate—even laughable—medical schools was published in 1910. During the next 20 years the number of medical schools in the United States fell from 148 to 66. But the significance for our topic is that the many poor schools had already allowed into the medical profession incompetents who did do damage to their patients. The medical profession had a bad image at the turn of the century, and it was an earned reputation in many instances. Iatrogenic addiction was an all too frequent expression of incompetence within the profession.

Physicians used various theories of addiction as a basis for their treatment of patients. Without entering into the details, I would divide them into two general categories: those theories which argued anyone could become addicted if given opiates long enough and those which maintained that only individuals with psychological or biochemical peculiarities could become addicted. The cures were divided into abrupt cessation of the drug, with or without some allaying substance such as atropine, and those cures which gradually reduced the dose. Addiction was considered either a habit which could be broken by will-power or a biochemical alteration of the body which required special treatment or even indefinite maintenance. Perhaps I should add here that addicts also were broadly divided into the pitiable and the vicious; generally, the iatrogenically addicted were pitiable; those who came into the habit by the route of pleasure or in a search for excitement were vicious.

Given this history, how can we analyze the various kinds of iatrogenic addiction? I would suggest three categories: The first is inadvertent addiction. In this class would come the use of addicting substances whose properties were not yet suspected by the medical profession. I suppose one might consider the use of the hypodermic syringe or the use of cocaine in the 1880s to be causes of inadvertent addiction. Even the early use of heroin led to unintentional addiction. But once an addicting substance has been identified, addiction would be, in most instances, negligent. Here we would include prescribing to meet the desires of the patient for a psychotropic substance when this was not in any way a necessity, prescribing to keep a patient or to gain a patient in a competitive health delivery system or prescribing with no thought whatsoever of the consequences. Witness the "script doctor" of yesterday and, unfortunately, today also. The final category I would suggest is intentional iatrogenic addiction. This would include addiction of terminally-ill patients, methadone maintenance and addictions created in the past for the treatment of alcoholism or in the effort to cure another addiction, as may have occurred when the excessive cocaine user, Dr. William Stewart Halsted, became morphine dependent.

To these three varieties of addiction—inadvertent, negligent and intentional—one could add the physician's self-addiction. The addicted physician always seemed more casual or at times even enthusiastic about providing drugs without restraint to patients. Health workers traditionally have had a high level of addiction or drug abuse, and addiction to opiates has been popularly considered the typical addiction. Regrettably, this has been a reality. In a way this is a kind of "iatrogenic addiction," but I prefer to con-

sider it in the context of our topic a factor which complicates the other forms of iatrogenic addiction.

The reality of iatrogenic addiction has led to legal reforms and changes in medical practice. The Harrison Narcotic Act was one. Later Supreme Court rulings continued this reaction against apparently careless or mercenary physicians and pharmacists through restraints on prescribing and dispensing. These limitations are familiar to all of us. For example, the regulations regarding methadone are in that tradition of fearing the minority of physicians who undermine responsible prescribing. But there has also been a response within the medical profession. I suspect it stems initially from a strong sense of guilt at the number of addicts created by careless provsion of drugs and anger at those relatively few physicians who violate norms of practice. The result here can be an excessive self restraint which results in inadequate pain control for patients. The fear on the part of a physician that he might be the cause of a patient's addiction even in instances of the terminally ill is not an unknown phenomenon. To understand the power of this restraint in the medical profession we must go back to the era of O'Neill's play and the horror of iatrogenic addiction which frightened both patients and physicians alike. The tradition of watchful distrust has not ended.

Presently, iatrogenic addiction has expanded from the opiates to include sedatives and anxiety-reducing medications such as benzodiazepines. These addictions are often much more life-threatening than addiction to opiates. We have moved from inadvertent to negligent stages of iatrogenic addiction with one after another new tranquilizer. The future, however, appears to offer increased risk of physician-induced drug dependence. I offer this observation on several grounds. The production of drugs attacking anxiety in the latter half of the 20th century continues unabated. For our century, the problem of anxiety holds a place similar to that held by pain in the 19th century. Better and better chemical methods are developed to deal with a symptom whose root causes are difficult to locate and modify. Great temptations are held out to physicians who are able to relieve symptoms in spite of the dangers inherent in the drugs' multiple and often addictive effects.

When I speak of "temptations" faced by physicians in practice, I do not want to imply that the decision to provide drugs with potentially addictive consequences is typically calculating, mercenary or careless. The patient who wants surcease to anxiety or pain presents the most reasonable and appealing request to a physician. The desire to provide relief and to respond to a patient's anticipation of effective care is natural. Often the road to an addictive state starts with a gradual slope. One coercive pressure on the phy-

sician is the spoken or unspoken but understood knowledge that the patient can obtain the desired relief from another physician who may profit from an easier prescribing policy. In this way, the few physicians with no hesitation to prescribe whatever is requested may have a broad effect on other physicians in a community. All these factors which lead to unfortunate prescribing are soft persuasions, but they have a cumulative effect. As improved psychotropic drugs are marketed, the demand from patients will increase and the immediate benefit which a physician can bestow on a grateful patient will also grow.

Anticipating more and better anodynes which nevertheless may not address underlying causes of mental distress, we are also entering a period of abundance of physicians which can be compared to the supply of 1900. This increased production of physicians is not the result of many poor schools as it was a century ago. It is a planned increase with the hope of improving the national distribution of physicians and reducing the costs of medical care. There seems to be some question whether the increased number of physicians is leading to lowered costs, but I do not doubt that the rapid increase in the number of physicians will increase competition for patients. In 1900 there were 173 physicians for every 100,000 persons in the United States. This fell after the Flexner report to 125 in 1930, but has been rising since then and passed the 1900 ratio in the mid-1970s. By 1981 the figure had reached 200/100,000 and is still rising rapidly. It is estimated the ratio will reach 247 by 2000.[18] These considerations lead me to wonder whether we may not be facing a second era of increased iatrogenic addiction and a subsequent round of fear and restrictive reaction to the health professions. How this might be averted is a goal of our symposium.

Addictive effects of drugs and physicians' prescribing practices encompass fields as diverse as pharmacology, economics and morality. They must all be addressed in the campaign to reduce needless addiction. If the health professions cannot respond adequately to this challenge, the public justifiably will mandate external controls.

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Questions and Answers

QUESTION: You commented on the medical profession and economics. What about morality?

DR. MUSTO: Morality enters the decision process at several points. There is the eternal question of the morality of addiction itself. The doctor's fear of causing addiction is one reason patients in pain at times receive less than optimum pain relief from physicians. The issue of morality also enters into the question of treatment for addiction, dividing the methadone programs from the drug-free programs. Physicians', therapists' and patients' views on the morality of addiction affect important decisions and must be taken into account.

QUESTION: Along the same lines, it is easy on the one hand to give a narcotic analgesic to a terminally ill cancer patient to maintain him. But another patient with a similar pain problem that will not lead to his demise makes us aware that giving those drugs will lead to other harmful disorders. It becomes a moral decision because one realizes that this patient is going to live another 20 years or so. Although there are medical aspects to that decision, those aspects are minimal when compared to other therapies these patients receive.

DR. MUSTO: I agree that this kind of decision is a heavy burden for a physician. Shortcuts to the decision have been employed. At times, especially in the 1920s and 1930s, physicians believed that a "normal" person could not become addicted, that a patient had to be "psychopathic" in some way to get pleasure in addition to simple pain relief from an opiate. The attending physician could then estimate the patient's personality as an aid to deciding whether to use much morphine. The larger question concerns a total view of the patient's pain problems rather than just which opiate to use. This point is stressed by many experts on pain relief, for example, Dr. Robert Twycross of Oxford and St. Christopher's Hospice. Still, the physician is often left with a lonely and difficult decision regarding pain relief by medication, and too often the patient receives less relief than reasonably possible.

QUESTION: At this time, do we know the percentage of physicians addicted to opiates?

DR. MUSTO: In a recent report of 4,000 physicians studied, 1½% were known drug addicts. The health professions are quite vulnerable to drug abuse.

QUESTION: One fear today is that an addicted patient will become a street addict, with crime and loss of function and family life. Years ago, when addiction was being criticized so vociferously in the lay press and in the medical profession, opium was widely available. There weren't the laws that forced people to go underground to get narcotics. The question is, was there a drug problem and what was it about the addicted patient that generated so much negative press within the medical profession and the public?

DR. MUSTO: Prior to the federal laws against easy access to opiates and cocaine, especially the Harrison Act of 1914, the public was very concerned about the personality effects of addiction and also the impact on crime. I have quoted Eugene O'Neill on the image of addicted individuals, but it is also interesting to note that the crime rate was said to have been raised, although the drugs were much cheaper and more easily available than later. The reasoning was that certain drugs, especially cocaine and heroin, impelled the user to commit crimes. Another assumed connection was that criminals took a drug to get up their courage before committing a crime. The relation between laws against drugs and the crimes committed to obtain the drugs is another question, one which has been difficult to settle.

QUESTION: Were there any studies or series of iatrogenically addicted patients that documented whether they either lost function or disrupted family life or sunk to the level of the opium den?

DR. MUSTO: I have studied the records of the patients at the New Haven

morphine maintenance clinic which operated from 1918–1920* as well as the history of individuals reported singly. There is no question that many people were able to handle their lives while on a maintenance dose of opiates, just as individuals on methadone maintenance today often lead stable, productive lives.

QUESTION: I think that as long as we continue to use the term addiction to encompass all the different states that people have been talking about—including misuse, abuse, dependency on medication—it will be impossible to resolve the moral, physiological and medical aspects of that definition. I think it behooves this group to try to differentiate these states according to a terminology that fits the different subgroups.

DR. MUSTO: Users of drugs have traditionally been divided into two categories: average, normal, good people and evil, perverted, abnormal people. The iatrogenic addict has usually fallen into the more desirable category. It is important to make distinctions among the various populations, but difficult to convey these distinctions to the public.

QUESTION: In the legal system, what is the difference between medical addiction and iatrogenic addiction? Was it a Supreme Court decision that allowed the medical addict to receive drugs?

DR. MUSTO: In 1919 the Supreme Court decided that provision of narcotics to anyone *not* medically addicted, that is, addicted due to pain or because of some specific illness, was illegal. A prescription for drugs to maintain a patient who was merely addicted was not, in the Court's opinion, a true prescription. Exceptions and permissions to maintain were worked out with local narcotic agents. As a result, a respectable person stood a better chance of legal maintenance than someone who fell into the undesirable category I mentioned earlier.

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