PART I

Overview

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Introduction

> Good afternoon ladies and gentlemen. This is your pilot speaking. We are flying at an altitude of 35,000 feet and a speed of 700 miles an hour. I have two pieces of news to report, one good and one bad. The bad news is that we are lost. The good news is that we are making excellent time. – Anon.

Not so long ago, it would have seemed obvious where medical science was headed. Medicine's historic contributions to human health are legendary – vaccines, insulin, anesthesia, electronic heart pacemakers, the heart–lung machine, and many others. Entire diseases, such as smallpox and polio, have been eradicated, or nearly so. Such impressive achievements gave no reason to question clinical progress; indeed, they fueled expectations for still greater accomplishments in the future.

In many ways, medicine has met those expectations, even surpassed them. Modern medicine's technical capabilities are truly extraordinary. Many major organs can now be transplanted. Mechanical devices can partially or substantially replace a person's failing joints, heart, lungs, and kidneys, and there are synthetic substitutes for blood, veins, and skin. Machinery can sustain bodily functions after vital signs have ceased. Researchers are working on developing fully implantable artificial hearts, lungs, eyes, and bladders, and are experimenting with human brain transplants. Through gene splicing, scientists can modify the genetic makeup of living organisms, literally creating new forms of life with desired traits in the laboratory. We are poised on the threshold of applying these techniques to humans – human genetic engineering.

But amid these spectacular accomplishments are new worries and concerns, troubling signs that all is not well in the house of medicine. One of the most visible is the issue of costs. The United States now spends over $1 billion per day on medical care. Total medical expenditures constitute nearly 11 percent of the nation's gross national product, double the fraction spent on health in 1960.

Despite sustained governmental and private efforts to control costs, the price of medical care in 1986 rose at *seven* times the rate of inflation.[1] This relentless cost escalation has led some observers to look more critically at the resources being devoted to biomedical research and development, which supply the future armamentarium of medical practice. There is growing agreement that we simply cannot afford an endless parade of fabulously expensive new lifesaving or lifemaking technologies. Somewhere we have to draw the line.

Soaring medical costs have also prompted new scrutiny of what we are getting for our health dollars. The answers are disturbing. Too often, enthusiasm for the latest scientific breakthroughs has led to exaggerated expectations and uncritical acceptance. Medical history is full of examples of promising new techniques that later proved disappointing, if not dangerous.[2] With improved methods of statistical assessment, it has been possible to evaluate medical innovation more rigorously, and many have been found wanting. According to a federally commissioned study, less than half of the drugs sold between 1938 and 1962 were effective for their claimed therapeutic purposes.[3] Similarly, careful evaluation of a broad range of modern medical and surgical innovations has shown that only half offered improvements over standard practice, even without considering costs.[4] Ineffective drugs and therapies still find their way into general use because adequate assessment is lacking.

Problems have arisen from seemingly safe, even conventional medical practices. Many "miracle drugs," potent weapons in the war against disease, have proven to be double-edged. Indiscriminate use of antibiotics, for example, has led to the development of new strains of antibiotic-resistant bacteria, which are more difficult and costly to control. The tragic consequences of diethylstilbestrol (DES) and thalidomide, drugs given to pregnant mothers that led to death or disfigurement of their children, serve as a poignant reminder that no proof of risk is not the same as proof of *no* risk – an elementary principle of statistics too often ignored amid the hopes and hoopla accompanying the latest therapeutic advance.

Furthermore, we now know that medicine's contribution to the health of the population as a whole is really rather small in comparison to the role of social and environmental conditions. Analyzing trends in morbidity and mortality over the past three centuries, Thomas McKeown has shown that for most diseases, the introduction of effective medical procedures had little if any

detectable effect on death rates, whose downward course seemed to be governed primarily by improvements in nutrition, living standards, and personal behaviors such as reproduction.[5] McKeown contends, therefore, that Western medicine's preoccupation with technological and therapeutic intervention is misguided, and that more attention should be given to the effects of social and economic circumstances, which he predicts will be the dominant determinants of health in the future as well. Marc Lalonde, the Canadian Minister of National Health and Welfare, offered a similar recommendation in a widely circulated book proposing a redirection of Canadian health resources based on current patterns of mortality and morbidity. "There is little doubt," Lalonde concluded, "that future improvements in the level of health of Canadians lie mainly in improving the environment, moderating self-imposed risks and adding to our knowledge of human biology."[6]

Although modern medicine no longer seems the panacea it once did, there is little agreement about what to do about it. Some would redouble our commitment to basic research, arguing that important breakthroughs are just around the corner. Others call for a more comprehensive and rigorous system of evaluation for new medical technologies to prevent dissemination of those that are ineffective or harmful. The present federal administration has instituted sweeping changes in health care financing to try to curb medical inflation. None of these strategies, whatever their merits as partial solutions, gets to the heart of what is ailing medical science. New issues continue to emerge, while old problems remain unsolved. Meanwhile, public confidence in medicine, once the object of almost boundless hopes, has plummeted.

What do we want for our medical future? The question is rarely asked. Yet decisions about medical innovation and care involve not only scientific and economic considerations, but also social and moral choices: They influence who will live, and who will die. They are, ultimately, society's alone to make. A forest products company advertises that gene splicing could produce "miracles" in the future, including "the flowering of a 'better' human being." "But who," asks the advertisement, "is going to decide what makes a 'better' human being?"[7]

Of all the dilemmas facing modern medicine, this is the greatest: finding suitable ways to ensure that medical innovation responds to and reflects the interests of all sectors of society. When a reporter asked Dr. Robert Jarvik, one of the leading developers of the artificial heart, whether the news media had overlooked any issues

in the publicity surrounding the program, he thought for a moment and then replied that there was one: "What does the public really want? The assumption is that the lab is working in the public interest . . . It's always *assumed* that [the artificial heart] is needed and wanted . . . but no one has really asked."[8]

Many of the questions raised by modern medical technology are new, and require new answers. We can no longer rely on old assumptions and approaches to solve the current problems; indeed, many of these problems flow directly from the failures of past policies. This book attempts to draw lessons from four innovations that illustrate these new problems and uncertainties. We have chosen examples from very different areas: a drug – DES; a medical device – the artificial heart; public health – the 1976 swine flu immunization program; and basic science – genetic engineering. These innovations have all been, to varying degrees and at varying times, controversial. DES and genetic engineering have evoked concerns about actual or potential physical harms, while swine flu and the artificial heart raise questions of cost, equity, need, and effectiveness. These controversies – their origin, trajectory, and ultimate impact on policy – illuminate the nature of public concerns about medical innovation and the most effective forms of public influence and action. We focus especially on the implications of the attempted interventions for medicine's present dilemmas and potentially fruitful new directions.

The cases

DES is a synthetic estrogen that was prescribed to millions of pregnant women in the 1940s through early 1970s in the belief that it helped prevent miscarriages. Although studies published in the early 1950s indicated that DES did nothing of the kind (it may even have increased the likelihood of complications), its use declined only slowly. In 1971, physicians discovered a previously rare form of cancer – clear-cell vaginal adenocarcinoma – in daughters of women who had taken DES during pregnancy. Other reproductive disorders were subsequently discovered in both DES sons and daughters, as well as higher rates of breast cancer and precancerous changes in the women themselves. Despite the discovery in 1971 of the association with clear-cell cancer, two other uses of DES continued throughout the 1970s: It was prescribed as a "morning-after pill" contraceptive in many hospital and college clinics, and was

also widely used by livestock producers as an animal growth stimulant. Spanning the entire post–World War II era, the DES story illustrates how differing social climates, government policies, and attitudes about professional behavior can shape drug development and regulation. It raises important questions about the role of the pharmaceutical industry in federal decisionmaking, the ethics of human experimentation, and compensation for victims injured in the course of medical and scientific innovation.

The second case study describes the quest to develop an artificial heart – a totally implantable mechanical device capable of replacing a failing human heart. Government-funded research began in the mid-1960s amid high expectations. Initial plans called for mass production of mechanical hearts by 1970, at a total development cost of $40 million. More than twenty years and $200 million later, the program had not yet produced a satisfactory totally implantable device, and the implants that were performed were marred by persisting technical problems and the occurrence of multiple, crippling strokes among most of the recipients. With its history of exaggerated promises and unforeseen scientific difficulties, the story of the artificial heart offers useful insights into the process of technology development and the ethical questions posed by clinical experimentation on desperately ill patients. It highlights the societal dilemma of allocating resources to high-cost new devices of unproven benefit in an era of cost-control efforts and cutbacks in both public and private medical care.

Third is the tale of a public health effort of unprecedented scope, the 1976 swine flu immunization program. Fearing a "killer" pandemic of swine influenza, the government launched a massive campaign to produce and distribute enough vaccine to inoculate the entire U.S. population, all within a matter of months. From the beginning, the campaign floundered on technical and policy problems; yet, despite growing doubts among experts and increasing public criticism, the mass immunization campaign went ahead. The swine flu epidemic never occurred. However, the vaccine itself proved to have serious side effects, including the paralyzing Guillain–Barré syndrome and some fatalities. All in all, the swine flu program was a fiasco. The case study explores how and why things went wrong, examining the interaction between politics and policy, the snowballing of perceived public health risks, and the dogged determination of program officials, once committed, to carry on in the face of mounting evidence that victory would spell defeat.

The final case study is of genetic engineering – a pathbreaking scientific technique developed in the early 1970s that allows scientists to modify the genes of living organisms. This technique and related methods are providing exciting new understanding of basic genetic function, and at the same time are transforming production processes in such diverse industries as energy, agriculture, and pharmaceuticals. From the outset, however, genetic engineering has been embroiled in controversy over the enormous new powers it conveys and their unknown implications. Scientists sounded the first alarm about possible dangers shortly after the technique's discovery. The debate soon escalated as local communities, and the federal government, sought a voice in determining proper safeguards. Although many of these early fears later proved groundless, uncertainties remain, and controversy has flared periodically throughout the technology's rapid development. In the early 1980s, the mushrooming of commercial biotechnology led a number of communities to pass legislation requiring private companies to follow federal guidelines. More recently, field tests involving the deliberate release of genetically engineered organisms into the environment have touched off a new round of public protest and local opposition. This case study illustrates the changing forces affecting expert and lay perceptions of risk and benefit, and conflicting notions of the accountability of science to society.

A one-time wonder drug that caused unforeseen harms, a sophisticated new medical technology whose financial and ethical costs could outweigh its medical benefits, a nationwide public health effort against a phantom epidemic, and a revolutionary laboratory technique that alters life itself – the four case studies paint a troubling picture of brilliant medical and scientific accomplishments intermingled with unexpected problems, unrealistic expectations, and deepening moral and social dilemmas. Viewed separately, each case provides intriguing clues about what inspires and directs the search for medical and scientific knowledge, and about how and why that search can go astray. Taken together, the cases have much to say about the dilemmas of modern medicine.

Although the cases involve innovations in diverse areas, they share many common patterns of decisionmaking that characterize contemporary biomedical science in the United States and elsewhere. A particularly striking feature is the dominant role of tech-

nical and scientific experts in decisionmaking, even on issues with important social or ethical components. The case studies reveal some of the weaknesses of that approach. Also apparent in the cases is the increasingly blurred distinction between "science" and "technology"; for genetic engineering and some aspects of the artificial heart, they are often one and the same. In all four cases, there were aspects of scientific activity, and of uncertainty, that were critical to the technology being developed or applied.

All of the innovations ran into difficulties or setbacks of one sort or another, ranging from the health problems associated with DES and swine flu vaccine, to the technical miscalculations and delays of the artificial heart program, to the public opposition and controversy provoked by genetic engineering. Obviously, these problems vary greatly in magnitude. Despite its occasionally stormy history, for example, genetic engineering is widely viewed as a major scientific advance with far-reaching implications. Rarely is the path of any medical innovation entirely smooth or trouble-free.

Careful scrutiny of the problems encountered in the cases can shed new light on how and why the policy process works by clarifying how and where it breaks down. The study of dysfunction is a time-honored tradition in many fields, including biomedical science itself. As a noted biologist put it in 1912, many important discoveries have emerged from "probing the actual causes of bodily disturbances and the actual removal of such causes."[9] In psychological research, the study of visual illusions and judgment biases has improved understanding of the process of perception, and studies of forgetting have helped explain the way that memory operates. So, too, at the level of organizations and societies, a better understanding of failures in the biomedical policy process can reveal important dynamics in the structure and process of decisionmaking and can suggest possible remedies.

Our investigation of the four cases focuses on the chain of events, including both decisions and "nondecisions," that led ultimately to difficulties or disappointments. When there was uncertainty, did it result in skepticism and caution or in optimism and risk-taking? What were the consequences? Most important, were the problems encountered inevitable, given the evidence and understanding of the time, or could they have been avoided?

Knowledge of many of the outcomes of key policy decisions suggests where to look for errors in decisionmaking, but not, of course, whether they will be found or what they will be. Such

"errors" must be judged in light of the information and options available at the time, not by today's standards or with the clarity of hindsight. The task of historical analysis, according to one respected historian of science, is "to see the past in the same terms as those who lived in it, yet at the same time stand apart from those perceptions and evaluate their implications for the functioning of a social system or the initiation of change in that system."[10] Merely because certain adverse outcomes occurred does not mean, a priori, that they were inevitable. Indeed, one of the dangers of hindsight is, in the words of historian R. H. Tawney, that it "give[s] an appearance of inevitability to an existing order by dragging into prominence the forces which have triumphed and thrusting into the background those which they have swallowed up."[11] Each of the case studies therefore gives special attention to attempts to oppose the prevailing course of decisions, including those that were sooner or later "swallowed up" by more powerful forces. Subsequent events reveal the merits of some of these attempted interventions.

In drawing lessons from these cases for the future, it is useful to distinguish between errors in the *way decisions were made* and those caused by the *state of available information*. Did problems occur, in other words, because certain facts were simply beyond the reach of existing knowledge or, rather, because known information was disregarded or knowable information not obtained? The circumstances that prevented effective use of available information are crucial to understand if future policymaking is to be improved.

The case studies examine both formal policy processes and also the more informal side of policymaking – the lobbying and liaisons that took place behind the scenes. In general, we emphasize bureaucratic and political roles rather than personalities or other idiosyncratic factors. This "structural" interpretation of events is usually more easily reconstructed from historical documents and other sources, and is likely to be more helpful in defining remedial organizational and procedural policies.

On the other hand, there are certain individuals in the cases whose own personal stamp on history must be recognized. For example, the efforts of a single DES mother, Pat Cody, launched a nationwide network of "DES Action" groups which have provided critical services and assistance to DES victims. The courageous decision of a few scientists to alert the general public to the possible risks of genetic engineering opened an unprecedented

chapter in American science policy. These examples remind us that individual people *altered* the course of past events in these cases, and that such individual influence is possible in the future as well. Structural and political constraints are essential in understanding the forces that shape behavior, but some individuals will always stand out and apart.

It is worth emphasizing that this investigation does not, and cannot, try to assess how common the problems and uncertainties in the four cases are, or will be, in other areas of medical innovation. Unfortunately, few studies exist that trace in detail the evolution of biomedical decisionmaking, including options not pursued, and the responses of different groups as problems emerged.[12] It seems safe to say that general questions concerning costs, risks, efficacy, and equity have wide application, whereas some of the issues raised by the creation of new life forms, the appearance of second-generation harms from DES, and the development of a mechanical heart pose questions that are new in degree if not in kind. By examining how both familiar and novel questions have been handled in four different cases, this book seeks to clarify the range of dilemmas we face as a society and the choices we cannot avoid.

Organization of the book

To set the stage for the case studies, the book begins, after this introduction, by describing the enormous changes that have taken place in both medicine and the larger society over the past few decades and the policy dilemmas they present. This discussion serves as a brief synopsis of the issues raised by the cases and an overview of the main lines of argument running through the book. The following four chapters trace the histories of the four innovations, from their inception up through roughly the mid-1980s. These four case studies present the "facts" of each case as accurately as possible, describing the events and decisions relevant to what we consider the critical policy questions.

The remaining chapters then look in greater detail at some of these policy questions. Chapter 7 discusses the way risks are – and are not – identified, communicated, and controlled in individual medical encounters and for society as a whole. It shows how the concerns of patients and citizens are systematically undervalued relative to the interests of professionals and private industry, and