The Technological Imperative in Medical Practice:
An Anthropological Study of Therapeutic Plasma Exchange
by

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THE TECHNOLOGICAL IMPERATIVE IN MEDICAL PRACTICE: AN ANTHROPOLOGICAL STUDY OF THERAPEUTIC PLASMA EXCHANGE

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ABSTRACT

Therapeutic Plasma Exchange (TPE) is a costly, dramatic, machine-based treatment for a number of serious autoimmune diseases such as myasthenia gravis. A patient's old plasma is replaced with new. Using the development of TPE as a case study, I explain how the technological imperative -- the rapid development and quick, often uncritical adoption of new equipment in western medical practice -- is generated and maintained by social forces.

I begin with the assumption that western medical knowledge and practice is as open to social and cultural interpretation as any other medical system. A combination of research strategies, including ethnographic techniques of in-depth interviewing and participant observation, were employed. Twelve TPE treatment units in two countries (U.S. and U.K.) were studied. Informants included patients, innovating physicians and nurses, representatives of equipment manufacturers, and government officials. Archival sources, including the medical literature and the lay media, were utilized.

I review the history of TPE, documenting its exponential rate of growth in the late 1970s and demonstrating the many forces which helped generate enthusiasm for a new therapeutic approach. I next discuss the stimulus provided by the for-profit medical equipment industry, describing its role in providing technical support and speeding the communication of information about TPE in its earliest stage. The many pressures experienced by seriously ill patients furthered the rapid expansion of TPE. Physicians, honoring the primacy of research interests as well as responding to their desperately ill patients, gave the new technique increased momentum.

An examination of the social differences between "experimental" and "routine" treatment settings reveals how the meaning of a new technology as the standard of care evolves as the treatment process is routinized. Through a description of actual ward rituals I describe the process of routinization, demonstrating how the meaning of a new technology derives from the social setting itself.

A moral imperative to provide treatment is experienced by physicians when they are faced with a decision about whether to prescribe a therapy which feels routine. The social inevitability of therapy takes on a moral tone; the experience of a technological imperative becomes a moral imperative for action. Once the use of the procedure is perceived as a standard of care, its use becomes a moral as well as a technical obligation.

Approved 25 July 88. M. Margaret Clark

Preface

HOW I CAME TO STUDY THERAPEUTIC PLASMA EXCHANGE

The choice of a doctoral dissertation topic is not always a completely rational and scientific process. My decision to study a new medical technology, therapeutic plasma exchange, was influenced by a wide range of factors, including emotional issues, intellectual curiosity, and pure serendipity.

My interest in the use of "machines" in medicine dates from my experiences as a pediatric nurse. While caring for patients, from premature infants to adolescents undergoing open heart surgery, I found myself nursing the machines as often and with as much intensity as I was nursing the children. Long before becoming a trained social scientist I discovered in an informal, impressionistic manner what Anselm Strauss and others have been researching carefully: that the use of sophisticated equipment in hospitals has transformed the nature of caring for patients. As a participant I discovered that the organization of both medical and nursing work was in a state of profound change

because of advances in the diagnostic and therapeutic armamentarium of medicine.

When I worked as an intensive care nurse I was exposed to a wide array of medical equipment. After becoming proficient with the more mundane advances, such as cardiac monitors and ventilators, I began to feel that I could handle anything. Nurses learn to be engineers as well as experts in direct patient care. I could troubleshoot a malfunctioning EKG machine, an infusion pump, or a suction machine all in a morning's work. And some of the machines even ran smoothly, at least part of the time.

However, there was almost always a new piece of equipment on the wards guaranteed to cause trouble. I recall spending an entire night (11 P.M. to 7 A.M.) arranging to have the missing supplies for a new extracorporeal membrane oxygenator machine sent to the Minneapolis airport by air freight and then sent to the hospital in a taxi.[1] The scene in the neonatal intensive care unit was dramatic, with everyone awaiting the arrival of the missing part. After it arrived, a total of six nurses per day were required to care for the patient and the machine. In spite of the difficulties we were all excited to be part of the "cutting edge" of medical care. The child's death seemed almost irrelevant to our effort to intervene.

My reactions to the use of high technology medicine were shaped further by the experience of working with a new peritoneal dialysis machine.[2] While working in a pediatric intensive care unit I was informed that we would soon be receiving this new piece of equipment. The introduction of the machine required a great deal of organizational effort since all staff members had to be trained to use the machine by a technician from another city. Learning to operate the machine was difficult and took a significant amount of time.

From the beginning I was perplexed by the goals of the pediatric nephrologists who sponsored the new machine. Peritoneal dialysis is an old technique in medicine which can be performed quite easily manually. Although time consuming, the manual procedure is simple and relatively safe.

The new machine purified city water directly from the tap by a process of reverse osmosis. It was complex and cumbersome. Was my resistance to the machine based on good sense, or was it a conservative reaction against any form of change? Of course the resistance from the nursing staff had little or no impact and we all proceeded with our training, eventually proceeding to treat real patients.

My personal view of the impact of the new peritoneal dialysis machine is influenced by the memories of one particular night at work. A three year old child came close to death because of malfunctions in the machine. I worked for eight hours with a pediatrician trying to correct what

seemed to me obvious problems in the application of the technology to a very small child. Designed for adults, it simply was not suited for use in pediatric patients where measurement of fluid status must be very precise. In our zealousness to use the machine, rather than dialyze the patient manually, we were causing the child to drown in his own body fluids.

Mishap followed upon mishap every time we used this particular machine. I recall standing in the middle of the intensive care unit with a frightened child in the bed next to me, both of us soaking wet after the machine had concluded one of its numerous "explosions," spewing water over a ten square foot area. Luckily the child's parents were not present to share the scene and wonder exactly what we were doing. Of course the company-provided service representatives were nowhere to be found at 4 A.M., and when they called in to offer help the company technicians often had less knowledge of how the machine actually functioned than did the nurses.

None of these problems, regardless of the magnitude of the catastrophe, seemed to affect the physicians' overall resolve to make use of the new equipment. The fact that the procedure could be carried out more easily and safely using the old fashioned manual method seemed of no account. It was then that I first began to sense that the forces favoring the adoption and use of new technologies were

formidable. The medical machines I was working with seemed to take on a life of their own.

Almost ten years later another event confirmed my earlier observations. While conducting a vigil in an intensive care unit with my seriously ill mother I was horrified to watch as another patient was almost killed by a malfunctioning peritoneal dialysis machine. The patient survived only to have a new nephrologist order the nurse to "try again" with the machine despite the fact that it was a holiday weekend and the machine had not been repaired. I kept thinking back to that child of ten years earlier. The only change was that the machine belonged to a new generation of equipment - sleeker and more sophisticated looking. Were the same mysterious pro-technology forces in operation again? And what were the forces: economic incentives, desire for prestige, or an expression of basic cultural values? Trying to understand these issues became a consuming interest to me.

My interest in medical machinery developed in concert with a concern about the crucial ethical issues inherent in modern medicine. What had happened to the patient's voice in these dramatic encounters between health professionals and medical innovations? As a nurse I became acutely aware that ethical issues often surfaced in tandem with the need to make decisions about the use of life-sustaining equipment. Because of my clinical experience in pediatrics I originally decided to conduct a study of ethical decision-

making in neonatal intensive care as my dissertation topic. With its frequent use of advanced medical technology, the neonatal intensive care unit seemed an ideal setting for such a study. At the time I was choosing a subject these issues were becoming of great concern both within medicine and to the general public. I planned to include a cross-cultural component in my research, studying NICUs in San Francisco and Dublin, Ireland. In fact, this was the project I defended in my oral qualifying examination.

Before I could begin, however, I was preempted in my choice of a research site. A medical sociologist from another university started an almost identical study in the NICU I had chosen to observe in San Francisco. My first reaction was fury and distress. How could someone be invading my territory? Then I heard about two or three other NICU studies being conducted around the country, and my despair turned to relief at being "saved" from entering an increasingly crowded research arena.

At the same time, I became concerned about the issue of objectivity in fieldwork. I worried that I might be unable to maintain the necessary cultural "distance" if I worked in the familiar environment of the NICU. Certainly I would have the advantage of knowing the local language and culture but could that seeming advantage become a barrier to accurate observation? In a symposium I organized for the American Anthropological Association meetings on issues of ethics and objectivity in fieldwork the discussant, Oliver Osbourne,

appropriately criticized the tendency for medical anthropologists who are also health professionals to work in known clinical settings where they are "comfortable." He argued that this resulted in the loss of cultural distance essential to good fieldwork. In the end these issues pushed me away from research in the NICU.

Luckily, there was an almost simultaneous pull from another source. Dr. Christine Cassel, a physician I knew through the University of California, San Francisco bioethics group, told me about her work with a new and fascinating medical technology called plasmapheresis, or therapeutic plasma exchange (TPE). She was involved with the first American medical group to use TPE as a treatment for myasthenia gravis (Dau, et al. 1977). Dr. Cassel said she was surprised that more attention was not being paid to this new technique, and she expressed deep concern about the social, ethical, and economic issues associated with a rapid increase in the use of TPE. When I informally surveyed physician friends about this procedure very few were aware of its implications or even of its existence. I became intrigued.

After a series of exploratory interviews with TPE participants I realized that a study of this recent innovation in medicine would have a number of distinct advantages and was, in fact, a logical extension of my original desire to study the NICU. As I mentioned above, one of the key issues in the NICU, indeed in bioethics

generally, is the appropriate use of technology. Issues such as whether to place a baby with severe respiratory distress syndrome on a ventilator can be agonizing for all parties involved. On one level, the necessity for making this decision is "caused" by the availability of the ventilator. By its very existence the machine becomes ethically coercive; a "technological imperative" for its use appears to come into play. Yet it is not at all clear why the mere existence and availability of a machine results in a moral imperative for its use. It became apparent that my original questions about ethical decision making in the NICU were not adequate because they were asked too late, after the use of the technology was well accepted by clinical practitioners. Perhaps the clues to the use of new technology in ethically complex situations might be easier to follow much earlier, before the procedures become part of standard medical practice. Hence, I reasoned, a study of a therapeutic innovation not yet accepted as a standard of care might shed light on the development of a technological imperative for its use. A dissertation investigating the case of TPE, a technology not yet accepted as standard therapy, seemed a logical extension of my previous interests.

As a research topic TPE had the additional advantage of being a subject area about which I knew virtually nothing. Adult medicine and immunologically mediated diseases (those treated with TPE) were not my particular strengths. Aside

from a basic familiarity with the inside workings of hospitals I had no preconceived ideas about the field which might interfere with assuming the anthropologist's "naive observer" point of view. I thus was able to meet Dr. Osbourne's criticism about studying too close to home.

Serendipity -- my discussions with Dr. Cassel -- played a role in my originally hearing about TPE. I was also served by chance in that the first reports about the use of TPE were published almost simultaneously in the U.S. and in London. Thus a complete account of the use of the development of the technology would require fieldwork in England, providing me with the opportunity of studying in an unfamiliar medical care system, one very different from our own. It all seemed too good to be true when my husband's sabbatical plans coincided with my desire to do fieldwork in London.

Thus, helped along the way by disasters, serendipity, and the desire to be a "real" anthropologist, I happened upon a dissertation topic.

Acknowledgements

I have incurred innumerable debts in the course of researching and writing this dissertation.[3,4] I would like to begin by thanking Christine Cassel for her enthusiastic introduction to the subject of TPE. Her initial help allowed me to make the difficult decision to change thesis topics.

When one begins a major study with almost no knowledge of the subject area, your informants are of the utmost importance. My most substantial debt is to the many participants in the development and use of TPE who spent countless hours educating me about their field, patiently being interviewed and observed in what must have seemed a never-ending process. These informants include physicians, patients, nurses, technicians, equipment manufacturers, and government officials. For reasons of confidentiality I cannot name any of these people specifically; however, their cooperation is what made this study possible.

Within the stimulating intellectual environment of the University of California, Berkeley and San Francisco campuses my thinking about medical technology progressed from the initial simplistic and naive questions of a clinician to the disciplined and analytic approach of a well-trained medical anthropologist. Many people contributed to this transformation. My specific thanks go to: Jonathan

Showstack, Phillip Lee, Phyllis Fetto, and Michael Nevitt of the Institute for Health Policy Studies; Anselm Strauss and Carolyn Wiener from the Sociology program; and Bernard Lo and Andrew Jameton from the Medical Ethics Division. They lent an attentive ear to the earliest formulations of this project, adding the differing perspectives of their disciplines.

My greatest intellectual debt is to the original members of my dissertation committee. George Foster of the Berkeley campus shaped the initial stages of my development as an anthropologist and has remained an enthusiastic supporter. Anne Davis of the School of Nursing attended to my growth as both a nurse and a researcher. Albert Jonsen of the Division of Medical Ethics introduced me to the field of bioethics and has been a constant source of ideas about the complexities of technology use in medicine. My greatest debt, however, is to Margaret Clark, who has shaped not only the dissertation but every phase of my graduate school career. She spent innumerable hours discussing the ideas presented here in their earliest, roughest forms and refused to lose confidence in my abilities as an anthropologist -- even when I did my best to convince her to the contrary.

Without the emotional support and practical help of many friends and colleagues there would be no acknowledgements to write. Between the beginning and ending of this research project my life has changed enormously, saddened by the deaths of both my parents and a grandmother

who helped raise me, enlivened by the births of two children, Samuel and Miriam, and made more complicated as I undertook the first major commitments of my professional career. More individuals than I can name have provided assistance. Some, however, merit special attention. Susan and David Pike aided my entry into both English life and the National Health Service, providing service as cultural interpreters. On this side of the Atlantic many friends provided varying combinations of intellectual challenge and practical help. I would like especially to acknowledge the assistance and support of Judith Barker, Sally Glaser, Deborah Gordon, Eric Juengst, Judith Justice, Maurice Kamins, Sharon Kaufman, Linda Mitteness, Jessica Muller, and Helaine Weinstein.

Three people deserve special recognition. Without the help of Barbara Stoops and Margaret Wrensch this dissertation would never have been completed. Their many contributions cannot be measured or adequately repayed. And finally, I would like to thank my husband, Stephen Arkin, for his support during the years this project has consumed. His experienced advice, "a dissertation consists of pages," is in large part responsible for the pages that follow.

Notes

1. ECMO is a machine that substitutes for the function of both the heart and lungs, similar to the bypass machine used during open-heart surgery but applied for indefinite periods of time.

2. Peritoneal dialysis is one method of substituting for a malfunctioning kidney. The dialysis solution is instilled and removed from the peritoneal cavity via a catheter inserted through the abdomen.

3. The research on which this dissertation was based was supported by: a National Research Service Award from the Division of Nursing, U.S. Public Health Service; the Wenner-Gren Foundation for Anthropological Research; and the Graduate Division, University of California, San Francisco.

4. Portions of the text of this dissertation have been published in Biomedicine Examined. Margaret Lock and Deborah Gordon, editors (see Koenig 1988). I would like to thank both Lock and Gordon for useful criticism of this manuscript.

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Chapter I

TECHNOLOGY USE IN MEDICINE:

THE PROBLEM, THEORETICAL FOCUS AND METHODS

Diseases desperate grown by desperate appliance are relieved, or not at all.

Shakespeare Hamlet IV.iii.

Introduction

While leaving the operating room after assisting with an early implantation of an artifical heart into a human being, Dr. Robert Jarvik, one of the inventors of the new device, commented to the press that the surgery had gone so smoothly it seemed "routine." The New York Times reported on February 18, 1985:

> Though it was only the second time the Humana team performed an artificial heart implant, there was a sense of the routine. "Boy this is a dull operation," one of the nurses who had participated in Mr. Schroeder's operation said, according to Dr. Jarvik. "That was great," Dr. Jarvik said, "because nothing exciting is going on, there didn't seem to be any danger, any great risk here."

On reflection these remarks seem truly extraordinary. To describe the physical removal of a man's ailing heart and its replacement with a mechanical substitute as "routine," indeed, "just a day's work," expresses something of the power of medical technology over the modern imagination. Images of dramatic technological progress dominate our understanding of modern medicine (Reiser 1978). As a culture we are fascinated with the details of medicine's most recent miraculous advance. The limits of technology seem boundless. Although increasingly aware that progress sometimes occurs at significant cost, both social and economic, we eagerly await news of the latest test-tube baby or liver transplant.

What accounts for the rapid development and quick adoption of new equipment in western medical practice? "The landscape of modern health care is filled with machines" (Reiser and Anbar 1984:3). Clearly, some new medical procedures (vaccines, for example) offer such significant improvements over existing practices that there is little question about their use. More often, however, the true nature of new procedures and equipment is extremely difficult to evaluate. In an attempt to explain the seeming primacy of technology in modern medicine many health economists and policy analysts have postulated the existence of a "technological imperative" in medical practice; these commentators believe that the mere existence of a dramatic new medical device provides a mandate for its continued

use. (The phrase technological imperative has long been used in engineering and related disciplines as a shorthand term for the powerful tendency to choose complex, highly technical, and occasionally "over-designed" solutions to problems.) Victor Fuchs, who first applied the phrase "technologic imperative" to the field of medicine, attempted to account for this preference for the latest machine by discussing the power of "tradition" among physicians; he speculated that physicians had been "imprinted" during training to provide the best possible medical care, generally meaning the newest and most technological care (1968; 1974). The idea is both powerful and captivating.

In this dissertation I will examine the social processes which contribute to the operation of a technological imperative in medical practice. I will be asking how people construct understandings of the complex technologies which enter their lives. My focus will be on the meaning of medical technology, specifically on the changed meaning which new machines develop as they are used. In order to explain the significance of this changed meaning I must define one additional idea, that of the "experiment-therapy continuum" in medicine. This concept, developed by Fox and Swazey (1978), speaks to an inherent tension in the use of new medical technologies. What is their meaning? Are they experiments or are they treatments? New technologies must traverse this continuum, changing from a status of pure experiment to the standard of

care. I believe that this transformation of meaning is an inherently social process which sustains the technological imperative. Social forces speed the progress of new medical technologies along the experiment-therapy continuum.

There are no simple or easy scientific rules for determining when a new treatment has become an accepted standard therapy. It is by definition an ambiguous process. Yet physicians must make treatment decisions daily which take this distinction into account. One physician complained, "I can't find out what experimental is in medical practice. That's a very difficult and a very, very basic question. I've asked a variety of people..."

A recent example illustrates how the "experimental" label on a new therapy can be changed for social or political reasons. An Assistant Secretary for Health announced during a congressional hearing that henceforth, liver transplants for certain ill children would be considered "a nonexperimental procedure" (Iglehart 1984). This decision, made for political not medical reasons, shows that the position of a new technology on the experiment-therapy continuum may be subject to social negotiation.

In order to investigate these issues, I conducted a case study of one recently developed medical technology: therapeutic plasma exchange (TPE). TPE is a dramatic, machine-based treatment for a number of serious diseases. Through the vehicle of TPE, I will document how the technological imperative in medical practice is generated

and maintained by inherently social forces. In this introductory chapter, I will first discuss the rationale for the study, justifying my focus on technology use in medicine. I then explain the theoretical approach of the research and place it in the context of other social studies of medical technology. Next, I provide a detailed description of the technique of TPE to orient the reader, followed by an account of the rapid increase in the use of this technology shortly after its development. This section provides a direct, numerical demonstration of the technological imperative. Finally, I describe the methods used in conducting the research and provide an overview of the dissertation as a whole.

Medical Technology as a Focus of Study

The ever increasing use of technologically sophisticated equipment in medicine has caused much concern among health professionals, policy makers, and the lay public. The media coverage of the first artificial heart implant in 1982 suggests the range of opinion in this controversial area. Reports ranged from unabashed praise for the daring and skill of the surgeons and the courage of Barney Clark to thoughtful concern about the social and ethical issues raised by the availability of "heroic" forms of therapy. Other commentators expressed simple wonderment

about who was going to foot the bill for the next generation of medical miracles.

A few of the voices raised in this debate took the form of mindless "doctor bashing,"[1] or an almost hysterical criticism leveled against any and all technological advance. Let me say at the outset that I do not join with these modern day Luddites in their campaign to smash the sophisticated machinery of clinical medicine and return to a pristine "golden age" of humanistic (and technologically unarmed) family doctors. This naive approach neglects the very real benefits of modern medicine.

Nonetheless, serious and problematic issues surround the unprecedented growth of medical technology. Of most concern to health policy makers and government officials is the issue of cost. In America, we are now spending more than eleven per cent of our gross national product on health care and increases in the cost of medical care continue to rise at a rate greater than that of inflation. Although the exact relationship between the use of advanced technology and rising health care costs is a complex economic problem lacking simple answers, there is general agreement that increasing technology use is one cause of the dramatic rise in expenditure (Schroeder and Showstack 1979).

Less pressing to policy makers but of equal import is the role of medical technology in the changing character of clinical medicine and nursing. Mechanic (1977) discusses how technological innovation results in changed

organizational structures in the hospital. One result is the increasing bureaucratization of medical care. The complexity of the modern hospital alters the experience of giving and receiving care. Technical tasks become predominant. An example is the changed nature of the childbirth experience since the inception of electronic fetal monitoring and associated advances.

The predominance of technology is especially clear in the area of chronic disease. The modern patient with a chronic illness faces a dramatically altered "disease trajectory." This term, coined by Strauss and his group (1985), suggests the experience of the chronically sick over time in multiple, technologically oriented encounters with the health care system. The typical patient is likely to encounter as many machines as human faces. The potential (if not the reality) of dehumanized care is ever present.

Many of these new machines have the ability to alter the natural history of a disease. In particular, the life-sustaining capabilities of modern medical equipment pose difficult ethical dilemmas for patients, physicians, and society as a whole. Today's successes with intensive care technologies and complicated surgical procedures were unimaginable as little as ten years ago. The ability to sustain life indefinitely has called into question the existing sociocultural and biomedical norms requiring that "everything" possible be done for the patient in the battle to preserve life and prevent death. This is a new

phenomenon in medicine. Only recently has serious attention been paid to the question of when to stop treatment or withhold an available therapy (President's Commission 1983; Hastings Center 1987).

On a societal level these advances in medical technology have forced a reexamination of basic cultural beliefs. Values basic to a society, such as what defines a life or is considered death, are under intense pressure as a result of technological advance (Parsons, Fox and Lidz 1972). Thus the study of new medical technologies is vital to an understanding of changing cultural values in American society.

The issue of the relationship between cultural values and technology is extremely complex. Equally difficult and abstract is the question of the relationship between technological advance in medicine and basic health levels in a society. The question could be phrased: Does the use of high technology medicine lead to significant reductions in disease morbidity and mortality levels? We tend to assume a direct relationship between progress in biomedical technology and health. However, some analysts have questioned this basic assumption, suggesting that the 20th century orientation towards the treatment of individual episodes of disease (as opposed to an emphasis on prevention and general social amelioration) may have had less impact on morbidity and mortality levels than most realize (McKeown 1979). The work of McKeown brings into question the usually

implicit assumption that advances in the technology of medicine automatically lead to therapeutic success.

There are serious practical ramifications of the technological imperative as well. New treatments commonly diffuse into widespread clinical practice before evidence is available about their actual usefulness. "Marginally useful, expensive technologies are developed, while unmet needs abound" (Banta 1983:1365). Examples can be cited in the areas of both surgical procedures and therapeutic equipment. Two particularly notorious cases are the eventually discredited but for a time widespread use of a "gastric freezing" machine during the fifties to treat stomach ulcers (Fineberg 1979) and the quick acceptance and extensive use of lobotomy for the treatment of mental illness in the 1930s, 1940s, and 1950s (Valenstein 1986). Hindsight makes it clear that these procedures were not only ineffective, but in many cases actually harmful. Remarkably, the physician who developed the lobotomy procedure received the Nobel Prize for medicine in 1949, indicating the transient nature of medical orthodoxies.

Examples are not limited to the infamous or to the distant, non-scientific past. Many more recent innovations have been adopted and diffused widely prior to conclusive evidence of effectiveness. The efficacy of coronary care unit technology in improving the outcome of acute myocardial infarction has been questioned in numerous studies (reviewed in Waitzkin 1979). Likewise, electronic fetal monitoring,

now believed to be useful in the management of high-risk pregnancy, was widely adopted in the situation of normal deliveries despite evidence that it failed to improve the survival of low-risk infants (Banta and Thacker 1979). This list could be extended but the examples cited are sufficient to clarify the nature of the problem: once a new technology is developed, the forces favoring its adoption and continued use as a standard therapy are formidable.

Theoretical Approach

Traditional social science approaches to technology range from an extreme form of "technological determinism," in which technology is viewed as a determinant of culture, to a view that the influence of technology can only be understood in terms of the meanings which people give to it. The reality, as is usual in the case of extreme formulations, is much more complex. Clearly, the use of technology cannot be independent of its social context. Especially in the case of medical technology, with its potential for evoking strong feelings carrying potent symbolic references to the body, life and death, the relationship between the machine and its user is multi-faceted.

Despite the great potential which social studies of medical technology hold, Aiken and Freeman (1984) and Banta (1983) have documented the lack of interest in the science

and technology of medicine among social scientists concerned with health. With the exception of the work of Fox and Swazey (1978) and Fox (1959), the field is barren. Earlier social science studies dealt with more narrowly defined questions, such as the study of medical innovation and diffusion (Greer 1977; Rogers 1981). These works were concerned with pragmatic topics such as identifying "barriers" to the diffusion of new techniques. Most importantly, early studies accepted the inherent value of new medical techniques without question (ibid.). In the past few years more critical studies have begun to appear, such as Plough's (1981, 1986) work on renal dialysis and Guillemin and Holmstrom's (1986) study of neonatal intensive care.

The relative lack of interest among social scientists is compensated for by a large literature in economics, health policy, and in the emerging field of health care technology assessment (McKinlay 1981, 1982; National Research Council 1979; Institute of Medicine 1985; McNeil and Cravalho 1982). This keen interest in technology use in medicine is accounted for primarily by concerns about the rising costs of medical care, although other issues, such as clinical safety, are also important considerations.

Anthropologists have long understood the absolute importance of social and cultural knowledge in comprehending the medical systems of their traditional subjects, tribal or peasant societies in the third world. Ethnomedicine has

been a common focus of research. What has not been undertaken is a study of biomedicine itself. We have not taken "biomedicine as an ethnomedicine" (Gaines and Hahn 1982). The reasons for this are complex. Our own society and its sophisticated technologies, part of a powerful scientific paradigm, have been "off limits" to the kind of investigation routinely performed on the medical systems of other societies. Lock has stated the issues clearly:

> Because contemporary medicine in industrialized societies is based upon a scientific foundation, certain assumptions have been made about this type of medical knowledge which have led to its exemption from social analyses. In the first place, it has been assumed that the biomedical model is the representation of reality, clearly not complete, but nevertheless slowly but surely moving towards a final explanation of the causes, diagnosis, and treatment of diseases (1984:121).

I begin with the assumption that western medical knowledge is as open to social and cultural interpretation as any other medical system (Comaroff 1982). As pioneering social studies of modern biomedical science have demonstrated, even our knowledge and understanding of "pure science" topics -- such as the biochemical structure of hormones or genetic disease -- can be viewed as at least partially social constructions and not simply as biological fact uninformed by cultural considerations (Latour and Woolgar 1979; Yoxen 1982).

The Technique of Therapeutic Plasma Exchange

The study reported here is based on a two year investigation of TPE[2], in which I conducted extensive observational fieldwork in eight cities in the United States and United Kingdom. I visited TPE treatment units and research facilities, as well as related settings such as medical equipment manufacturing companies and scientific research meetings. During this period I observed numerous TPE treatments as they were carried out, conducted a detailed review of the medical literature, and interviewed many of the key participants in TPE research and treatment. (My research methods will be described in detail in a separate section below.)

Although when first observed TPE appears intimidating and complicated, in reality the basic principles are quite simple. A large centrifuge machine (called a cell separator) is used to remove one part of the patient's blood, the liquid component, or plasma. This is replaced with new plasma, obtained from blood donors. At the same time the patient's own red and white blood cells are returned. The machine itself appears daunting because of the large array of tubes, bottles, blood pumps and flow regulating devices necessary to accomplish the task of plasma exchange (see figures 1, 2, 3, and 4).

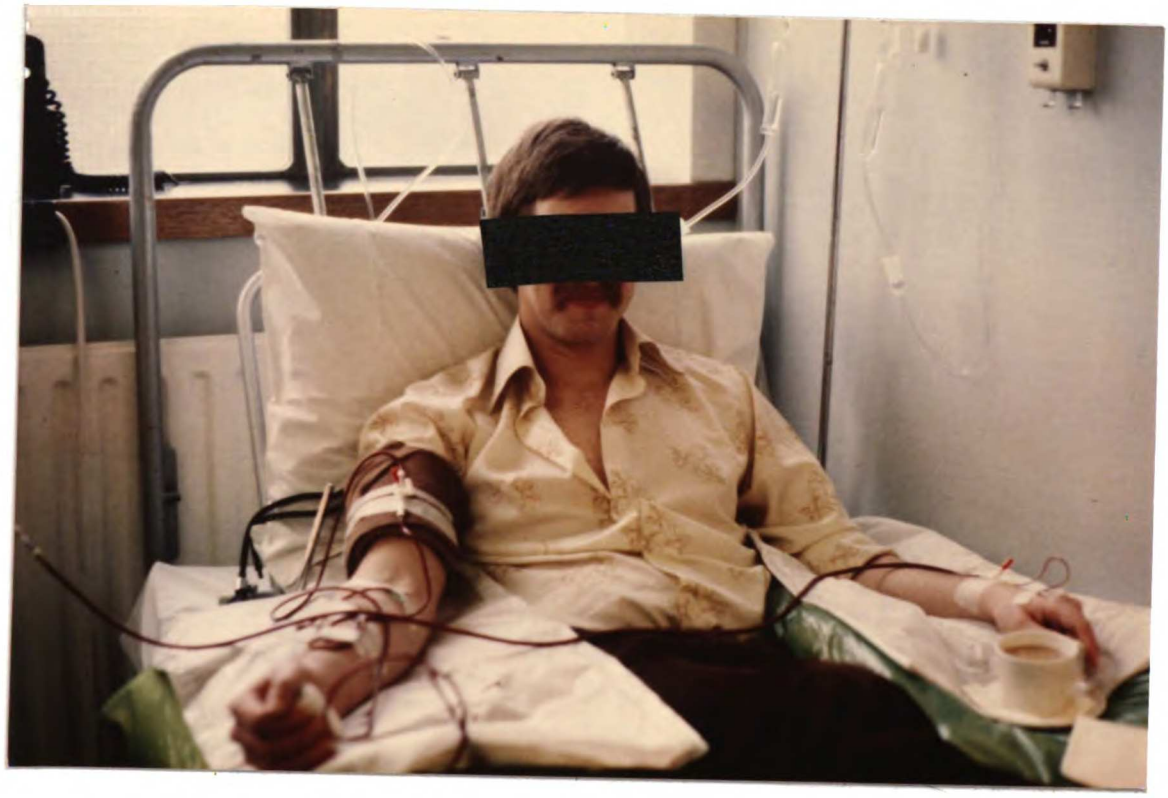

FIGURE 1. Patient "hooked up" to a TPE machine.

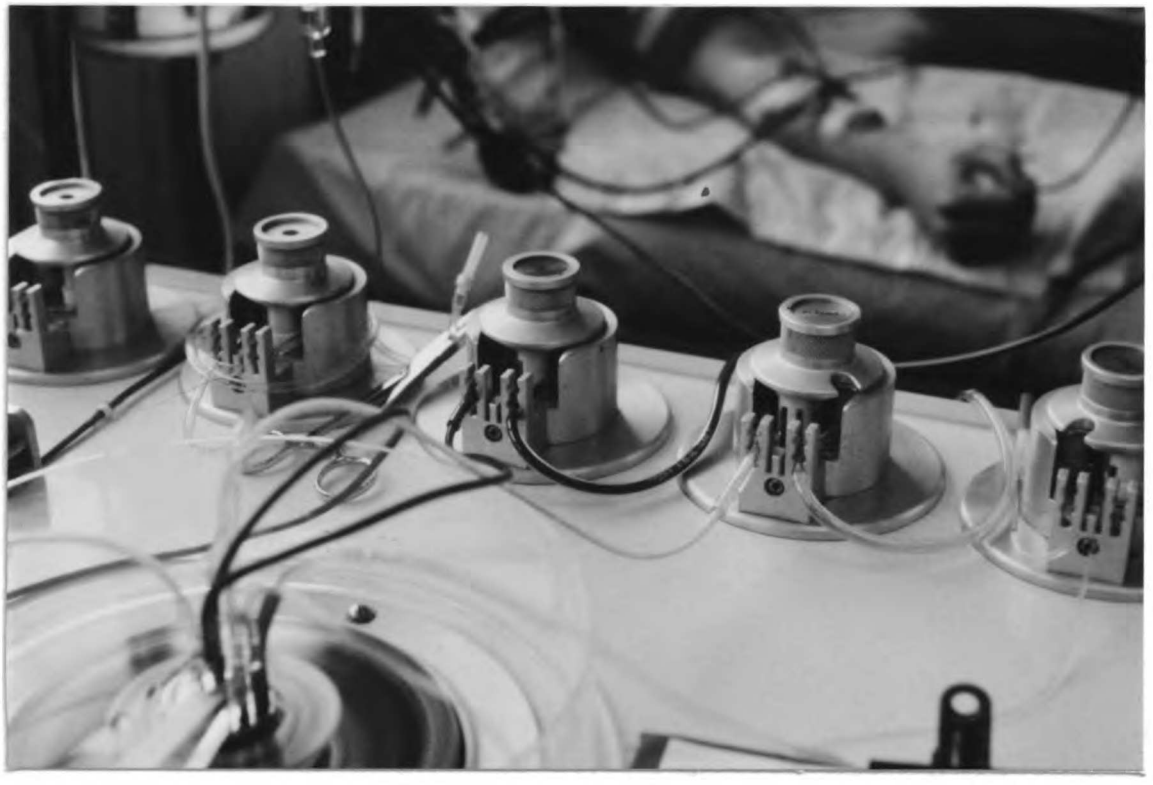

FIGURE 2. Top view of an I.B.M./N.C.I.-type machine, showing blood pumps and centrifuge.

FIGURE 3. Nurses operating the machine.

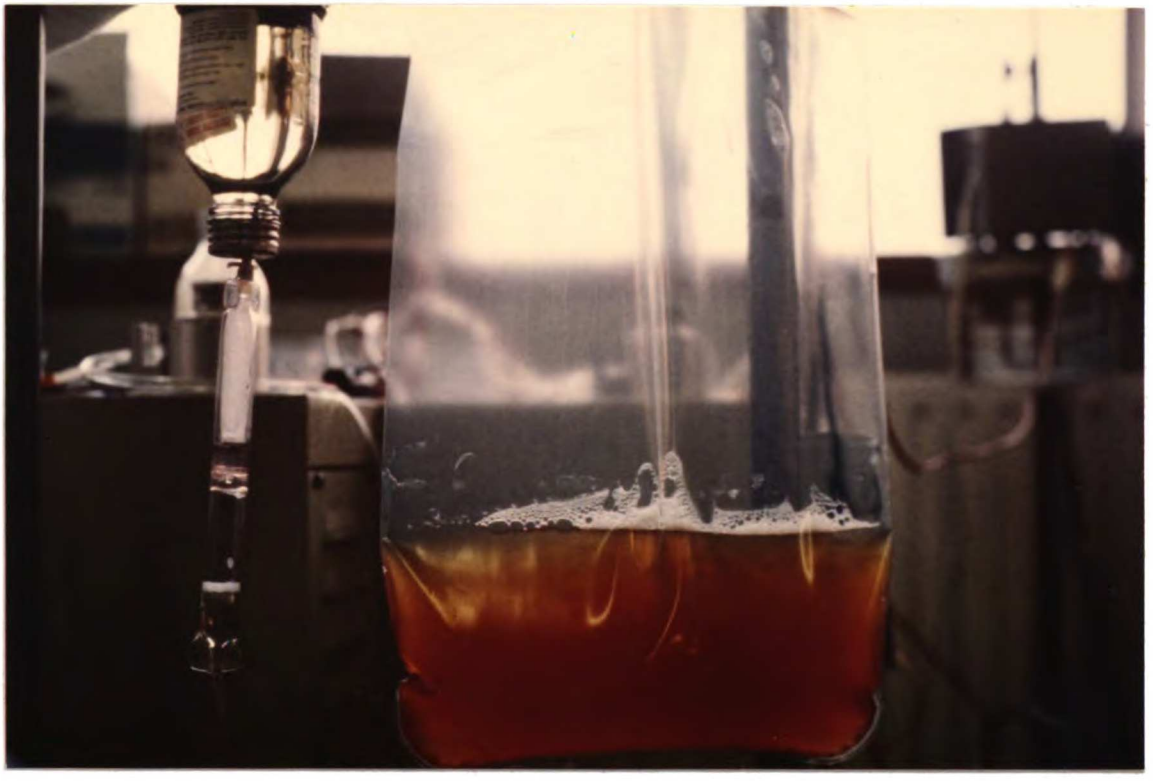

FIGURE 4. Clear plasma substitute (upper left) replaces patient's old plasma (center).

TPE is used primarily for a class of diseases called the autoimmune disorders in which the body produces harmful substances, generally either immune complexes or antibodies to its own tissues. Disorders which have been treated with TPE include myasthenia gravis, systemic lupus erythematosus, rapidly progressive glomerulonephritis, multiple sclerosis, rheumatoid arthritis, and many others, some obscure and some quite common (see Table 1).

TABLE 1

Conditions Treated With TPE

ABO Incompatible Bone Marrow Transplant Preparation
Acquired Immunodeficiency Syndrome
Amyotrophic Lateral Sclerosis
Asthma
Autoimmune Hemolytic Anemia
Burns (severe with shock)
Cancer (disseminated)
Crohn's Disease
Cryoglobulinemia
Dermatomyositis
Eaton-Lambert Syndrome
Fabry's Disease
Factor VIII Inhibitors (in hemophilia)
Glomerulonephritis (rapidly progressive)
Goodpasture's Syndrome
Guillain-Barre Syndrome (acute and chronic)
Hemolytic-Uremic Syndrome (adult)
Hepatic Coma
Hypercholesterolemia (familial)
Hyperviscosity Syndrome (various forms)
Idiopathic Thrombocytopenic Purpura
Insulin Antibodies (in diabetes)
Myasthenia Gravis
Multiple Sclerosis
Pemphigus
Poisons (mushrooms, paraquat, etc.)
Polymyositis
Post Transfusion Purpura
Pruritus (intractable)
Primary Biliary Cirrhosis
Psoriasis
Pure Red Cell Aplasia
Raynaud's Phenomenon
Refsum's Disease
Renal Transplant Rejection
Rh Incompatibility
Rheumatoid Arthritis
Systemic Lupus Erythematosus
Thrombotic Thrombocytopenic Purpura
Thyrotoxicosis
Vasculitis (various forms)

The frequency of treatment varies in different diseases, with patients receiving TPE daily for some forms of acute renal disease or monthly for neurological conditions. Therapy is generally not as intensive or long term as renal dialysis. The antibodies (or other harmful substances) collect in the plasma and are removed by the machine along with the old plasma. The new, "clean" plasma is free of disease causing proteins.

The theoretical rationale for TPE as a treatment is that in some diseases there is an accumulation of a harmful element in the plasma component of the blood. This harmful element may be an antibody directed against the body's own tissues (an autoantibody) or a damaging complex of an antigen plus an antibody (an immune complex). The pathophysiology of the disease myasthenia gravis is illustrative of the basic mechanisms at work in autoimmune disease. I will explain the rationale for use of TPE in treating myasthenia gravis to aid the lay reader in understanding the scientific basis of the treatment.

The production of antibodies is one of the body's most important defense mechanisms. The body responds to foreign invaders, such as bacteria or viruses, by producing specific antibodies against the unfamiliar organisms. In certain autoimmune diseases, for unknown reasons, the body begins producing an antibody against "self," confusing its own cells with foreign tissue.

In myasthenia gravis an autoantibody forms against part of the neuron, thus blocking the transmission of chemical messages from nerves to muscles. The part of the neuron which receives the messages becomes blocked with the autoantibody, precluding the transmission of acetyl choline (a neuro transmitter). The result of this blockage is severe weakness of all the body's muscle groups. Serious disability can result, including loss of the ability to breathe or swallow.

Because these harmful autoantibodies cannot be removed selectively from the blood, in TPE the entire plasma component (including the autoantibodies and up to four liters of plasma) is removed by the machine. The removed plasma is replaced with non-diseased plasma substitute which is obtained from blood donors and then commercially processed and purified. A number of valuable blood constituents such as the protein albumin, clotting factors, and "good" antibodies are lost as an unintended side effect.

TPE is accomplished by the use of a sophisticated-looking machine which separates blood into its major components by spinning it in a centrifuge. As with any centrifugation process the separation takes place because of the different weight of the individual blood components. The machine used is called a "cell separator;" a number of models are available from different manufacturers. In addition to a centrifuge, the machine consists of a series of pumps to move the blood around, a system for keeping the

blood from clotting while outside the body (anticoagulation), switches for diverting the different blood products in different directions, and alarms to ensure the patient's safety in case of any system failure.

The first step in the procedure is gaining access to the patient's circulation. Access is obtained by inserting large needles into the veins, usually the antecubital veins, or by surgical placement of an arteriovenous shunt or fistula such as those employed for kidney dialysis. Next the blood is pumped from the patient, anticoagulant is added, and separation of the plasma from the other blood components takes place in the centrifuge. To make sure the patient maintains an adequate blood pressure, only a small amount of blood is removed at any one time; patients are also given extra fluids. Once separated, the patient's old plasma is diverted to a waste container. The new plasma is then returned to the patient along with his or her own red cells, white cells, and platelets. Once the patient is "hooked up" to the machine the treatment takes about two to four hours during which a nurse or specially trained technician is in constant attendance monitoring both the machine and the patient's response to treatment.

The dramatic nature of TPE is difficult to describe in words; one must imagine a patient connected to a large and complicated looking machine by means of which the patient's blood is removed by circulating it through many feet of tubes. A number of medical personnel are in constant

attendance, checking the machine and the patient, and adding bottles or bags of new plasma. One physician informant described TPE as "the ultimate Walter Mitty-like experience. A patient's lying there in bed and attendants move levers back and forth...the machine goes toponka, toponka, toponka...It's all a sort of medical fantasy."

Rationale for Studying TPE

The innovation of TPE provides an instructive case through which to examine the social and cultural elements sustaining a technological imperative in medicine. The procedure, used for serious and debilitating disorders for which few treatments are available, is costly and dramatic. Yet at the same time its actual contribution to the treatment regimens of various autoimmune diseases is very difficult to evaluate. The high cost comes from the expense of plasma substitutes, the cost of the machine and disposables, and the labor intensive nature of the therapy.[3] Estimates of the cost per procedure range from $400 to $1500 (ECRI 1985) with patients often requiring many treatments over a prolonged time period. Although some of the disorders for which TPE is used are rare, others, such as rheumatoid arthritis, are quite common. Since it is estimated that one to two per cent of the U.S. population suffers from rheumatoid arthritis the potential total cost if even a fraction of this population were to be treated is

staggering. Hence TPE provides a good illustration of a new technology with the potential to greatly increase overall health care costs.

Another interesting aspect of therapeutic plasma exchange is the inherent "messiness" of the procedure. From the beginning, it was unclear whether TPE would prove generally useful or be completely abandoned after a period of initial enthusiasm. Although early reports indicated that TPE seemed to palliate the symptoms of some autoimmune diseases the technique is very nonspecific, offering little hope for definitive, curative therapy. Lewis Thomas could have had TPE in mind when he coined the phrase, "half-way technology" (1971).

Half-way technologies are not necessarily ineffective; rather, they are capable of only limited tasks. TPE does accomplish the removal of harmful substances from the blood. However, it does this in a very inefficient manner, causing the loss of valuable blood components at the same time. Simple removal of autoantibody will never be the ultimate solution to autoimmune disease; that will come only with increased knowledge of what triggers the body to begin producing antibody against itself. TPE bears the same relationship to autoimmune disease as dialysis bears to kidney disease: it is only half-way to the goal of cure.

Furthermore, because of the nature of the diseases treated, the evaluation of TPE is extremely subjective. Often investigators must rely on the patient's own

assessment of improvement, such as a decrease in morning stiffness for arthritis patients. Even the more objective measures, such as the length of time a myasthenic patient is able to hold his hand out in front of him, are subject to interpretation by the physician and the enthusiasm of the patient. Formal evaluations are complicated by the possibility of a potent placebo effect. In spite of its dramatic appearance the ultimate place of TPE in medical therapy remains unknown (AMA 1985; Shumak and Rock 1984).

In addition, TPE shares with other half-way technologies the problematic concern of potential iatrogenic harm. As with dialysis, risk to the patient is not inconsequential. There are serious dangers associated with the need to gain vascular access, such as bleeding, clotting difficulties, and infection (Shapiro and Shapiro 1987). The long term effects of depleting the body of plasma are unknown. And of most concern, a number of deaths have been reported as a consequence of TPE (Ibid.). Because the actual effectiveness of TPE is far from clear cut and its safety not well established, it provides a good opportunity to examine the social and cultural processes which support the technological imperative. TPE is by no means a magic bullet in the treatment of serious autoimmune disease.

A Rapid Increase in the Use of TPE

Early in the development of therapeutic plasma exchange its use increased very rapidly, even though its ultimate usefulness remained uncertain. Because the extent of this increase and the factors that may have contributed to it are central to my analysis of the technological imperative, I will discuss the rapid expansion in use of TPE at considerable length and document the methods I used to measure it.

Following the introduction of cell separation equipment in the late 1960s and early 1970s a gradual increase in the use of TPE began. Then, beginning in the mid 1970s, the number of TPE procedures dramatically increased. Although it is impossible to pinpoint an exact cause, I believe the increase was a direct result of the intellectual breakthroughs leading to the spread of TPE to autoimmune disorders such as myasthenia gravis and Goodpasture's Syndrome. Undoubtedly there was also an association between the increasing availability of machines world wide and the number of procedures performed; the upswing was preceded by the introduction of a cheaper and simpler cell separator machine.[4] (The scientific and technical development of the procedure will be discussed at length in Chapter II. This section is limited to documenting numerically the rapid increase in TPE's use.

Valid information about the number of TPE treatments performed during the early stages of the technology's development is unavailable. With an innovative technique there is simply no one keeping track. There are no governmental reporting requirements and it is impossible to use insurance company records because records of that kind are not available until a later stage of development. Often regulatory agencies or other government organizations are unaware of what is happening "in the field." The lack of an early warning system means that efforts at technology assessment often are not undertaken until after a new technology has diffused widely into practice.[5] Heyse reports that when the federal government began looking into the financial impact of TPE they first estimated that the number of procedures in 1979 was in the hundreds; they later discovered that the actual number was at least 16,000 (Edelson 1982:76).

Because of the lack of direct evidence, I have developed a number of indirect measures to estimate the actual number of TPE procedures performed and thereby demonstrate its rapid increase in use. I will include three types of information to document this rapid increase: estimates put forth by various organizations, data on procedures performed in individual treatment units, and data on the increase in publications about TPE in the medical literature.

First, a number of organizations have attempted to reconstruct the growth of TPE for specific purposes. Market research organizations tried to obtain information on the actual number of procedures performed in order to guide investors interested in companies producing TPE machines and disposable equipment. Such a firm, Scoville Associates, developed a retrospective estimate of TPE procedures performed; they showed an increase from 5,000 procedures in 1977 to 40,000 in 1980. The order of magnitude is significant; between 1977 and 1980 the number of TPE procedures carried out in the United States increased by 500 per cent. An equipment industry informant who wished to remain anonymous reports similar figures, suggesting an increase from 12,000 procedures in 1978 to 40,000 in 1980. Another market research firm (Montgomery Securities) believes that the figures could have been much higher. In 1981 they estimated that as many as 80,000 procedures were performed in 1980. Although it is difficult to determine the validity of these estimates it is likely that the figures from private firms are accurate because they had the financial resources to invest in conducting informal surveys, as well as the economic motivation to collect accurate information for their customers. The one organization making estimates which had an actual reporting mechanism was the American Blood Commission. Tweny one thousand therapeutic apheresis procedures were reported to the commission in 1980 (Epstein 1983). This figure is

undoubtedly low because it excludes TPE procedures performed by physicians in specialties outside of the blood banking community. Shumak and Rock (1984), physicians intimately involved in the development and use of TPE, estimated the number of procedures in 1982 as 80,000. These estimates are summarized in Table 2.

Table 2

Estimates of Number of TPE Procedures in U.S.

YEAR	NUMBER OF PROCEDURES	SOURCE
1977	5,000	Scoville Associates
1978	12,000	Anonymous Industry Source
1979	16,000 (reported)*	Montgomery Securities and American Blood Commission
1980	40,000	Anonymous Industry Source
	40,000-70,000	Montgomery Securities
	21,327 (reported)*	American Blood Commission
1982	80,000	Shumak & Rock 1984)

* The reported figures are most likely undercounts.

A second type of information is actual data I collected from individual TPE treatment units on the numbers of procedures they performed. I was able to obtain this information from a small number of treatment units in both the U.S. and in England, all of which became involved in TPE relatively early. Figure 5 shows the increase in number of procedures in these TPE units.

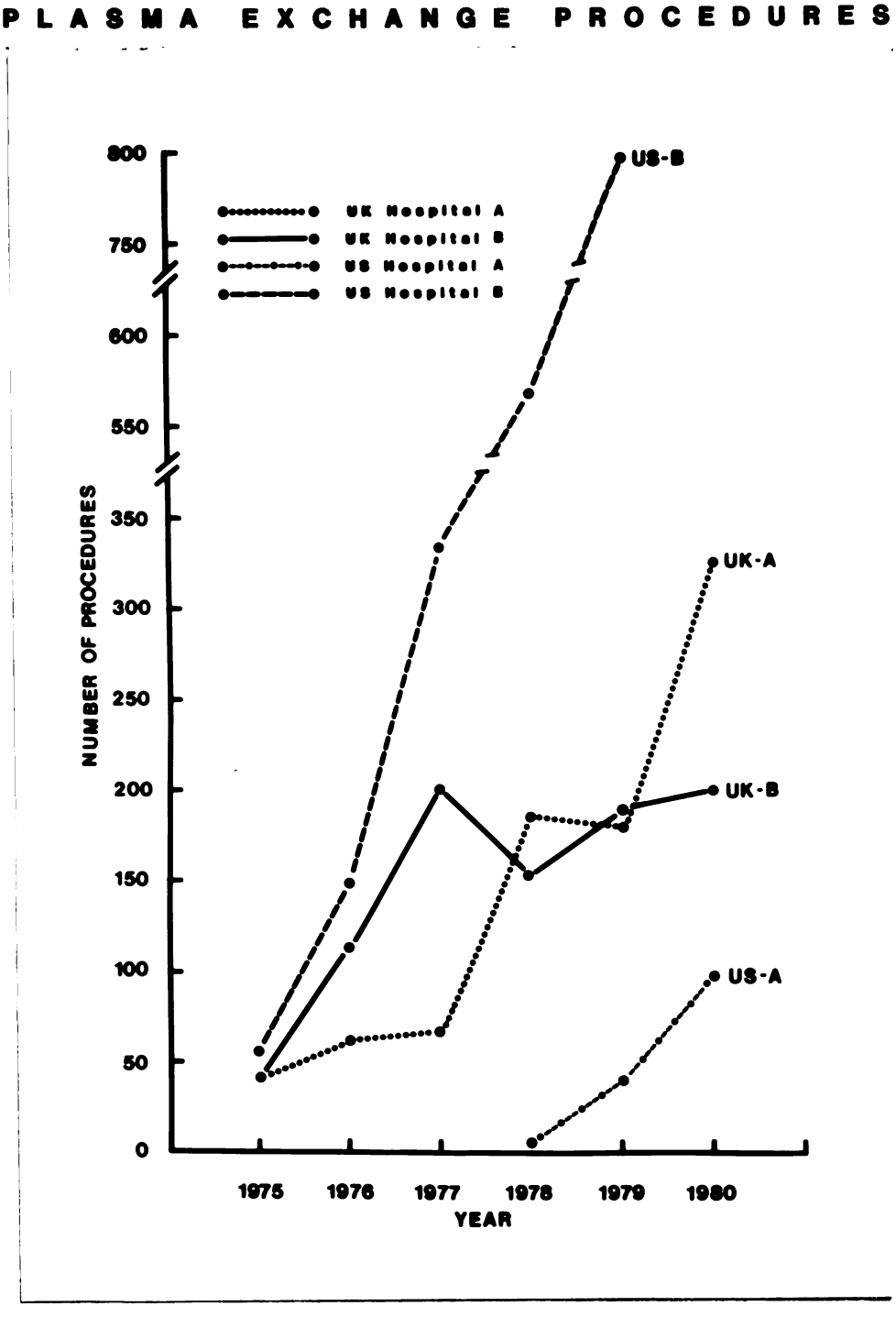

FIGURE 5. Total number of TPE procedures performed per year in four hospitals.

Although it is impossible to know how closely each unit approximates the overall growth curve, taken together, these figures demonstrate the rapid increase in use of TPE. In many cases these increases were dramatic, with the use of TPE quickly expanding to the capacity of the unit as defined by machine availability, nurse-technician time, or some other limiting factor, such as availability of plasma replacements. A technician at the Mayo clinic, which began performing TPE at an early date, described his perception of the increase: "Seventy-five [1975] was when it started escalating; it's almost doubled every year. The chart is just amazing, it's almost a straight line up for each year."

Because of the lack of reliable data on the actual increase in use of TPE I devised an indirect method to gauge the expanding interest in the procedure in the medical community. Using the National Library of Medicine's "Medlars II" computerized data base I conducted a computer search to locate all citations in the medical literature dealing with therapeutic applications of plasma exchange.[6] As the shape of the graph in figure 6 indicates, there was a gradual increase in citations in the mid-seventies followed by a very rapid increase in the number of publications about TPE in the late seventies.

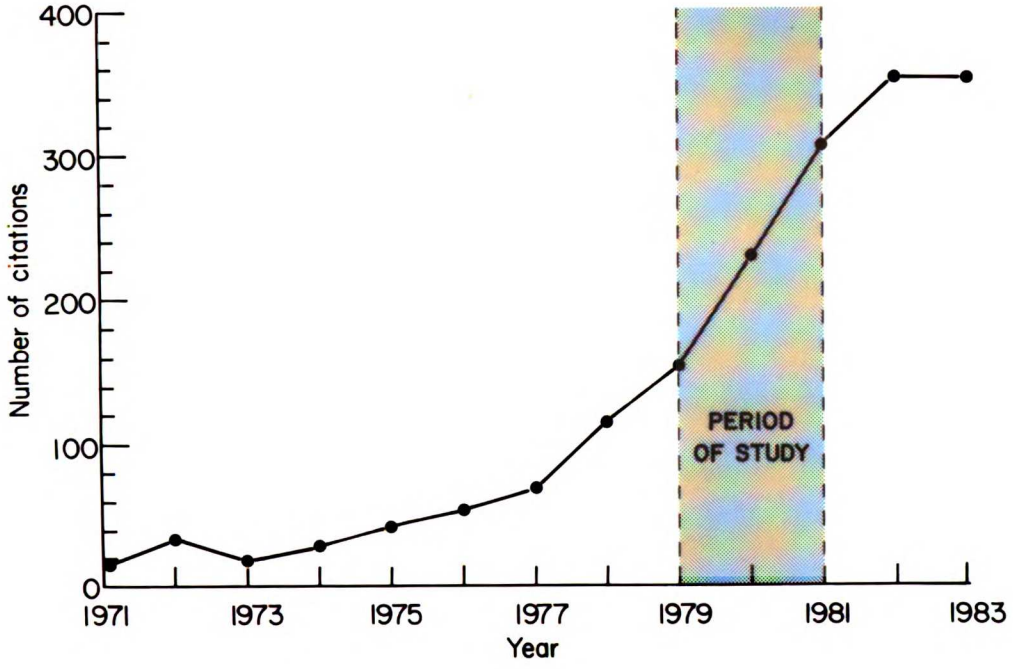

FIGURE 6. Citations of TPE in the medical literature, 1971-1983.

The slope of the curve is highest during the period of data collection for this study (shaded area of graph), indicating the most intense interest. Because of the lag time in publishing articles in medical journals this method probably places the peak interest at approximately six months to one year later than it really occured.

The increasing interest in TPE described above was the result of two distinct kinds of expansion. The overall increase in numbers of procedures performed resulted from extending the use of TPE to more and more types of patients within a particular disease category. For example, at first TPE might be applied exclusively in the most severe cases, only to be later extended to less extensive disease as the efficacy of the technique is supposedly "proven." In addition, increasing numbers of patients were treated as the technology extended from the research centers in which it was first used into the broader medical community. For example, many neurologists began treating patients with myasthenia gravis in their own hospitals rather than referring them to major medical centers. This resulted in an expansion in the overall number of procedures performed.

A second major source of increasing use of TPE was the application of the technology to a wide variety of <u>new</u> disease categories. Table 1 (earlier in this chapter) lists forty diseases in which TPE has been applied. This listing was constructed from published sources and is almost certainly an underestimate. Many of the diseases listed are

either known, or presumed to be, of autoimmune origin. In some instances TPE was tried briefly and then abandoned; in others it continues to be used. Although many of these conditions are extremely rare, taken together, they represent a major expansion in the use of TPE.

The different methods of estimating the increasing use of TPE which I have described offer convincing evidence that a sudden and rapid increase in both interest and actual use of the technology occurred. In the mid to late 1970s TPE was used more often and in an increasing number of diseases and was widely discussed in the medical literature. The expansion in the use of TPE resulted from numerous factors: advances in basic science, availability of the equipment to perform the procedure, and an array of complex and interesting social and cultural elements which will be discussed in subsequent chapters. The rapid expansion, occurring before the technology was evaluated, provides evidence for the operation of a technological imperative. (See Appendix A, Status of TPE in the 1980s, for an account of more recent changes in the use of TPE.)

Methodological Approach

The general methodological approach of this research is that of ethnography. Since the exact methods employed by anthropologists often appear mysterious to readers from outside the discipline, I shall be explicit in describing

the actual data-gathering and analytic techniques employed in this study.

Put most simply, the primary aim of an anthropological field study is to provide an understanding of the culture and social organization of a paticular group. The naturalistic methods of anthropological fieldwork provide effective means of obtaining information on how people view their world and act within it. For researchers in quantitatively-oriented basic science disciplines the ultimate goal is to define exact relationships between ever more minute bits of information, such as the relationship between oncogenes and cell growth. The anthropologist, on the other hand, maintains the challenging goal of setting forth a broad, holistic account of the culture under study. Even a specific case study like this aims at the total picture, including a wide range of salient "variables," any one of which could be studied in much greater depth.

In this dissertation the object of study is an international research community. Because of the speed of communication of information and constant interaction among physician investigators, it is necessary to view the "community" in which these physicians and other actors work as international in scope. This is an extension of the traditional anthropological understanding of a community as a small, relatively isolated group of people. The anthropological ideal of a small, geographically bounded group was rarely met; even isolated island populations were

invariably found to have encounters with outsiders. Today it is even more important to recognize the complexity of interactions which occur. A complete anthropological account includes essential information about the particular historical situation of a group as well as explaining how the group is situated within a complex web of social, political, and economic forces.

A combination of research strategies was necessary to study the initial development and early stages of growth in the use of TPE. This study relies primarily on traditional anthropological techniques of participant observation and interviewing. Other investigative methods were developed in the course of the fieldwork. It was obviously impossible to talk with every early user of TPE; thus a process of informal "sampling" was developed to guide data collection.

The first sampling process isolates TPE in a temporal sense. This study is time-bound. Although I discuss the historical development of TPE in detail, the major focus of the ethnography is the specific time period 1979 through 1981. This time frame includes the stage of most rapid growth in the use of TPE, the time during which I collected first-hand data. Thus the analysis and conclusions set forth here are limited to this early point in the innovation process.[7]

The study is also bounded geographically. Although the formal subject of the ethnography is the international research community in which TPE evolved, the innovation

process was studied in only two countries: the United States and England. These two countries were chosen for three reasons. The first is simple expediency. It was necessary to collect data in a limited number of settings; using England and the U.S. eliminated problems of language or access. Second, the first clinical use of TPE for autoimmune disorders occured almost simultaneously in the U.S. and England in the mid 1970s. By choosing to work in these two countries I was able to include many of the early users of TPE in the study. Finally, working in two medical "cultures" with totally different organizational structures allows use of an important anthropological technique: the comparative method. By constantly analyzing and comparing the use of TPE in the two medical systems the social and cultural features of the innovation process become more visible. This technique was particularly valuable in studying TPE because of differences in the economic basis of health care in the two countries. Unlike their American counterparts, English physicians receive no direct financial benefit from the use of technologically-based treatments.[8] Thus, although an explicit comparison of TPE in the U.S. and in England is not a goal of this study the use of the comparative method enhances our ability to discern social and cultural issues.[9]

Other sampling techniques evolved as the research proceeded. When this study began, there were few sources of information about TPE. In early 1979 when I polled

physicians about their knowledge of TPE most had never heard of the procedure. Thus it was difficult to obtain information. My first strategy was to develop a series of informants. This was done by reading the early literature and talking with as many of the first users of TPE as possible. I used a network approach to develop a group of key informants who, in turn, helped me to find other users of the technology.[10]

Physicians were the primary informants for the study. A total of twenty-five physicians were interviewed about their involvement with TPE. These informants might best be considered a "series" rather than a formal sample because they were not selected randomly. However, once I recognized that there were certain sub-categories of physician innovators, such as blood bank directors, nephrologists, and neurologists, I made a systematic effort to include physicians from all these categories.

The physician interviews were semi-structured and consisted primarily of open-ended questions. (Appendix B contains the interview schedules used with all categories of informants for the study.) A number of the physicians in the series were interviewed more than once. The interviews varied in length from forty-five minutes to two and one half hours. The majority were audio recorded and transcribed. Most physicians (and other health professional informants) were undisturbed by the tape recorder and simply turned it off if they wished.

Physicians, the key actors in medical innovation, were the primary informants. However, there are many other critical actors in the process. In addition to the physicians, I interviewed other TPE participants, including patients receiving therapy, the nurses and technicians who actually operate the equipment, representatives of the companies that manufacture TPE products, and a few additional actors, such as government representatives. These additional informants were also identified by a network method; most often they were associated with the physicians participating in the study. I also contacted directly some of the major commercial manufacturers of TPE equipment. In total I interviewed 15 nurse/technicians (the people who actually operated the TPE equipment), 20 patients, and 15 company representatives (from five different medical equipment firms.) These interviews also consisted of open ended, semi-structured questions. In instances where recording was not done (patients generally were not audio recorded because of technical difficulty) the interviews were dictated or typed up from hand written notes.

An equally important source of data is the written record of TPE, including both the formal medical literature, and the coverage of TPE by the popular press. During the past ten years hundreds of articles have been published in the medical literature, including case reports, research results, editorials and letters. This literature is a

valuable source of information on a number of topics, including communication of information (who cites whom) and the participant's view of the procedure (who expresses concern about safety or enthusiasm about the procedure).

While the medical literature provides a "professional" account of the evolving technology, the reporting of this literature in the popular press provides the lay view of the procedure. In order to understand the perspective of potential patients receiving information through the media, I collected and analyzed the popular accounts of TPE in magazines and newspapers such as Time, Newsweek, and the New York Times.

Other sources of written documentation include advertisements and brochures prepared by the medical equipment companies, market research reports written by financial analysts, and correspondence between patients seeking treatment and physicians. My basic strategy with documents was to collect everything I could find dealing with TPE and later analyze the contents of the material according to categories. Data from all sources was coded and analyzed using content categories developed in the course of the research.

In studying a complex process like the development of a new medical technology it is difficult to be a participant observer in the classic sense. One cannot be present for every crucial stage in the innovation process or be in contact with every physician researcher. Yet I did not want

to ignore the important step of directly observing the social setting of innovation: the TPE treatment unit. Thus, in addition to interviews and work with the literature, I conducted participant observation fieldwork in TPE treatment units.

A total of twelve TPE units were studied, four in the U.K. and eight in the U.S. Because of the nature of the international research community under study, I chose to observe a large number of centers rather than remain in one unit for the entire study. The majority of units were observed for short periods of time, usually a few days. However, five units were studied more intensively, for time periods ranging from two weeks to three months. A total of six months was spent doing daily observation in TPE treatment units. I conservatively estimate that I observed over 200 TPE procedures being performed.

Direct observation allowed me to study the response of patients to treatment as well as the general social interaction in the unit. During the longer periods of observation, when I stayed in a unit for a number of weeks or months, I was able to observe the interaction of unit actors with important outside participants in the development of TPE. Most importantly, I was able to study the social interaction of physician investigators and medical equipment manufacturers.

Although the TPE treatment units were the primary setting of participant observation, I also was able to observe less formally in other settings. In visits to the headquarters of the medical equipment firms that manufacture TPE equipment I was able to take a brief look at their organization and functioning. I was also able to observe one major international plasma exchange conference. This helped me to understand the process of communication of information at scientific meetings.

A final source of data for the project was quantitative information obtained from the TPE treatment units visited and from the medical literature. As described earlier, data on the numbers of procedures performed in TPE units was collected in order to document the increasing use of TPE.

To summarize, the procedures employed in this research were eclectic and opportunistic. Classic anthropological techniques of participant observation and interviewing were adapted to the unique situation of studying TPE. Unusual archival sources of data, such as market research reports, the lay media, the professional medical literature, and materials produced by medical equipment companies were all exploited. This array of techniques was necessary in order to study the interacting social worlds of TPE participants, ranging from small treatment centers, to international research meetings and the headquarters of multi-national corporations.

Limitations

The anthropological case study approach has limitations which are well understood. The most serious limitation is that generalizability to other, similar issues cannot be assumed. The knowledge gained from studying TPE may not be immediately relevant to other medical technologies. This problem is common to almost all research within the ethnographic tradition of anthropology. It is my view that the loss of generalizability is more than compensated for by the power of an anthropological case study approach. Other forms of research would not allow the discovery or identification of crucial social and cultural influences on the development of an innovative medical technology. The power of ethnography lies in its ability to identify new variables which may prove to be important but are not yet understood well enough to be studied in a quantitative fashion. Since the social and cultural forces which affect the development of medical technology are not yet fully understood, an anthropological study is a necessary and important first step.

A more serious limitation arises from my sampling procedures. Since I was studying the process of innovation in medicine, I talked almost exclusively to physicians, patients, and nurse/technicians who had already made the choice to use TPE. This choice was justified by my interest in documenting the social and cultural forces which speed

the adoption and use of new therapies. Naturally I needed to talk to physicians and patients who had made the choice to use the technology. Unfortunately, this meant that I did not interview systematically physicians or patients who had made the choice not to use TPE. Since non-users are ultimately an important part of the overall environment of a new technology this creates a natural bias in the data and analysis presented here. This bias is unavoidable because my major concern is with the social setting of early innovation, including the behavior of enthusiastic users.

A final qualification concerns the scope of the study. In medicine, the underlying American cultural preoccupation with mastery of the body via ever more sophisticated equipment is supported by important political and economic considerations. The systems of financing and delivering health care in American society have favored the hospital as the setting for providing services and the use of high-technology devices. For example, American physicians are reimbursed for their services in a fashion which is dramatically skewed toward the use of machines and procedures as opposed to more cognitive services, such as interviewing patients or providing counseling about health behavior (Schroeder and Showstack 1979). Although these issues are important in furthering our understanding of the technological imperative, they will not be developed in great detail in the dissertation. Where relevant, I will mention structural and economic features of the health care

system which contribute to the technological imperative. My major focus, however, is on the meaning of technology for those who use it and social process at the level of individual treatment units.[11]

Overview

The overall structure of the dissertation is described below. I begin with a broad, historical overview of the technology of TPE, eventually narrowing the focus to the social interaction of specific treatment units.

Chapter II reviews the historical origins of TPE, examining the scientific and intellectual antecedents of the new procedure and the development of the equipment necessary to perform it. This chapter provides the necessary context for the material which follows.

Following this review, Chapter III explores the relationship between the biomedical equipment industry and innovating research physicians. I discuss how this tenuous relationship is maintained through a system of social exchange. The resulting social organization allows for the maximum flow of information about new medical technologies, a social feature which supports the technological imperative.

Chapter IV moves to an examination of the two key partners in medical innovation: research physicians and patients in need of therapy. The meaning of TPE for each

group is the focus. For physicians, this meaning is complicated by the tensions inherent in their dual roles as researchers and clinicians. The patient's desperate need supports the technological imperative. I review how patient demand for treatment is a potent force in moving new therapies along the experiment/standard therapy continuum.

The actual social context of innovation is analyzed in Chapter V. I discuss the social differences between "experimental" and "routine" treatment settings. An explication of these differences reveals how the meaning of a new technology evolves. Through an examination of actual ward rituals I discuss the process of routinization, demonstrating how the meaning of a new technology derives from the social setting itself. The role of the nurse as "ritual specialist" is highlighted.

The conclusion (Chapter VI) explains how the social process of routinization is transformed into a "moral imperative" to provide new treatments. Once the meaning of TPE as a standard therapy is established, a treatment imperative is experienced by individual clinicians as they care for their patients. The social implications of a moral imperative to provide innovative medical care are the main focus of the conclusion. The technological imperative has consequences in two areas: In the health policy arena, implications for the overall cost of care, clinical safety, and the potential effectiveness of technology assessment programs are reviewed. And finally, I discuss the

implications of the technological imperative for bioethics, highlighting potential limitations to patient autonomy in decision-making.

Notes

1. This is a useful term employed by the English to describe people, including social scientists, who blame physicians for a wide variety of social ills.

2. A number of terms have been used in the medical literature to describe this procedure, including "plasmapheresis," "plasma exchange," "therapeutic haemapheresis," and "therapeutic apheresis." Many alternate spellings exist as well. For consistency, I will use the term therapeutic plasma exchange, and the acronym TPE, throughout this dissertation.

3. The expense of TPE comes from four sources: 1) the capital outlay for purchase of a cell separator (approximately $20,000, depending on the machine selected), 2) the cost of the disposable plastic products (software) needed to operate the machine, 3) the salary cost of trained personnel to administer the treatment, and 4) the high cost of the commercially produced plasma replacement products.

4. These hypotheses are hard to test because the exact number of machines sold at any particular time is the most difficult type of information to obtain from the equipment manufacturers. They consider such information proprietary because it is directly relevant to issues such as their overall "market-share."

5. The policy implications of this phenomenon will be addressed in the conclusion.

6. My thanks to Lydia Jensen of the University of California, San Francisco, Medical Library for valuable assistance with this complex task.

7. It is important to keep in mind that the arguments presented here about the social context of technology development apply only to this early phase of TPE's development, the upswing portion of the curve when a new technology is in the early phases of clinical use. The social forces which define the latter stage, the stage of critical reflection and disillusionment, have not been examined. These would require a separate, complex study.

8. They are, of course, as influenced by the non-monetary benefits of association with a new technology -- such as increased prestige -- as are American physicians.

9. An explicit comparison of the development of TPE under the English National Health Service with the setting of American fee for service medicine would require additional systematic (and quantitative) research beyond the scope of this dissertation.

10. Throughout the dissertation I alternate between using individuals' real names and pseudonyms. In Chapter II, where I discuss the actual historical development of TPE, I use the actual names of both individuals and organizations. Much of the material discussed here would be available from published sources or is a matter of public record. In the remainder of the dissertation I do not use any real names, but make use of pseudonyms for all individuals and equipment companies. The latter chapters are based on my interpretations of confidential interview materials or observations.

11. These political and economic issues are well known and discussed at length in the literature of health policy, health services research, and health economics (see, for example, Iglehart 1984, Institute of Medicine 1984, McKinlay 1982, McNeil and Cravalho 1982, Fuchs 1974).

Chapter II

THE HISTORICAL DEVELOPMENT OF THERAPEUTIC PLASMA EXCHANGE

> Daily experience satisfies us that blood letting has a most salutory effect in many diseases, and is indeed the foremost among all the general remedial means.
>
> William Harvey

In order to understand the social context of an evolving technology an account of its actual development is essential.[1] The history of TPE is especially important because the events leading up to the eventual clinical applications of the technology were extremely complex. Innovation resulted from a combination of forces, including: breakthroughs in basic scientific research, advances in the medical equipment industry, and experimentation by clinical researchers. This account of the development of TPE refutes the naive assumption that advances in medicine are always rational, predictable, or linear. The history of TPE is more accurately depicted as a collection of false starts, chance events, promising anecdotes, expressions of wild enthusiasm, and disappointments.

In this chapter I discuss the historical development of TPE from three separate perspectives. I begin by relating the "intellectual" history of TPE, discussing the advances in basic science that were essential for the eventual

clinical use of the technology. Second, I will review the development of the "hardware" (blood cell separation equipment) necessary to carry out TPE. Third, I will describe how the technical advances, together with increasing medical knowledge, resulted in the development of plasma exchange as a therapeutic modality. Since many of these events took place simultaneously and in scattered places around the world I am left with the task of creating analytic divisions which often seem quite arbitrary. Thus the reader should bear in mind that the separation of this historical presentation into categories such as intellectual history and equipment development, although essential, ignores the true complexity of the process of clinical innovation. In reality there is a constant interface between basic science, technology, and clinical application. The historical account is meant to provide the background for understanding the analysis of the social context of TPE which will be presented in later chapters.

The history of TPE brings up many important issues which have been of concern to historians of science. The basic idea of removing large quantities of plasma and replacing it with substitutes appears to have arisen almost simultaneously in the minds of many clinical scientists. Some of these workers were explicitly aware of the progress others had made, but many were not. It was certainly not the case that a single dynamic innovator made a "discovery" and started down a path of research which others soon

followed. Rather, as Kuhn (1962) has suggested, the set of ideas necessary for the innovation to occur were "in the air" and were taken up quite rapidly by a number of researchers.

Sources

This account of the historical development of TPE was drawn from three major types of source material. I relied chiefly on interviews with the physicians and medical equipment industry executives who were directly involved with TPE from its inception. I also made extensive use of the original scientific literature, consisting primarily of case reports about early use in patients and descriptions of the new technology. Finally, since this project began a small amount of secondary literature has become available, including Hamblin (1979); Lowenthal (1976); and Millward and Hoeltge (1982). I have been able to make use of that literature in constructing this account.

The Scientific Origins of Therapeutic Plasma Exchange

Blood-Letting and TPE

TPE is a mechanical system that removes trouble-causing substances from the blood. When thinking about TPE it is hard to avoid the parallels with blood-letting, a form of therapy found in many of the classic medical traditions of the world. In the West phlebotomy dates back to the

Hippocratic corpus and was used well into the era of scientific medicine. One of my English informants volunteered, "it is only since World War II that leeches have disappeared from the pharmacies of some London teaching hospitals." The modern use of TPE to remove harmful substances from the blood has much the same logical basis as the traditional use of phlebotomy to restore a balance of bodily humors. The underlying premise is easy to grasp: something harmful is removed and balance is restored. The harmful element may not be inherently dangerous; it may be detrimental only when produced in excess.

In modern blood-letting the imbalance is located in the body's immune system, not in the four basic elements of humoral pathology. In spite of the logical similarities of the techniques, I do not mean to suggest that TPE grew directly out of the practice of blood-letting. Clearly this is not the case; the practice of excessive bleeding fell into disrepute in the late ninteenth century. Nonetheless it is curious that modern technology has stumbled upon a form of therapy so widely employed on an empirical basis in previous time.

Plasmapheresis in the History of Medicine

In fact, the first authors to employ the term "plasmaphaeresis" in an English language article speculated that their new method might be an improvement on "...the time honored but often debatable venesection of medical

practice" (Abel, Rowntree, and Turner 1913-14:628). These researchers speculated that a method as widely used as blood-letting must contain a basis of truth. Dr. John Abel and his associates at Johns Hopkins devised an experimental method of withdrawing blood from dogs, separating plasma from red cells and returning the red cells with Locke's solution. They called their procedure plasmaphaeresis, from the Greek "aphaeresis."[2]

Discontinuity in Medical Innovation

Abel and his associates were engaged in basic experimental pathology. Although their ultimate goal was the "relief of toxaemia," their research had no practical objective. In fact, Abel developed the first apparatus for performing renal dialysis (Comroe 1983:61). However dialysis did not "catch on" in 1914 and neither did plasmaphaeresis. Willem Kolff is generally credited with developing dialysis in occupied Holland during World War II. Although Abel preceded Kolff by thirty years his achievements were ignored. Similarly, Abel's work in plasmaphaeresis also fell on infertile ground. It was not until the 1970s that TPE was seriously applied in clinical medicine.

Many modern physicians working in the field of plasma exchange cite Abel's work as the origin of their field but it is clear that there was no continuous line of scientific development. The citing of Abel is almost ritualistic, an

after the fact justification. These physicians cite Abel and then jump immediately to literature in the fifties, sixties, and seventies (without demonstrating any links) as they attempt to create a rational history for their work.

The ability to apply the technologies of dialysis and TPE in clinical medicine took many years and numerous other scientific achievements. In his study of the scientific advances leading up to cardiac surgery Comroe (1983) demonstrates how often there is a lag between discovery and application. One example is the vascular surgery techniques which make possible modern heart transplantation. Comroe describes how Nobel laureate Alexis Carrel, in the first decade of the twentieth century, "...performed every feat and developed every technique known to vascular surgeons today", including heart transplantation in animals (1983:180). Of course it was not until 1968 that a human heart was successfully transplanted. The technical ability to perform a medical procedure is necessary but not sufficient for its use in clinical practice. In the case of TPE the technical ability to carry out the procedure preceded its widespread use by many years.

Related Scientific Developments

Comroe's detailed discussion of the "intellectual history" of open-heart surgery is immediately relevant to the case of TPE. Many of the advances necessary for John Gibbon's heart-lung bypass machine were also prerequisites

for the clinical use of an extracorporeal technique such as TPE. A few of these include: knowledge of human blood groups, an effective anticoagulant, an understanding of asepsis and aseptic technique, and a pump whose design and material would not damage human blood cells. To exhaustively review the discoveries necessary to accomplish a plasma exchange one would need to go back, at the very least, to William Harvey's 17th century discovery that the blood circulates. One of my physician informants, after describing how he happened upon the use of TPE for a particular type of kidney disease, emphasized that the technical details were trivial compared to the "seventy years of experimental pathology" that had informed his view of the disease under study.

Other Blood Manipulating Technologies

The idea of removing an obviously harmful and known substance from the blood is one intellectual antecedant of therapeutic plasma exchange. Another variant of this, the concept of exchange transfusion, is also relevant to the history of TPE. Exchange transfusions were done manually in the years before TPE was developed, removing and replacing one unit of blood at a time. This technique was used in treatment of hemolytic disease of the newborn. Here the noxious substance (maternal antibody to the infant's red blood cells) was quite well understood.

The idea of manipulating the blood for very specific purposes was common currency in medicine by the 1960s. The use of the heart-lung machine to oxygenate blood during open heart surgery has already been mentioned. In addition, renal dialysis came into widespread use during that decade. In dialysis the patient's blood is removed and forced to flow past a semi-permeable membrane. A solution of basic body salts on the other side of the membrane (the dialysate) allows the passage of unwanted electrolytes, such as sodium and potassium, from the patient's blood into the electrolyte bath. Although the basic principles underlying dialysis are very different from the principles of TPE, both depend on similar means of manipulating the blood outside the patient's body. Physicians specializing in renal disease found it particularly easy to accept the idea of TPE because of their familiarity with dialysis, which sped the acceptance of TPE in its early stage of growth.

Use of Plasmapheresis in the Hyperviscosity Syndromes

The more immediate clinical history of TPE begins with the use of plasmapheresis in the management of the hyperviscosity syndromes. In a disease such as Waldenstrom's macroglobulinemia, the underlying pathology is caused by a neoplastic disorder of B lymphocytes (a type of white blood cell) which results in an excess production of a monoclonal gammaglobulin. To put this more simply, one specific type of protein in the blood (IgM, an

immunoglobulin) is over-produced to such an extent that the blood becomes too thick (hyperviscous). The results of this are serious circulatory problems, visual disturbance, and neurological symptoms. Although treatment of the underlying disease is usually not successful, the symptoms of the disease can be handled by simply removing the excess protein which circulates in the plasma.

The simple removal of protein from the blood in order to counter symptoms caused by its excess presence is the most direct antecedent of modern TPE. In the 1960s, when this treatment was first applied, it was done using manual methods and without replacement of the depleted plasma (Solomon and Fahey 1963; Lawson 1968). The manual methods employed were derived from the basic technology of blood banking; blood was removed by gravity, as if for a donation, centrifuged, the plasma discarded, and the patient's own red cells returned.

This procedure, which is technically the only correct use of the term plasmapheresis, was originally developed during the Second World War when large quantities of plasma were needed. Plasmapheresis in a blood bank, or non-therapeutic plasmapheresis, is a method of blood donation which allows the donor to give more plasma, and donate more frequently, than if red cells were also removed. Thus plasmapheresis, a method developed for use in blood collection, was modified for therapeutic use.

Physical Removal of Noxious Substances and Expansion to Machine TPE

Following the first therapeutic trials in the hyperviscosity syndromes, TPE was adapted for use in a number of other diseases which involved the physical removal of harmful substances from the plasma. The substances removed included metabolic by-products, various poisons, and excess cholesterol. In the early 1960s this work was all carried out using manual plasmapheresis methods described above. When blood cell separator technology became available, most researchers turned to the machine to increase their speed and efficiency. However, the use of the machine to perform TPE was not a major intellectual breakthrough; the basic idea, removal of unwanted substances, did not change.

The earliest published use of TPE utilizing the blood cell separator machine was an attempt to treat acute liver failure with plasma exchange. In liver failure there is a buildup of metabolic by-products in the circulation. This 1969 attempt, which made use of an early cell separator prototype (the I.B.M./N.C.I machine, described in the equipment development section below), was initially reported in a French medical journal (Buckner, et al. 1975). Another early application was Thompson's work in using TPE to treat an extremely rare hereditary disease called type II-A familial hypercholesterolemia (Thompson, Lowenthal, and Myant 1975). Patients with this condition have such high

levels of cholesterol in their blood that they usually die from heart disease in early childhood. As in the use of TPE for hyperviscosity, the basic principle underlying treatment was removal of an unwanted substance.

Expansion to Antibody-Mediated Disorders

Although some of this early work led directly to newer uses of TPE, other attempts, such as the work in liver failure, proved to be without merit. Results of these early trials were published in relatively obscure journals and not widely read. The one area in which activity continued was within the field of hematology. Because many of the early cell separator machines were physically located within blood banks and administratively controlled by blood bank physicians these physicians were best able to see the potential for new applications of the technology. It was hematologists and blood bankers who began using TPE to treat immune disease, which ultimately proved to be an important step.

One such early application was at the University of Minnesota, where TPE was used for several rare conditions in the early 1970s. These conditions included "traditional" applications such as hyperviscosity but also extended into antibody-mediated diseases. For example, the Minnesota group used TPE to treat hemophilia patients who were producing antibody against (and hence destroying) the Factor VIII transfusions which kept them alive (McCullough, et al.

1973). These researchers later expanded their work to other antibody related diseases such as thrombocytopenia (in which platelets are attacked) and hemolytic anemia (in which red blood cells are attacked) (Branda, et al. 1975). Citations in their early publications indicate that they were aware of the previous literature about TPE in liver failure and the hyperviscosity syndromes. Although the Minnesota group's reports were some of the first to document use of TPE in autoimmune disease, they were published in a blood bank specialty journal, Transfusion, and thus were not widely circulated.

Another early application by hematologists was the use of plasmapheresis (with manual methods) and later of actual plasma exchange (with the machine) to treat Rh disease (Powell 1968; Fraser, et.al. 1976). In order to allow the mother to carry a baby to term, plasmapheresis was used to remove the Rh antibody circulating in the mother's blood. This application also came from the blood banking community because of their experience in collecting blood from Rh sensitized women in order to manufacture a diagnostic reagent and later for production of anti-D to prevent Rh disease.

An Intellectual Breakthrough: TPE and Autoimmune Disease

The most significant intellectual leap in the development of TPE came with its application to the autoimmune diseases. TPE's earlier uses in the

hyperviscosity syndrome and related diseases involved a fairly straightforward idea: removal of a substance, such as IgM protein, cholesterol or Rh antibody, that was causing harm because of its presence. But these early applications did not lead to more general use of TPE. One physician informant commented, "...although they have prior claim to the use of the technique, they didn't see it for what it could be, a technique used in all sorts of different diseases."

Similarly, although the early use in antibody mediated disorders like Rh disease and removal of anti-Factor VIII antibody in hemophilia were important, these diseases are caused by classic production of antibody in response to a foreign antigen, unlike autoimmune disorders in which the body attacks its own tissue. Although the disorders are both caused by antibody production, in Rh disease, for example, where the antigen is of foreign (non-self) origin, the basic mechanisms are well understood. I believe that the significant intellectual leap occured when researchers decided to apply plasmapheresis to the field of autoimmune disease. This advance was made possible by a burgeoning knowledge base in the field of clinical immunology. Since the growth of TPE was intimately tied to advances in clinical immunology, it is crucial to understand, briefly, the state of the field.

An Expanding Fund of Knowledge in Immunology

The 1970s were a period of rapid expansion in knowledge about the autoimmune diseases. The concept that an auto-immune process could be responsible for a particular type of pathology was first advanced in the late 1930s (Burnet 1972:109), but it took decades before knowledge of the immune system and experimental techniques were available to demonstrate the validity of this hypothesis. The first laboratory proof of autoantibodies in human disease came in 1957 when Gadjusek and Mackey reported finding a high titer of antibody to human tissue extracts in a case of macroglobulinemia (Ibid.:4).

Sir MacFarlane Burnet, a Nobel prize winner for his theory about the nature of antibody production (the "clonal selection" theory), states, "As of 1971 every pathologist and every academically minded physician is aware that a steadily growing number of subacute or chronic diseases are being spoken of as auto-immune, i.e. resulting from misdirected immune responses against tissues or cells in the body" (1972:2). Thus, at precisely the time cell separation technology became available the intellectual concept of autoimmunity as an important cause of disease was coming of age, acquiring increasing validity within the scientific community.

The validity of autoimmune disease theories arose from both expanding basic knowledge and clear experimental evidence of the existence of autoantibodies. Unequivocal

proof became available only when a scientific technique for measuring autoantibodies was developed. Rosalyn Yalow's Nobel prize winning discovery of radioimmunoassay made possible the measurement of minute quantities of autoantibody in the circulation. Before the development of radioimmunoassay, techniques of autoantibody measurement were extremely crude. The ability to measure precisely the level of autoantibody in the blood was crucial to the development of TPE.

It is my opinion that the expanded paradigm of TPE use to autoimmune conditions was a significant leap which accounts for the rapid growth of the technique documented in Chapter I. This was an important new idea that spurred rapid geometric growth rather than a logical next step in an arithmetic expansion curve. My opinion is supported by some of my physician informants, but others saw the development as gradual. The difference related, at least in part, to the sub-specialty of the physician. Hematologists, especially those who had been involved with the earlier use of the machine for granulocyte (white blood cell) transfusion (described below), saw the innovation process as more continuous. Other physicians, such as neurologists and rheumatologists, became familiar with the process only later. Thus not all physicians and researchers will support my interpretation, varying according to their own vantage point during the development process.

Two Important Publications

TPE first attracted significant interest in the medical community when it was applied to two important autoimmune diseases: Goodpasture's Syndrome, and systemic lupus erythematosus (SLE). In April 1976 two articles on TPE appeared in the same issue of the widely circulated British medical journal The Lancet. Lockwood and collaborators (1976) reported the results of using plasma exchange in seven patients with Goodpasture's Syndrome and Verrier Jones' group (1976) reported on eight patients with SLE treated with plasmapheresis. (Goodpasture's Syndrome is a type of severe, sudden kidney failure. SLE is a chronic connective tissue disorder.)

The use of TPE for SLE can be traced directly to the experience of treating Rh disease discussed above. Dr. John Verrier Jones, who published the first work on TPE for SLE, had been exposed to the technique when he worked with an early researcher in Rh disease in Bristol, England. Verrier Jones treated his first lupus patient in July, 1974. He described this attempt as a move of "desperation." (See Chapter IV for a discussion of the "desperation reaction" experienced by physicians developing new treatments.) Lockwood's first use of TPE will be discussed in detail below.

The two attempts to treat autoimmune disease reported in the same issue of The Lancet, although independent of one another, occured almost simultaneously. Verrier Jones

treated the first SLE patient in July, 1974; Lockwood and his colleague Peters treated the first (published) Goodpasture's Syndrome patient in August, 1974. Both physicians were responding to a similar intellectual climate of opinion as well as basic advances in equipment technology and clinical immunology.

Independent Invention vs. Diffusion: Issues of Priority in Scientific Discovery

Because the invention of TPE involved putting together a number of preexisting discoveries and ideas it may be impossible to ascertain the exact chronology of discovery. In fact, it seems that the idea appeared spontaneously to a large number of clinical researchers in different parts of the world at about the same time. Many of my physician informants emphasized that the use of TPE was not a major intellectual achievement. Rather, they used phrases such as, "...it became quite obvious that you could turn [the machines] round the other way and use them to get large volumes of plasma off" and "...[it was] just a natural outgrowth." Once established, the procedure spread very quickly. One researcher used the term "epidemic" to describe the rapid expansion of TPE. He stated, "before we knew it, everyone was doing it." This very rapid expansion also increases the difficulty of sorting out the exact chronology of development.

Despite these provisos that TPE was not a major intellectual discovery, I found in my research a great deal of physician interest in the question of priority. The scientists would verbally state that the issue mattered little and yet also reveal that they had given the idea considerable thought and in some cases gone to a great deal of trouble to determine exact priorities in discovery. This is a matter of no great surprize and fits in well with Merton's discussion of the importance of priorities in scientific work (Merton 1973).

Although the search for truth suggests a scientific disinterest in the immediate rewards of research activity, hubris is an expected, and valued, personality trait in scientists. The ideal of pure science conflicts with the absolute value placed on originality, revealed in the (partly disguised) but omnipresent concerns about who did TPE first, with what machine, and for which new and interesting disease.

The need for "firsts" thus in itself becomes a force in the technological imperative. On the positive side, innovation is stimulated. However, on the negative, physicians race to associate themselves with "new" techniques before they can be properly evaluated. (You get credit for a "first" even if it doesn't pan out.)

My physician informants would emphasize the many "firsts" that had occured in their institutions, while at the same time stating that, "it's largely a game, really."

But a game of deadly seriousness. One physician researcher had his secretary telephone a number of the first people to publish in the field in order to determine the exact dates on which their first patients were actually treated. A number of physicians attempted to persuade me that the idea to use plasma exchange had been their own. Even if they recognized that others had used the technique earlier they were keen to identify themselves with new and original work. For example, one physician told me, "I had two occasions when I thought quite independently that it would be a useful thing to do." He continued, stating that he later realized that, "[we were] making it up as we were going along, rediscovering something that had been discovered years ago."

Hammersmith Hospital and TPE: A Case Study

Since there is much more to scientific discovery than the dry reporting of results in scientific journals I will continue the story of TPE and autoimmune disease by describing the exact sequence of events in the first use of TPE at one particular hospital. This hospital, the Hammersmith Hospital and Royal Postgraduate Medical School in London, is very important because the use of TPE in two autoimmune diseases, Goodpasture's Syndrome and myasthenia gravis, was originated by research workers connected with this institution. Their use of TPE to treat Goodpasture's

Syndrome was a very early and influential, although not technically the first, use of plasma exchange in a documented autoimmune disorder.

The Hammersmith Hospital is a major research facility with strong ties to the Medical Research Council (M.R.C.), the British equivalent of the National Institutes of Health. As a prestigious London teaching hospital Hammersmith has far more resources devoted to it than the average district general hospital. Although it serves a particular region and population base, it also receives referrals from throughout the country for specialized services. This type of hospital is best described as a flagship in the National Health Service hospital fleet. Hammersmith is the site of an M.R.C. funded leukemia research unit. Because of this interest in cancer therapy (primarily granulocyte transfusion), in 1971 the M.R.C. leukemia unit purchased the first cell separator machine manufactured by the Aminco company that was sold in England. (See the equipment development section below for a description of the different machines.)

Thus, the equipment necessary to carry out TPE was available; the next stage was intellectual, leading to the important publication in Lancet mentioned above. As the physician credited with the idea of using the machine to treat Goodpasture's Syndrome, Professor D. Keith Peters, stated, "my unit was...certainly not directed toward something like plasma exchange." (Peters was a senior

colleague of C. Martin Lockwood, the first author of the Lancet paper.) Rather, the nephrologists working at Hammersmith were investigating the underlying mechanisms of glomerulonephritis. Peters is a renal physician with strong interests in immunology. When asked to account for the development of TPE in autoimmune disease, Peters commented, "I suppose it's really chance favoring the prepared mind."

The "prepared mind" came from familiarity with advances in experimental pathology; according to Peters, "it was common currency by the early seventies that things in the circulation were damaging the kidney." "Chance" came as the result of a lunch between Dr. Peters and a hematologist from the M.R.C. leukemia unit, John Goldman, shortly after the arrival of the new blood cell separator. Divisions between departments are not absolute at Hammersmith. As Peters stated, "we're a relatively tight, small community on this site; [one sees] a great deal of one's colleagues."

At this lunch, Goldman described to Peters how easy it was to do various maneouvers with the cell separator. Peters claimed that the next step, the intellectual one, was relatively simple. "...It suddenly dawned on me that plasma exchange, which I had in fact been thinking about separately, would be a very easy thing to do, in patients, because of the cell separators...The moment I thought it was technically easy, it was in my mind." He added that his previous thoughts on the topic had dismissed the idea of plasma exchange as too difficult, "a right performance."

The lunch between Goldman and Peters which led to the first use of TPE in Goodpasture's Syndrome has acquired the status of an "origin myth" in succeeding groups of physicians working at Hammersmith. A number of physicians mentioned "that lunch between Professor Peters and Goldman" when I asked them to recount the history of TPE as therapy.

The idea itself still had to overcome considerable opposition. Goldman, for example, reports that he first told Peters, "That's silly; it won't work." Nonetheless, the renal team proceeded, making use of Dr. Goldman's machine. When they eventually reported an apparently successful treatment back to Goldman he remained sceptical, telling Peters that he did not believe their results.

One of the intellectual barriers that needed to be overcome in order for TPE to be tried in humans resulted from experimental data from animals which showed that removal of antibody from the circulation might actually cause a rebound effect, resulting in levels of antibody higher than before the original attempt at removal. The commercial production of antibody for medical uses, for example tetanus antibody, depends on this phenomenon. The Hammersmith team debated these issues, eventually rejecting the notion of rebound antibody synthesis. Peters made this decision on the basis of a belief that autoantibody production mechanisms were poorly understood and might be quite different from the response to foreign antigen injected into an experimental animal. (This has turned out

to be correct.) In addition, they decided to combine the TPE procedure with immunosuppressive drug therapy to counteract the rebound phenomenon.

With this much accomplished, they proceeded to treat their first patient with Goodpasture's Syndrome, albeit in a "half-hearted" way. This patient already had fairly advanced disease, indicated by lack of kidney function, and did not improve as a result of the treatment. (The importance for later research of the first patient's response will be discussed in depth in Chapter IV.) It is significant that they did not attempt TPE again for two years after this "failure." Also, at this point, in 1972, there was no way of knowing whether the TPE treatment was actually removing the antibody. The next necessary step was a reliable way of measuring the amount of antibody in the circulation so that the effectiveness of the treatment could be judged.

This piece of the puzzle came from an independent source, over 10,000 miles away. In 1973, Curtis Wilson of the Scripps Clinic and Research Foundation in La Jolla, California, had developed a quantitative radioimmunoassay for the autoantibody present in Goodpasture's Syndrome. (The antibody is technically called anti-glomerular basement membrane antibody, or anti-GBM Ab). As Peters recalls, the field of immunopathology was fairly small in the early seventies and he had a personal acquaintance with Wilson, making it, "very easy to get in touch with him." Ease of

communication within the international research community is an important element in medical innovation.

In August 1974 a patient with Goodpasture's Syndrome was transferred to Hammersmith Hospital. Since the disease is extremely rare, a researcher wanting to study the disease must frequently wait for a long period of time before an appropriate patient is located. This particular patient was referred to Hammersmith because of the availability of plasma exchange. The patient's referring physician had asked if Hammersmith had anything "new" to offer that the referring hospital could not provide. This patient was the first person successfully treated with TPE for Goodpasture's Syndrome. The Hammersmith team performed the procedure "in the dark," meaning that they were unable to determine directly if the patient's antibody levels were falling. They sent samples of the patient's blood to La Jolla where Curtis Wilson performed the new test to measure the amount of autoantibody in the circulation. The results of these studies were not obtained until after the patient had shown clinical improvement, demonstrated by improving kidney function. After the fact, the researchers were able to document that the patient's improvement was directly related to the reduction in antibody produced by the plasma exchange. Contrary to the usual clinical course in Goodpasture's Syndrome, a serious disease with a very high mortality rate from uncontrollable lung hemmorhage and/or kidney failure, the patient recovered kidney function.

These successful results were published the next year in the British Medical Journal as a case report (Lockwood, et al. 1975).

Because this first use of TPE in Goodpasture's Syndrome was extremely important, I will summarize the factors, both intellectual and structural, which made the innovation possible. First, the disease itself had only recently been "solved" and in a scientifically elegant fashion. It had been shown that antibody removed from a diseased individual would produce the syndrome in experimental animals. As one of my informants said, "Koch's postulates were met."[3] Thus, the appeal of using TPE for Goodpasture's Syndrome came from the idea of directly removing the newly identified pathological agent. Furthermore, it was immediately possible to document this removal through a quantitative radioimmunoassay, which gave the clinicians confidence that their approach was correct. Added to this is the fact that Goodpasture's is an immediately life-threatening disease. Thus the clinicians had great incentive to try "something" to save the patient from the prospect of imminent death by lung hemorrhage or loss of kidney function.

These factors were of general importance, but specific to the situation at Hammersmith was the intellectual climate of open communication which aided the original idea. Equally important were the availability of the cell separator machine and the fact that there was enough administrative flexibility in the hospital to permit the

machine's use by another group of physicians for a totally unproven purpose. Yet another important element was the N.H.S. referral system which allowed for the transfer of patients with extremely rare diseases to a single center where their disease could be studied. Quickly seizing the opportunity provided by their early success, the Hammersmith team acted swiftly to get their results in press. They also developed their own radioimmunoassay for the autoantibody so that blood samples would no longer need to be sent to California. And finally, they were able to obtain a grant from the M.R.C. which enabled them to buy their own cell separator, hire a technician to operate it, and assign one of the physicians originally connected with the project to continue work as a research fellow.

From their start with a single successful patient with Goodpasture's Syndrome, the Hammersmith group continued to use plasma exchange as a therapeutic tool. Of great importance was their extension of TPE to other diseases of autoimmune origin, most notably, myasthenia gravis. As with Goodpasture's Syndrome, myasthenia gravis is a disease which is caused by the body producing antibody against its own tissue. In the mid-1970s this etiologic theory was first confirmed experimentally by the isolation of the actual autoantibody in work carried out by Jon Lindstrom at the Salk Institute (and almost simultaneously by other researchers.)

Professor Peters next turned to myasthenia gravis for a trial of TPE because it is not as immediately life-threatening as Goodpasture's Syndrome, and thus he hoped to be able to learn more about the actual effects of TPE alone compared to the immunosuppressive drug therapies which were given simultaneously to supplement TPE. When the initial patients with myasthenia gravis actually improved it provided the first direct evidence that the autoantibody believed to cause the disease (antibody to the acetyl choline receptor site at the neuromuscular junction) was responsible for the disease process.

The Hammersmith group treated their first myasthenic patient in April 1976, publishing the results in The Lancet later that year (Pinching, et al. 1976). Another English group had actually tried TPE in myasthenia first (Finn and Coates 1977). However, their patient did not respond and the work was not published until after the other successful reports appeared. (There is some dispute about whether this patient actually had myasthenia.) The following year, an American group at Children's Hospital in San Francisco published their results of TPE in myasthenia in The New England Journal of Medicine (Dau, et al. 1977). By this time, the idea of applying TPE in the treatment of autoimmune disorders was well established. In short order the idea of TPE was transfered to many other diseases of either proven or suspected autoimmune origin, including

multiple sclerosis, Guillain-Barre Syndrome, and rheumatoid arthritis.

Increasing interest within the medical community was illustrated by the appearance of editorials devoted to the use of TPE in the clinical management of autoimmune disease. In the period immediately following this medical "discovery," editorials appeared in widely read, non-specialty journals such as The Lancet (in 1976), the British Medical Journal (in 1978), and the New England Journal of Medicine (in 1977). These editorials coincide with the period of rapid increase in use of the technology, discussed in Chapter I. They also signify an important marker in TPE's progress away from an experimental status, towards general acceptance. With this level of public discussion in the medical community, the technology began to be taken seriously by other clinicians and investigators.

The Development of Blood Cell Separation Equipment

The clinical and intellectual history of TPE predates the invention of the cell separator machine by many years because plasma removal and exchange can be performed manually. But it was only with the development of automated equipment that the procedure began to be used extensively, because the manual procedure is enormously tedious and time-consuming. A description of the manual procedure is helpful in comprehending the impact of the machine. First, the

patient donates a unit of blood in the standard fashion, in which the blood drains by the force of gravity into a bottle or bag containing anticoagulant. Next, the physician or nurse/technician must carry the blood into an adjoining room where the blood is spun into its components in a standard laboratory centrifuge. In the meantime the patient is waiting, with an I.V. in place to keep the vein open. After centrifugation, the plasma is squeezed out of the top of the blood bag and discarded. Finally, the patient's red blood cells are carried back into the patient's room and reinfused through the I.V., again relying on gravity to accomplish the infusion. Once the blood is returned the process begins again from the beginning. Removing a significant volume of plasma, usually around three to four liters, might take over eight hours of full time work.

In contrast, a cell separator machine accomplishes the same task in as little as two hours. (Actual times vary considerably depending on the quality of the patient's veins, hematocrit, and blood viscosity.) One early investigator of TPE stated, "our own work would not have been contemplated without the existence of the cell separator." Thus, the availability of cell separation technology was a crucial factor in the rapid expansion of TPE once the notion of using this as a treatment gained intellectual currency. The fact that the machine predated the treatment, and that the machines were already in place

in hospitals throughout the world, eased its initial clinical application.

Original Purposes of Cell Separation Technology

Now I come to the complicated question of why and how cell separation technology was developed. The key point is that these machines were definitely not developed with the idea of using them to manipulate the body's immune system by plasma exchange. Rather, the machines were developed specifically for use in two other areas of medicine: the blood banking industry and in the treatment of cancer patients. The innovating clinicians who began work in TPE made small modifications in the pre-existing equipment in order to change its functions.

This pattern -- that of a new procedure developing from an existing technology -- is actually quite common in clinical medicine. It is difficult to predict the future use of a new device or drug; its ultimate use and importance may be very different from that originally envisioned. A recent example is the history of the drug cyclosporin A. Originally developed as an antibiotic, its use in preventing rejection of organ transplants was recognized later and it has revolutionized that field. There are equally dramatic examples in the area of medical devices. The heart-lung bypass machine that makes open heart surgery possible was first conceived as a method for treating pulmonary embolism (Comroe 1983). The respirator, developed to support

patients under anesthesia, soon expanded beyond the operating room, making possible the development of critical care units. The fact that TPE did not come about as the result of specific, targeted research programs is not unusual.

Two different types of cell separators were developed almost simultaneously in the two fields of endeavor: blood processing and cancer research. The two eventually merged, with both machines being utilized for general purposes. I will review the development of both types of machine, emphasizing the cooperation between university researchers and industry.[4]

Cancer Therapies and the IBM/NCI Cell Separator

I will begin by discussing the origins of the continuous-flow blood processor developed in the mid 1960s in a collaborative effort between the National Cancer Institute (N.C.I.) and the International Business Machines (I.B.M.) corporation. It was this machine, conceived as a means of improving the treatment of cancer patients, which ultimately was adapted for use in TPE. By the early 1960s many cancers, particularly non-solid tumors like leukemia and the lymphomas, were beginning to respond to aggressive new forms of treatment, primarily chemotherapy. The leukemias, which had been almost uniformly fatal in the early 1950s, were responding to aggressive therapies for the first time. However, the chemotherapy treatments available

were non-specific, wiping out important blood components at the same time as cancer cells. Hence successful therapy required the ability to replenish the patients' essential blood components until their own bone marrow was able to begin producing these elements again. Clinicians needed a method to replace white cells to fight infection and platelets to allow blood clotting, in order to support the patients during the aggressive chemotherapy treatments.

In May 1962 a chance meeting took place between a research physician at the N.C.I. and a research engineer from I.B.M. George Judson, the I.B.M engineer, was at the N.C.I. because his young son was undergoing treatment for leukemia. Emil Freireich, the N.C.I researcher, had been working on manual methods of harvesting both platelets and granulocytes (one type of white blood cell important in fighting infection) from donated blood. A collaboration was formed, and grew when I.B.M assigned Judson to work on the project at the N.C.I. In addition to personnel, I.B.M also supplied other assistance in the form of design and fabrication support. N.C.I reimbursed I.B.M for some of the costs. The immediate goal of the team was to develop a machine which would allow the collection of granulocytes for transfusion, a formidable task because white bloods cells cannot be harvested in the same straightforward way as red blood cells.[5]

A unique set of events was necessary for this collaboration to take place. First, it required the intense personal interest of Judson, the result of his son's illness. Second, it took the flexibility and cooperation of I.B.M. It certainly seems unusual that a large company, especially a company that is not (and was not) a major power in the medical equipment field, would respond so quickly to the needs of the situation. Of course I.B.M is known to be an unusually flexible company, and did have an early involvement in John Gibbon's original work on the heart-lung bypass machine.[6] There was significant scientific overlap between the engineering problems to be solved in the two machines. As Comroe (1983:34-35) points out, this type of collaboration between medicine and industry is highly unusual; industry is usually not willing to take financial risk until they are fairly certain of an ultimate profit.

A certain mythology has evolved around the story of the cell separator machine's development. It is a very American myth, emphasizing how a small group of innovating entrepreneurs overcame all odds and created something new. The story also emphasizes the values of ingenuity and fortitude. For example, Freireich recounts that the materials for the orginal model were obtained, "...almost exclusively from our local hardware store" (1975:xxix). He continues, "I can remember the long hours...spent bathed in human blood mixed with grease in order to develop a laboratory prototype of an instrument designed to process

large volumes of blood on a continuous flow basis" (ibid.:xviii). Indeed, there were a number of complicated technical problems to solve, including how to achieve adequate blood separation with high yields of cells, and how to maintain sterility with rotating centrifuge parts. The important features of this machine were its continuous flow design (blood could be processed continuously rather than in "batches") and the centrifuge bowl which required sterilization (a disadvantage).

Judson, Freireich, and Robert Eisel (an N.C.I. blood bank employee) worked on the project until 1965. At that time the first paper on clinical use of the machine was published and a public showing of the prototype cell separator was made at an instrument symposium. The machine was used to treat a patient with chronic myelogenous leukemia, a kind of leukemia in which huge quantities of white cells are the major danger to the patient. This was the first human trial of the machine in a situation where the patient might actually gain benefit from the procedure (in this instance, reducing the level of leukemic blood cells).

In 1965 Freireich left the N.C.I., moving to the M.D. Anderson Cancer Center in Houston. There he conducted one of the three field trials of the newly developed cell separator. From 1966 to 1975 IBM offered the cell separator machine for sale, although they did not market the machine aggressively.

During this period, another group, the American Instruments Company (Aminco), obtained the design specifications for the I.B.M./N.C.I. machine. These specifications were in the public domain because of the federal funds (from N.C.I.) used in development. A company executive told me that you could buy the design specifications for $75. Aminco, with the help of Robert Eisel, who had worked on the original project at N.C.I before becoming an Aminco employee, developed a streamlined version of the cell separator which they called the "Celltrifuge." This machine was marketed in 1970.[7] Lowenthal estimates that by 1974 there were approximately 100 machines in use throughout the world (1976). Thus it took about ten years from the first idea of a machine to availability of cell separation equipment in major medical centers throughout the industrialized world.

By the late 1970s, when my study began, the market was very complicated. IBM reentered the field with a new machine in 1978 and Fenwall, a division of Baxter-Travenol, also developed a new machine which began to be sold in 1979. A third competitor was the cell separator developed by the Haemonetics Corporation, as described below.

The Blood Banking Industry and Haemonetics Corporation

While the I.B.M./N.C.I. collaboration was taking place in Bethesda, a parallel series of developments was occuring in the Boston area. The researchers involved were not part

of the major assault on cancer but had been working for years on more general issues in blood banking, particularly how to separate blood into its main components and store the components for later use. The storage problem is especially acute for the red blood cell, which maintains its oxygen carrying capacity for a limited period of time. A long term goal had been to devise a method for freezing red blood cells without damaging their function. However, the freezing of red cells proved to be extraordinarily complicated.

The story of the cell separator machine eventually manufactured by Haemonetics Corporation dates back to a machine developed in Sweden in the late 19th century which revolutionized the dairy industry. In 1878 Carl Patrick Gustaf De Laval patented an open, continuous-flow centrifuge for separating milk from cream. During World War II the great demand for plasma led Dr. Edwin J. Cohn of Harvard to adapt this machine, which was operated by a hand crank, for the separation of plasma from whole blood. This early work served as the model for the first blood cell separator machine developed in the period following World War II.

In 1949, Cohn began work on the design for a machine to collect and fractionate blood into its basic elements. This early work had numerous goals, including the collection of blood in its "natural" state for basic research purposes as well as collection and separation of blood for preservation and transfusion. (Blood can be preserved more easily after

being broken down into its component parts.) The ultimate result of this research and development effort was the "Cohn Fractionator," a complex refrigerated centrifuge (Tullis, et al. 1956).

As in the development of the I.B.M./N.C.I machine, a collaboration between academic medicine and industry proved essential. Cohn approached the Arthur D. Little Company (a research and development firm in Cambridge) for "free help in solving some of his problems." This was how Allen Latham, Jr., the founder of Haemonetics Corporation and the key person behind the development of the Haemonetics Cell Separator became involved. In an interview Latham told me, "I was sent over [by Arthur D. Little], as the junior person, to see what it was all about." After this initial exposure to Cohn, Latham continued to work in the field of blood processing, concentrating on the issue of preservation of the red cell.[8]

After Dr. Cohn's death Latham worked for 15 years with Dr. James L. Tullis, also of Harvard and associated with the Center for Blood Research. Latham's major innovation was in engineering a disposable bowl for blood cell separation. Earlier machines (e.g., the I.B.M./N.C.I. described above) had all used centrifuge bowls which required sterilization before re-use, a major disadvantage when working with blood products because of the difficulty of removing contaminating protein particles and the risk of disease transmission, particularly hepatitis. In the late 1960s, the Latham Blood

Processor (with a disposable centrifuge bowl) was ready for market (Tullis, et al. 1967). This machine was based on the Latham centrifuge bowl and, in contrast to the I.B.M./N.C.I. machine, it operated on a batch system rather than continuously processing the blood. A small volume of blood was collected, processed and returned to the patient.

Latham's employer, the Arthur D. Little Company, decided against marketing the machine and bowl, and in 1970 they sold the manufacturing rights to Abbott Laboratories. However, because of a major problem at Abbott (contamination of intravenous fluid solutions they manufactured) they elected not to produce a machine. Thus, in 1972 the patents for the Latham bowl were incorporated into a new company, with Latham at the head, called Haemonetics Corporation. In 1973 the company introduced the Model 30 Blood Separator, a machine which eventually came into widespread use for plasma exchange.

In summary, I have briefly outlined the simultaneous development of two types of cell separators: the I.B.M./N.C.I., first available in a developmental form in 1966 (and made widely available in a modified version, the Celltrifuge, by the Aminco Company beginning in 1970) and the Haemonetics Model 30, available commercially in 1973 (but preceded into the market place by the earlier and very similar Latham Blood Processor). These developments are summarized in chart form in Table 3.

Table 3

Development of Cell Separation Equipment

1878 De Laval continuous-flow cream separator

Haemonetics Cell Separator		I.B.M./N.C.I. Cell Separator	
1950's	Cohn Fractionator developed	1962-1965	Judson/Freireich Collaboration at N.C.I.
1968	Latham Blood Processor (Model 10)	1965	Public Showing of Machine
1972	Haemonetics Corporation formed	1966-1975	Machine Offered for Sale
1973	Model 30 Introduced	1969	First use for TPE (estimated)
1975-1976	First use for TPE (estimated)	1970	Aminco version offered for sale
		1978	I.B.M. re-enters market (Model 2997)

These two engineering feats were based on different initial goals (enhancing cancer therapy and blood processing), resulted in machines with different engineering specifications, and took place in relative isolation from each other. The I.B.M./N.C.I. machine developed out of the interest of an I.B.M. executive with a personal commitment to cancer therapy, tied to the N.C.I.'s role in the ongoing "national war on cancer." In contrast, the Haemonetics machine developed out of one engineer's interest in the preservation of red blood cells and dedication to the idea of disposable components in the blood banking industries. By the early 1980s, a wide variety of blood cell separator machines had become available. Over a half dozen machines were being produced by a number of manufacturers. However, with the exception of membrane filtration devices which are not based on centrifugation of blood,[9] most of them were either modifications (with improvements) or exact duplicates of the two original centrifuge designs.

Summary of Development

Thus, the expertise of American engineering was brought to bear in an effort to solve particular clinical problems. However, as I have already shown, the machine was not designed with TPE in mind.[10] Rather, its use as a direct therapy in removing diseased plasma and replacing it with substitutes came about as an afterthought, primarily as the result of simultaneous innovations by a number of clinicians

in medical centers throughout the world. These physicians had access to the machines because they had been purchased by blood banks or clinical hospital departments to be used for supplying granulocytes and platelets to support cancer treatment programs. With a few modifications, cell separators were easily transformed into plasma exchange machines.

The basic idea is simple: a noxious element is removed from a patient's bloodstream. Therapies based on this fundamental premise have existed for centuries. The advent of TPE was both logical, because of advances in basic science, and serendipitous, facilitated by the technical development of cell separation equipment for an altogether different purpose. Increased understanding of the pathophysiology of a number of diseases led to a desire to remove the offending humoral substance, either excess protein, cholesterol, immune complexes, or autoantibody. While these advances in medical science were underway, breakthroughs in medical engineering were occuring, resulting in the ability to manipulate large volumes of blood outside the body. Perhaps inevitably, a number of clinical researchers put together these two types of advances and (almost simultaneously) "invented" therapeutic plasma exchange.

The medical equipment companies were surprised by this new development; they had not anticipated the expanding use of their machines for TPE. An executive with one company

told me, "It was several years after we had been marketing [the cell separator] that therapeutic plasma exchange came into our cognizance." This caused considerable stress within some of the companies manufacturing the equipment. I will discuss this issue, as well as the nature of the relationship between cell separator manufacturers and clinicians once TPE was "discovered," in Chapter III.

Notes

1. Since the completion of data collection for this project some of the initial enthusiasm for TPE has waned (ECRI 1985; Hamblin 1984; Shapiro and Shapiro 1987). This chapter focuses on the history of the early period of rapid expansion of the technology. See Appendix A for an account of recent reassessments.

2. The use of the word aphaeresis as a medical term (in English) goes back to the mid-eighteenth century. An early dictionary states, "Aphaeresis in medicine denotes a necessary taking away or removal of something that is noxious" (Lowenthal 1976:25).

3. Koch's postulates are the necessary conditions to "prove" the etiology of an illness.

4. In this section of the thesis I will use the actual names of the corporations involved because much of the information I will discuss is a matter of public record. Later, when I analyze the nature of the clinician/company relationship I will use pseudonyms to disguise the specific companies discussed.

5. I will not review the scientific issues involved in granulocyte transfusion, which are quite complex and really an issue peripheral to plasma exchange. Of interest is the fact that granulocyte transfusion, very popular at first, experienced its own technological imperative but fairly quickly fell out of favor as a treatment of severe infection during cancer therapy.

Technical difficulties made it almost impossible to tranfuse enough granulocytes to make a signficant difference clinically. Transfusions proved to add little to standard antibiotic therapy. It is a bit more than a coincidence that just as the machines were less needed for collecting granulocytes they began to be used for TPE.

The transfusion of platelets, on the other hand, has continued to be an important element in the clinical practice of oncology. Recent improvements, such as matching donors and recipients by HLA (human leukocyte antigen) type (in the same way organ donors are matched with recipients), have made platelet transfusion even more effective. Cell separators continue to be used to harvest platelets for transfusion.

6. From 1945 to 1961 I.B.M., through the direct intervention of Chairman of the board Thomas J. Watson, provided engineering help and paid for construction costs for Gibbon's prototype bypass machines (Comroe 1983:34-35).

7. Aminco was eventually purchased by a major medical corporation, Baxter-Travenol.

8. In order to freeze a red cell, it is necessary to mix the cells with glycerol, which must later be removed before the blood can be utilized. Latham became interested in deglycerization. During an industrial sabbatical he managed to arange a lunch with a very prominent Boston clinician who convinced him of the "fundamental importance of the red cell."

9. Rapid changes in the nature of the equipment used to perform TPE have occured in the 1980s. Systems based on centrifugation have been replaced (in some instances) by a new generation of equipment based on the principle of ultrafiltration. With these systems blood is separated into its components as it is passed under pressure through a membrane which allows only cells of a specific size to diffuse through. These new procedures have been greeted enthusiastically because they offer the attraction of selectively removing harmful plasma elements, thus both reducing the cost of the procedure (because you do not discard the beneficial plasma proteins) and increasing its specificity. This is accomplished by combining the plasma with specific reagents which bind with the harmful plasma element. For example, charcoal has been used to remove cholesterol and new antibodies can be created (using new techniques designed to create monoclonal antibodies) to bind with the harmful antibodies present in the circulation (Pineda 1984). There remain many technical and scientific problems to solve before these new systems will replace conventional TPE. For example, in some diseases the actual harmful element in the circulation has yet to be identified or proven to be of pathological importance.

10. Questions of how scientific discoveries are made, or how medical progress occurs, are not of theoretical interest only. The history of TPE also bears on the public policy debate about whether the funding of "pure" or "applied" medical research is the more fruitful investment of public funds. Does medical progress just happen, or can it be targeted, as in the recent assaults on cancer and heart disease? There is no simple answer. This issue is discussed at length by Swazey (1974).

Chapter III

THE BIOMEDICAL EQUIPMENT INDUSTRY

"We know how to make it and how to do it. We know how to translate ideas into product...We bring a lot to the party."

Medical Equipment Company Executive

As the history of TPE reveals, the development of a new medical technology is not solely the result of highly abstract and neutral scientific ideas colliding together in a value-free environment, resulting in new treatments which are evaluated in a purely formal, scientific fashion and proven to be effective. Many other forces are at work. The explosive growth of TPE described in Chapter I cannot be accounted for by scientific and technical factors alone. The "technological imperative" is partly generated from within the paradigm of medical science, but the history of TPE by itself does not provide an adequate explanation. One must also consider the social context of innovation and how that context forms the meaning of TPE for the participants in innovation.

In order to explain the overall development of TPE I shall now move to a dissection of the social processes of innovation. This requires a careful examination of specific moments in the technology's development, trying to isolate

critical points in the social context of TPE's development where the meaning of TPE as standard therapy or experiment is revealed.

In this chapter I will examine the role of the biomedical equipment industry in the development of TPE, focusing on the companies' role in facilitating the communication of information about a new, experimental therapy. Next I will explain the nature of social relationships between clinician innovators and the representatives of equipment companies, describing the reciprocal ties which bind together these partners in medical innovation.

Industry's Contribution: Technical "Know-How"

The first and most obvious contribution of the biomedical equipment industry to the development of new medical technology is the engineering skill and ability to solve practical problems which industry can provide. In modern Western societies industry supplies an institutionalized mechanism for constant invention. Although a small number of new techniques develop exclusively within the community of academic medicine, the complexity of many recent breakthroughs -- such as nuclear magnetic resonance imaging, laser surgery, and the artificial heart -- require a level of expertise which is most available in private industry. One clinical

investigator stated, "...the technology, circuitry, electronic wizardry that's now available in the corporate structure is something you just can't duplicate." Today's medical innovations require a partnership between industry and medicine. As discussed in Chapter II, in TPE the partnership between clinicians and engineers during the phase of initial machine development was extremely important. Both early types of TPE machines were cooperative efforts. This partnership is reflected in the name given to one prototype -- the I.B.M./N.C.I. cell separator.

The contributions of both industry and clinicians during the initial stages of development are crucial. Clearly, engineers cannot create medical equipment in a vacuum, without input from physicians. As one company representative said, "...if you do your homework before[hand]...you can stop design mistakes." Engineering expertise without clinical understanding is useless.[1] Likewise, physicians may have vague, general ideas about what they want to accomplish clinically but have little practical sense of how to carry out a specific task. Allen Latham, the engineer assigned to assist Harvard physicians working on cell separation during the fifties, commented on their lack of expertise, including "violation of basic engineering principles." Another company executive summarized the role of industry, "We know how to make it and

how to do it; we know how to translate ideas into product... we bring a lot to the party."

Although there are exceptions, the majority of medical products are collaborative efforts. Medical innovations do not spring fully formed from the engineer's drawing board, quickly gaining widespread acceptance within the medical community. The partnership between clinical medicine and industry begins during the period of initial innovation and equipment design and continues as the product moves into clinical use.

The Social Context of Collaboration

Throughout the career of a medical technology a relationship exists between the people in private industry who manufacture and market medical equipment and the clinicians who test it and later use it routinely in caring for patients. These relationships consist of concrete, daily exchanges between people, and are thus by their very nature social relationships. The raison d'être of the collaboration is a medical product which results from the recognition of a clinical need and the subsequent testing and marketing of the product. The activities surrounding this product require constant intercourse between research physicians and company representatives. As a result, these relationships have become highly patterned. It is my contention that the nature of the social relationships

between equipment manufacturers and clinical researchers is an important consideration in the development of the technological imperative. The nature of this relationship varies during the different stages of innovation. Although in reality the process is continuous, it will be divided here into two stages.

The first stage, which corresponds to the experimental period of a new medical technology, encompasses the early intense collaboration between clinicians and industry while the equipment is initially being developed. Company representatives jokingly referred to this phase of development as the "cocktail napkin design" period, alluding to designs sketched out over drinks in a pub near the hospital. Once a prototype product exists, these intense relationships continue as companies begin the process of "selling a product physicians don't yet know they need." My field research focused on these early stages of the relationship. After a technological innovation has become accepted as standard therapy, the social relationships shift into a later stage: "the era of the detail man," when company representatives see themselves (and are perceived by others) as ordinary salespeople engaged in classic business marketing techniques. This chapter will emphasize the social relations of the experimental stage.

Qualification about Quality of Data

Before continuing with the analysis of the complex social relationships between clinicians and equipment manufacturers I must interject a note of caution about the interpretation offered here. It is important for the reader to understand that the role of the biomedical equipment industry in the development and diffusion of medical equipment is poorly understood and remains, on the whole, an unexamined issue. A major federal government study on the diffusion of medical technology simply ignored the role of manufacturers, stating, "reliable data about the activities of equipment makers are virtually unattainable" (National Research Council 1979:vii). The authors of this study proceeded on the assumption that the development of new medical equipment, as well as demand for new technology, is generated within the medical community, in isolation from commercial interests.

This assumption is convenient, given the difficulty of conducting research into the role of industry. But considering the obvious importance of commercial interests in the development and marketing of medical equipment I believe it is basically untenable. Thus I have attempted to make an analysis of the role of equipment makers despite the fact that data are difficult to obtain. Although I am unable to provide a definitive quantitative assessment of the importance of industry in the technological imperative,

I believe I have identified central issues involved in company/clinican relationships. This is a crucial first step in developing further research on the role of manufacturers in the generation and maintenance of the technological imperative. The research presented here represents one of the first attempts to examine these issues systematically.[2]

The difficulties in data collection center around the companies' desire for secrecy about their research activities and marketing strategies. A closed atmosphere is necessary in order to maintain a competitive advantage. Because of the need for secrecy the role of the anthropological fieldworker was complex.

An additional issue compounds the analysis which follows. In deciphering the exact role of manufacturers in the process of medical innovation there is the added burden of clarifying one's perspective. Let us consider, for instance, the issue of communicating information. In the case of TPE each group of social actors, as well as the anthropologist, has their own view -- a classic anthropological dilemma of the emic versus the etic interpretation of social reality. An additional complication is that in this case there are two conflicting emic interpretations of reality -- the views of the manufacturers, who believe they play a major, positive role in communicating information to physicians, and the perspective of the clinicians, who see themselves as beyond

the influence of commercial interests, protected by a shield of pure science. In my role as anthropologist I must of necessity take on the task of constructing my own, etic account of the companies' role in communication of information. In doing this, I begin with the assumption that neither the clinicians' nor the manufacturers' account provides an adequate interpretation. My account will include the emic interpretations offered by informants combined with my own formulation of the social situation based on what I observed.

The Nature of Biomedical Sales

The common stereotype of a salesman flogging his wares is not applicable to the medical arena. Or, more precisely, it is more or less accurate depending on the phase of development of the product under consideration. There is considerable difference between the sales and marketing of new experimental technologies and proven and well established medical equipment. One company representative explained these differences to me by drawing an elaborate diagram representing a theoretical continuum of types of sales. At one end of the diagram he placed someone selling can openers to a local hardware store; at the other end was a "salesman," with a Ph.D. in physics, selling a new generation of linear accelerator to Stanford University. This informant placed the selling of TPE equipment toward

the mid-point of the diagram, closer to the Ph.D. in physics than the can opener salesman. The point of this exercise was to demonstrate to the anthropologist that medical selling is very different from ordinary sales work, and that a considerable amount of training, skill, and expertise is required.

Other company representatives continued my education in this area. It became clear that the meaning they give to their work is complex, and that medical selling has numerous divisions. The major division is between "innovative" selling (of "experimental" products) and the task of representing medical products which essentially "sell themselves." One representative contrasted his work in TPE with a previous position selling pacemakers, a medical product that is now quite well established. He emphasized that selling pacemakers is "a very different sort of thing" than selling TPE equipment. Pacemaker technology is at an established stage of technological development, its clinical application is clearly defined and pacemakers are purchased on a routine basis by hospitals. A salesman's main goal is to convince the physician of the virtues of his particular brand of pacemaker, not to sell the surgeon on the use of pacemaking equipment generally. It is more like selling packages of gauze bandages than an artificial heart.

By contrast, innovative selling (according to the interpretation offered by the equipment salesmen themselves), is exciting and dramatic. Certain stories

about engineers who had created new machines in their garage had attained the status of "origin myths" among other company employees. The stories were repeated to me over and over again. Company representatives talked about the salesmen involved in the early stage of innovation as "a special breed." Selling innovative equipment is not a nine to five job; the salesman must be willing to help with a patient in the hospital at two o'clock in the morning in order to interest a physician in a new machine -- and possibly make a sale in the process.

An executive with one of the plasma exchange companies explained the different type of salesman needed in the different phases of medical sales and marketing. Many "fast moving consumer goods" sell themselves. In the medical world the equivalent of the can opener salesman is the "detail man" for a drug company. The detail man needs some skill but does not need a complete understanding of how the product will eventually be used. The innovative salesman, on the other hand, must have this knowledge because of the need to "work with the end user." He must be knowledgeable enough to engage in the "cocktail napkin design" sessions in which the talents of industry and clinicians are blended. When one company made the decision to begin marketing the cell separator machine for plasma exchange, in addition to the more traditional use in blood component collection, a complete change in the sales force was necessary. A company executive complained that the old salesmen simply could not

operate in the new environment. They were used to having the machines "sell themselves" to physicians completely at ease with their use.

One method of cementing the on-going social relations between company representatives and those in clinical settings was a conscious hiring practice undertaken by a great many, if not all, of the TPE companies. The companies hired people with medical backgrounds (for example, training in nursing or medical technology) in order to improve the chances of their employees' function, meaning setting up social ties, with their counterparts who continued to work in the medical field. A salesman who is also a health professional is able to command more respect. One motivation for this was simple expediency. After the well publicized scandals in America when artificial hip joint salesmen were (allegedly) found to be actually performing surgery, many hospitals clamped down on the freedom of movement of company representatives. Informants told me that this rule was harder to enforce if the sales representative was also a nurse. Former health professionals were hired for a number of positions, including technical support as well as sales and marketing. One company specifically hired nurses with a background in operating heart-lung machines or dialysis equipment. Besides being easier to train about the intricacies of the equipment, these representatives were able to establish their professional credibility with their clients --

clinical researchers -- much more quickly. During the very early stages, the technical support personnel often worked side by side with local hospital workers in treating patients, sometimes using experimental protocols, sometimes not. Companies were explicitly trying to make the social relationships involved one of medical person to medical person, making the selling element more "soft" than "hard." Use of health professionals also neutralized at least some of the inherent tensions between buyer and seller. The sales person who is also a nurse is assumed to share the TPE nurse or physician's interest in the patients' welfare vs. profit motivation.

Their day-to-day involvement in the medical arena is personally gratifying for the company representatives. They become insiders in medical progress, engaged in an "educational dialogue" with physicians. Because of the information which representatives have, they feel that they are very important to the doctors who are their "customers." They view their role as "providing a service." The vast majority of the salesmen I interviewed emphasized the excitement of their work in the initial marketing of therapeutic plasma exchange equipment. As one representative said, "I'm in on the start."

The Clinician/Manufacturer Relationship: Inherent Tension, Distrust, and Mutual Need

The history of TPE and cell separation equipment described in Chapter II makes it clear that a successful biotechnology product requires an intensive collaboration between industry and clinical medicine. However, the social relationships between the clinicians and manufacturers which these collaborative projects bring about are not always easy. Although both sides stand to benefit from a successful product, they are also at odds because of conflicting basic goals. A description of social ties based exclusively on the notion of straightforward collaboration is insufficient to the reality of the situation. It is more accurate to characterize the relationship between industry and clinical medicine as based on mutual distrust and tension as well as the more obvious shared goals and interdependence. The very intense, reciprocity-based social relationships I observed were necessary to overcome underlying layers of suspicion and distrust. These strong bonds allowed the achievement of a mutually shared goal: development of a new technology.

An ambivalent relationship of this type -- the combined presence of distrust and mutual need -- is, of course, an extremely common form of structural relationship among unequals. It occurs often in modern bureaucratic

organizations as well as in tribal or peasant societies. Shared goals in no way guarantee a conflict-free social field. My task here is to explain the nature of the tension between physicians and company representatives. I believe this tension has its source in the conflict between a view of technology that celebrates potential benefit to patients and advances in basic science, on the one hand, and a very different view of technology that emphasizes the financial interests of a particular company, on the other. This division of goals is not always absolute or mutually exclusive. For example, industry people are not uninterested in the welfare of patients and sometimes physicians invest in medical equipment companies, hence becoming involved in products in a financial as well as a scientific way. But the basic tension created by pairing two groups, one interested primarily in truth and the other largely in profit, is the dominant structural dynamic.

There are important structural reasons for the tension and ambivalence between clinicians and industry. By itself, the medical equipment industry can carry out research and development only to a certain point. They do not have the ability to carry out the final step of refining a product and testing with human subjects. They lack this capacity for two reasons. First, only licensed physicians are legally allowed (in the United States) to conduct research with human subjects. This research is increasingly regulated and monitored. Medical equipment companies can

not practice medicine legally in any country. Secondly, even if companies were able to hire physicians to conduct specific research (something feasible considering the growing over supply of physicians and the increasing dominance of the for-profit sector in American health care), their work would lose the appearance of disinterested testing that is maintained by cooperating with physicians in academic medical centers or large community hospitals.

In addition to structural tensions, key variations exist in how the participants view their work. Physicians expressed over and over how foreign the company point of view seemed to them. For example, companies looked at the advent of hemodialysis -- with the need for large quantities of supplies -- as a "bonanza." They are constantly thinking in terms of the ultimate "market" for the new product. One executive said, "If this [TPE] becomes the greatest thing since sliced bread, then we want to be in on it." This perspective was viewed critically by physicians who found it difficult to comprehend. Physicians believed companies to be uninterested in basic research, their key motivation. Company research was described as conducted "under the cloak of fairly strict commercial secrecy." One doctor remarked, "...one has to be very wary of their [companies] ulterior motives on occasion."

Despite these tensions, the two groups have many interests in common. Physicians and company representatives share goals in that both sides can gain significant personal

benefit from their association with new medical products. Whether a person sits on the industry or medical side of the fence it is possible to significantly advance one's career by working with or actually developing a new medical technology. A number of innovating physicians became well known on a national and even international level through their work in TPE. One reason for this is that a new technology offers numerous possibilities for publications, the main avenue for success in one's own institution (i.e., promotion and tenure) as well as to stardom in the academic medical world. In a similar fashion, industry representatives are able to advance their position within their companies by successfully producing and marketing a new medical product which is a financial success. Hence, both the real and symbolic benefits of product development are strong enticements to association with new medical equipment.

Both sides understand the motivational structure of their opposite numbers. Indeed they not only understand it but consciously manipulate it for their own advantage. Company representatives, for example, were well aware of physicians' desire for scientific achievement and career advancement. One company representative described the typical research physician as "in search of the magic bullet" which will allow the physician to "get his name up in lights." As we shall see below, the understanding of

what motivates physicians was used extensively by the TPE industry in promoting products.

The Role of Manufacturers in Communicating Information

The technological imperative is generated and maintained by communication of information. Clinicians must gain access to information about a technology, including its specific clinical application. And because of the very high value placed on being conversant with the newest and latest treatments, the sooner this information is obtained the better. Physicians (and hospitals) are often judged by their array of up-to-the-minute clinical technologies. Patients who desired plasma exchange were frequently willing to travel great distances to hospitals and centers able to provide the "latest" technological fix for their disease. (See Chapter IV for a discussion of the importance of "patient demand" for treatment.)

Of great importance is the social context of information exchange. The communication of information about TPE is intimately tied up with networks of social interaction between physicians and company representatives, networks built upon and maintained by basic priniciples of reciprocity and social exchange. Indeed, information is the key item of exchange. Before describing these reciprocal ties in depth in the next section, I begin by discussing how information is actually transmitted in the setting of a new

medical innovation. This discussion focuses on the many ways in which the TPE equipment companies function as the hub of complicated communications networks. They perform this function through classic business marketing techniques as well as many strategies developed specifically for the medical equipment marketplace, such as publishing journals and sponsoring research meetings. The role of the salesman is crucial in both gathering and disseminating information.

Standard Marketing Techniques

Once a medical device has attained the status of a standard therapy it is marketed like any other product. Like any for-profit company, TPE equipment manufacturers must publicize their wares. The most obvious way in which companies facilitate information exchange about medical devices is through fairly standard mass marketing techniques. These techniques are designed to acquaint physicians, the ultimate "consumers" of all medical products, with a company's technology. Many of these strategies will be familiar to the reader because of personal experience with marketing campaigns for products ranging from computers to professional conferences. These relatively mundane strategies are employed late in the innovation process. Marketing techniques of this sort are effective only when the main message is conveying information meant to sell the customer on the merits of brand X over brand Y. They are meaningless when the

physician consumer is not already familiar with the product. The social relationships during this phase of development are not particularly interesting. I describe them briefly, moving quickly to the more interesting social relationships of the early innovation period.

One conventional marketing strategy used by TPE companies is the creation and circulation of informational brochures (usually very professional looking, full color materials) to physicians who might be interested. Mailing lists are compiled and sent to physicians in a particular sub-specialty. For example, all the nephrologists in a geographic area are contacted by mail. This initial inquiry would then be followed up by a visit from the TPE company's local representative. The same kind of material is often published as an advertisement in a legitimate medical journal. Once the cell separator was developed and available for sale, ads began appearing in specialty journals -- especially journals read by blood bank physicians. Early ads dealt exclusively with the machine's functions in blood banking. But by the late 1970s some ads began to include the capability of performing plasma exchange as one of the "selling points" of their machine.

In addition to distributing advertising literature, the TPE manufacturers spend a great deal of money preparing exhibits of their equipment for professional medical meetings. The materials exhibited in these meetings are, again, of very high quality and sophistication. In some

cases the companies actually displayed a machine in operation (hooked up to a live blood donor) in order to demonstrate its fine points to physicians. Often the meetings were underwritten, partially or in full, by the manufacturers. It is also common (in both the U.S. and the U.K.) to see mini "booths" set up in hospital corridors, a setting which allows salesmen of medical equipment or drugs direct access to practicing physicians -- the company's ultimate goal in this type of marketing.

At this stage the relationship between physician and representative is limited and very specific. The company representative might have certain information that a physician needs, for example, the exact specifications about a cell separator. But most of the physicians who approach the exhibits have already decided that they are interested in purchasing a machine. They are now at the stage of comparison shopping. Although social relations may be cordial, they are not based on the mutual need and dependence which we will see is characteristic of the earlier stages of innovation. Up to the minute information, although still important, is less crucial to both physicians and representatives later in development. Thus the catalogue of items available for exchange is limited. One physician joked that a cell separator salesman had made him the "generous offer of a ball point pen."

The relationship of this type of marketing strategy to the technological imperative is not immediately clear. One important factor is that on-going ties between manufacturers and physicians are maintained. Company representatives continued to call on TPE physicians even after the technology was fairly well established. As one executive told me, this gives the companies an "ear on the market." Even if the salesman may not be able to influence further the development of TPE, he might be able to pick up valuable clues about future innovation. One company informant described salesmen as "information vacuum cleaners." This strategy allows the medical equipment industry to be "Johnny on the spot," ready with new generations of equipment or even new products. This readiness to innovate is maintained through on-going social ties between clinicians, basic scientists and industry representatives at all levels. Thus the technological imperative is dynamic, operating over time, as well as static, applicable to a particular machine or device.

Maintaining on-going social relationships is not the only way in which marketing techniques support the technogical imperative; the marketing techniques themselves are influential. Physicians claim to be little influenced by the scores of pamphlets crossing their desks or the visits of TPE manufacturers. Nonetheless I believe that this company supported activity contributes to the changed meaning of a new technology like TPE. These materials

convey a certain legitimacy to the products represented. One result of the companies' efforts to produce sophisticated promotional materials for their products is to give them the appearance of a standard therapy. Experimental therapies are not advertised. A community hospital cardiac surgeon in a small town does not receive full color brochures inviting him to purchase the latest model artificial heart. (At least not yet.)

Although most companies make sincere, and economically prudent, attempts to back only products that are efficacious, in reality this is an extremely problematic issue. Ineffective technologies may be supported either inadvertantly or in an attempt to capitalize on the sale of a new device before it is fully evaluated. TPE equipment was promoted with standard marketing techniques long before definitive scientific information was available. The end result is the same whether a product is marginally effective, useless, or a panacea: the ubiquitous use and professional appearance of these standard marketing techniques contributes to the loss of an earlier experimental meaning attached to the technology - and hence to the technological imperative.

Communication of Information During Innovation

When an innovation is not yet established, the role of the manufacturer in communicating concrete information about the technology is much greater. Two methods employed by

companies are sponsoring research meetings and publishing what I will call "pseudo-medical journals." These marketing strategies are generally used early in the innovation period. Although research meetings may be supported at any stage, their function in facilitating information exchange is greatest in the earliest stages. Company representatives at different levels (ie. salesmen, executives, engineers) are involved in communication through these methods. In addition, salesman are also involved more directly, as on-the-spot communicators who are in constant contact with physicians all over the world.

Sponsoring research meetings. The TPE equipment industry aided the spread of information about the new procedure by financially sponsoring two types of research meetings: those produced and managed by the companies themselves and meetings organized by some kind of legitimate professional group. In the first type, the company actually controls the format of the meetings and the invitations to clinicians. The company pays for the travel expenses of many of the visiting physicians as well. At least one company included the cost of travel to these meetings as a "perk," included with the purchase price of a new machine. In the second type, the company makes a donation to a medical group to help underwrite the costs of a conference (or publications of the proceedings). In this case the professional group acknowledges the financial help of the companies but maintains control over the scientific program.

The company produced meetings may be elaborate three day events or consist of a single evening. One company salesman described a meeting he was organizing in London. All of the physicians from London and the surrounding area who were actively engaged in TPE were invited, at company expense, for an evening at an exclusive London restaurant. The salesman made it clear to me that everyone was invited, regardless of what particular brand machine they happened to use. The explicit rationale for sponsoring this meeting was to allow the company to aid physicians by providing a forum for communication of new ideas about plasma exchange and related topics. The clear motivation behind the company action is to speed information flow, eliminating impediments to physician investigators such as lack of funds for travel.

Similarly, another company sponsors regularly scheduled research meetings in a large American city. This meeting lasts for several days and includes physicians (and technicians) from all over the U.S. and occasionally from abroad. Those invited are carefully selected by the company. A company executive selects the speakers and designs the format. The company official responsible for one of these conferences described it as an "international meeting," with about fourteen speakers over three days. He said a typical meeting might have 350 to 400 participants. It is organized very much like an ordinary medical meeting. Sponsorship may actually be done through a non-profit arm of the TPE corporation. However, the overlap of officers

between corporation and non-profit organization makes this a division in name only. From the company point of view these meetings are providing a service to the medical community. They are well aware of the high premium placed on keeping up to date on the latest developments in one's field. Companies work very hard at maintaining their credibility in the medical world. One representative talked about the difficulties of overcoming physician ambivalence about the manufacturers' role:

> I think one of the hardest things we had to overcome with the [non-profit] Instititue was to convince people that the Institute was really there to provide educational support -- to provide educational back-up and education materials rather than it being a part of the company, oriented toward the [corporate] organization. And I think we've done that -- with a lot of hard work. I think what we have done is to develop the Institute into a viable organization that most people utilize now when they're interested in doing [treating with TPE] a patient with X type disease. They'll normally call us.

Education in this instance is additional information about the uses of the company's medical equipment. The dual purpose of these research events was recogized by both sides. They are effective publicity events for manufacturers as well as serving other functions, such as education. One physician summarized the functions of these research meetings. "It's a pleasant sort of social occasion. As far as the company is concerned, it's a publicity event, but it's also an educational event."

Physicians express their characteristic ambivalence about these company activities. One researcher complained at length about the problems of the industry-produced medical conferences:

> I guess one of the reasons it's frustrating is that most of the talks that are given at that meeting would not make it if they were sent in for peer review to be presented at a decent scientific meeting...If you happen to be known by the company you can get plucked out and put up there on the stage and you could say any damn thing you please once you get up there...Some guy who happens to have done three of them [TPE procedures], and the [company] people found out about it, so they got him to come and talk about it. But if you'd submitted that to the American Federation for Clinical Research...or the blood bank meetings, or the hematology meetings, they wouldn't have had a prayer to get on the program.

Another physician called this kind of program a "very effective promotional organization." A second warned about the need to view this sort of medical meeting with a "jaundiced eye" because the company is selecting the data presented, including screening out anything negative.

One may wonder why physicians and researchers attend these meetings given the scepticism expressed in the above statements. The answer is that their own purposes, viz. meeting colleagues with similar interest, can be met within the context of a company sponsored meeting as well as at an orthodox meeting. One physician stated that the meetings can be, "Quite interesting. Not so much as a chance to hear the public [lectures] as to actually talk to people working in the field and gather informal ideas and exchange

information." Thus, although this same physician expressed criticism about the "jamboree atmosphere" of this type meeting, he nonetheless participated, turning the event to his own advantage.

Company sponsorship of legitimate medical meetings is not problematic for the physicians because they believe that ordinary canons of scientific truth will operate if the work to be presented is subject to scrutiny by the peer review process. In these situations manufacturers make an outright grant to a medical organization. The large financial commitment made by the equipment industry for activities like this indicates the value they place on timely exchange of information among actively working physicians and researchers. The availability of information is a crucial element in the technological imperative. Company sponsorship of medical journals serves a similar function.

Pseudo-medical journals. Besides sponsoring research meetings, the equipment companies also underwrite the cost of certain journals. I have called the publications sponsored by the TPE manufacturers "pseudo-medical journals" because they resemble ordinary medical journals in almost all respects. They look like authentic journals, they are edited by physicians well known in TPE work, and they contain articles on a variety of topics dealing with TPE, often by experts. I encountered these journals often in my research visits to TPE units in the U.S. and England. Sometimes they seemed to be on every desk or laboratory

bench. There were at least two such journals, published by two separate manufacturers, devoted exclusively to the clinical uses of cell separation equipment. These included a great deal of material about TPE. A physician informant described one such journal:

> They have recently begun publishing a medical journal, medical in quotation marks, in which they have hand-picked their editorial board and indirectly have hand-picked the slant that the journal will take...[It is] very cleverly done, because you get the brochure...and if your secretary throws away the envelope...there is absolutely no way that you can tell that it is a business-controlled medical journal.

That statement expresses the major issue involved in industry sponsored publications: the management of information. By establishing this type of journal the companies are able to exercise a fair amount of control over the articles published. This is true in spite of the fact that efforts may be made to separate company profit-making activities from non-profit entities set up to support research. In at least one instance this separation was in name only since the person in charge of the company funded non-profit institute was also a highly placed executive within the corporation. The fact that manufacturers use these journals to circulate information about their new technologies is clear. One company informant stated explicitly that the idea of a company sponsored journal had been developed in order to advance the use of therapeutic procedures. He described how physicians who had seen the

publication would telephone him for further information about the use of TPE for a particular disease. By acting as a resource network for physicians working on similar diseases, companies disseminate information directly to physicians.

The attitude of clinicians to these journals is complex. On the one hand physicians frequently disparage them; they were described to me as "very marginal journals" or "a way to legitimize junk." The managed quality of the data presented was distressing to some physicians. One commented, "It doesn't tell the problems. It doesn't tell the complications. It doesn't tell that there might be some better way to do it." Another commented, "None of us is going to put our best work into a little bitty journal like this." On the other hand, physicians publish articles in the industry sponsored journals, subscribe to them, and accept invitations to industry sponsored events. When I asked one well known and eminent physician why he published in an industry sponsored journal (after he had expressed opinions similar to those quoted above), he replied that it is a scientist's "duty...the only way a scientist is known is by publishing what he does."

One physician who had functioned as an editor for an industry sponsored journal claimed to have complete editorial freedom, describing an incident when the company had attempted to prevent him from publishing a book review. The editor prevailed. Naturally, using outside specialists

as editors or advisors to industry sponsored publications adds credibility to these journals. It also opens up avenues of reciprocity. For the clinician, one's name becomes "known" and associated with a new procedure. This can be very positive. And of course the physicians are often paid for their time in cash, as well. (The nature of this reciprocity is detailed below.) There can be exploitation as well. One physician revealed that his name had been used as "editor" of an industry sponsored journal despite his never having seen the material before it was published.

On a more positive note, industry sponsored journals (and the research meetings discussed earlier) allow information to be exchanged very quickly, much faster than in a peer-reviewed medical journal. An executive with the company that first used this marketing concept told me that the advantage of articles published in the company journal is that they were not encumbered by a lengthy review process. He added that this meant, by necessity, that the articles were less "discriminating." Discriminating or not (and according to whom), information about new medical technology is communicated to physicians.

This company strategy contributes to the technological imperative by speeding the spread of new information or new uses of a technology. Perhaps all physicians who get this industry information are capable of making a careful evaluation of each article's defects; they certainly believe

this to be true. In any case, the technological imperative is supported even if an individual article is published in an incomplete state, with inadequate statistical analysis or lack of controls. These publications encourage physicians to try the new technology themselves to see what their own results might be. And by speeding information exchange (physicians are put into contact with each other through the companies and then carry on without their assistance) the technological imperative is supported. Unevaluated information and early experiences are the kinds of information most relevant to the technological imperative. As a technology is used more and more it becomes increasingly difficult to withhold its use from patients on the grounds of its experimental status.[3]

The role of the company representative in information exchange. Many of the communication tasks of company representatives are fairly mundane, such as traveling from hospital to hospital demonstrating new equipment. In addition to straightforward information exchange functions, such as distributing literature and demonstrating new equipment, sales representatives facilitate the communication of information in complex, informal ways. In fact, the less formal means I observed while conducting research in TPE treatment settings are probably the more effective method of speeding information exchange. The salesmen also facilitate information exchange directly by

passing along information throughout their network of clients.

I observed salesmen giving out a one page summary list of disorders for which TPE had been utilized; this was titled, "Conditions Treated with Therapeutic Plasma Exchange." Of course they distribute the company produced pseudo-medical journals, but they also distribute reprints of TPE articles from conventional journals as well. If a positive article appears in a medical journal, especially a prestigious journal, such as Lancet or The New Engand Journal of Medicine, it is in their best interest to make the details of the research reported known as quickly as possible. Thus the company will buy and distribute large numbers of reprints. One company executive said that they might purchase 5,000 copies of a major journal article to pass on to physicians through their sales network. Since it is difficult to keep up to date on literature, especially if the new field is complicated (and like TPE includes publications in a variety of journals), the representative can then make use of the journal articles as a potential item of exchange. For example, I observed one salesman show a series of articles on a new item of TPE technology to a physician in charge of a TPE treatment unit. When the physician expressed interest the salesman immediately offered to supply him with copies of the articles. One company kept an elaborate library which included most of the relevant medical literature. They also employed a librarian

to help keep the salesmen and other company executives up to date on new developments in the field.

A crucial, but less visible, function of the sales representatives is facilitating the exchange of informal, anecdotal information. Company representatives take on this role in the earliest phases of innovation, when information is still scarce and of great value. At this point in time the companies can make themselves very useful by keeping physicians who might not otherwise have a chance to meet in touch with each other. Because of their constant contact with many physicians working in a new field, the representatives appeared to be the hub of a complicated communications network. As I interviewed the company salesmen and executives I was very impressed with their intimate and detailed knowledge of the specific physicians working in plasma exchange. One executive I interviewed could recite the names of all physicians conducting work in TPE when I mentioned the name of a particular city. "Oh yes. If you get to Chicago you must visit Dr. X, Y, and Z." The names mentioned were the same ones I heard over and over again from my physician informants.

In the first stage of the information exchange circuit the company representatives and/or salesmen gather information in the course of their everyday work. Sometimes this is done formally, for example, through actual data collection for market research reports. The physicians who cooperate with industry sponsored market research activities

are often physicians who have on-going social ties with the company or specific sales representatives in some way, perhaps through work on another product. In the early development of TPE the companies relied heavily on their contacts with physicians who had used their equipment for other purposes in the past. In this way current physician contacts are used to gain information on future trends in technology. Many of my physician informants reported participating in this type of industry sponsored research.

But the majority of information gathering is not within the context of formal market research; rather, it is informal "learning from the customer." The information they gather about what physicians are doing in the area of plasma exchange is immediately disseminated as widely as possible. The companies are very much aware of the importance of both types of information gathering. In fact, learning these strategies is a major part of their orientation for new sales employees. One representative told me, "I spent the first two years learning...from the customers." An executive explained further, "The sales representative's the man in the trenches; he's up on the front line where he's in constant contact..."

The process of selling is intimately tied to the process of information exchange. One representative said, "I spend a lot of my time talking to doctors about what's going on. It's how you sell the equipment..." In practice, this type of information exchange works as follows: While

observing in a TPE treatment unit I heard a salesman engaging in casual conversation with the physicians. He mentioned to the group of renal physicians who were testing a new piece of equipment that "They're doing an acute rejection at Nottingham today." The overt reason for his presence was to help the physicians with the clinical trials with a new product, a particular model of cell separation equipment. However, he was also disseminating information about other uses of TPE in renal disorders. This type of "off hand" comment, such as, "They're treating vasculitis with TPE at the Royal Liverpool Hospital," was a major part of the interaction between salesmen and clinical staff.

The salesmen also seemed to be taking specific advantage of the relative prestige of the different institutions talked about. The representatives were especially delighted to be able to capitalize on the use of their equipment at prestigious research hospitals, which gave them a sort of automatic legitimacy. Physicians in less prestigious hospitals were informed of activities at major, well-known hospitals. Casual comments about new research activities were often followed up directly. The sales person might put a research physician in touch with the two other people in the world conducting research on a similar aspect ot TPE. For example, in England I observed a company representative give a physician the names and institutions of specific physicians involved in research on

developing specific immunoabsorbent columns to remove harmful blood components.

A reasonable question is what influence this type of information exchange actually has. Clearly, there are some physicians who are so centrally placed within their fields of specialization that they need little help from salesmen in "keeping up" with their specialty. They generally deny that "commercial interests" influence their behavior. But there are many other, less centrally-placed physicians who do not have access to the latest information. A salesmen bragged to me that physicians, early in the development of TPE, often did not know what they could do with their equipment until the company representative explained its capabilities. He claimed that a patient with Guillain-Barre syndrome had been treated with TPE at his suggestion.

The company role is enhanced by another factor, competition among physicians. One might think that physicians would communicate directly, without the need for intermediaries. This is often the case. However, the representatives stated that it simply took too long to wait for physicians to learn from each other. One complained, "frequently docs won't go across the street to work with each other." This salesmen then mentioned some specific examples from his own experience of physicians in direct competition for "firsts" in a particular field of research. The competition surrounding the first clinical use of the

artifical heart in Texas in 1969 is an apt example (see Fox and Swazey 1978).

A few physicians acknowledged the large role played by the companies in disseminating information. One well known clinician stated, "They have a very big role...[Blood Systems Corporation] is the classic example of a company that transmits a tremendous amount of information to the blood-banking community..." Another doctor described how the representative can function as a link between physicians who otherwise might not meet. He stated, "I've gotten a number of referrals through Blood Systems because a physician will tell me, I was referred to you by them."

It is crucial to note that the type of information exchanged during the experimental stage of a new technology's development is frequently of an untested, anecdotal character. This kind of knowledge is not available through medical journals or other formal sources and can only be exchanged through direct personal networks. The companies' conscious efforts to support these information exchange networks is an important component in the technological imperative.

The Nature of Reciprocity Between Innovating Clinicians and the Medical Equipment Industry

Reciprocity-based exchange is the cement which binds together these reluctant partners in therapeutic innovation

-- company representatives and clinicians. They exchange a wide variety of items, some with an explicit monetary value and some with totally symbolic value. Exchange binds together the participants in any social situation, even in settings where the participants appear to be (or at least claim to be) independent of one another. The nature of the items exchanged varies throughout the innovation process. The value of goods and services (both real and symbolic) is highest during the experimental phase of a new machine. For example, engineering support provided by a manufacturer is more important early in the course of development. The importance of exchange mechanisms in easing these generally ambivalent relationships during the development of TPE cannot be overestimated. I will next explicate the nature of the exchange process and describe the actual items exchanged. These social exchange mechanisms have many functions. They bind together the research participants, as we shall see. But more importantly, the exchange mechanism also contributes to the technological imperative by speeding the communication of information and the development of new products.

Types of Exchange

The most visable items of exchange are those that have monetary value. Examples of this type of exchangeable goods include actual cash payments, in the form of stipends, retainers, research support, funds for travel, and in some

cases actual gifts of equipment. On the whole, this type of tangible good tends to flow from the equipment manufacturers to the clinicians. A less tangible exchange item is the kind of technical support and expertise which engineers supply to innovating clinicians during the "cocktail napkin" design phase of research. After an initial exchange of basic ideas, a company may actually design and manufacture a prototype machine using their own resources. This happened in the development of TPE equipment when IBM supplied the prototype cell separator for trial. I encountered numerous later examples of this while conducting fieldwork. One physician told me, "Parker Biomedical...made a device for us." This example, from an early stage of innovation, shows how companies support the development of equipment.

But what is exchanged for what? Put most simply, each side has access to certain kinds of resources that the other lacks. Manufacturing companies are at a major disadvantage because they lack one of the most crucial items needed to develop medical equipment -- access to patients with the appropriate diseases. Without this they cannot develop realistic equipment or test later versions of their products. Thus cooperation from clinicians with access to patients is absolutely essential to their work. In order to get this access, they must keep up their side of the exchange relationship by supplying other goods and services required by the physicians.

From the physician's point of view there are a number of valuable exchange items which are controlled by the companies. First of all, there is a great deal of prestige associated with any "first" in the medical field. There are many physicians who could enhance their careers by participating in the development of an important piece of equipment. As mentioned earlier, company representatives are exquisitely aware of this dynamic within the field of research medicine. When I asked an executive to explain why clinicians were willing to take the time to test out his products, he stated that the answer is simple: "They're interested in being published with something new." I was told by a senior physician in England that one of his junior colleagues had built his career on the base of his early work in plasma exchange. And this was not an isolated instance; many physicians capitalized on their association with TPE during the early stages to gain increased prestige within their profession by publishing in a "new" sub-field of medicine. Access to prestige is thus a potential item of exchange controlled by the companies.

Likewise, manufacturers are interested in new products, although for different reasons. They share with physicians the motivation of increased prestige but they have an added interest in the financial success of a product. A company that is first on the scene with a new and important medical product can realize significant profits by being first into a new market. They can establish their reputation and

"market share" before competitors are able to begin production of a similar product. Of course there are risks associated with this from the point of view of both physicians and company representatives. If a new technology does not "pan out," either scientifically (from the clinicians' point of view) or financially (from the company's point of view) then their association can prove to be negative.

Relationships between clinicians and company representatives were often well established and on-going. The nature of the exchange process creates a mutually shared set of obligations and commitments. The ritualized exchange relationship helps to neutralize the inherent tensions that exist between the different parties to medical innovation. It holds them together despite the centrifugal force of the tensions in the relationship which act to pull them apart. The nature of the relationship can be discerned in the comment of one company representative. Making very clear the mutual dependence, he stated, "You need each other; it's a symbiotic relationship."

Clinicians, although caught in the same web of mutual need, may not be as willing or able to acknowledge the connection. Their ideology of scientific truth and disinterest makes them less aware of the social context within which they practice. Physicians often expressed the idea that their scientific values kept them above the petty concerns of the marketplace. Reciprocity may not be

explicity acknowledged. Take, for example, the following statement made by a clinician. "There's no real gains (sic) for us in trying out the product for a company, except our own research experience, and papers maybe." In this statement, the speaker denies that he is influenced by the items of most value in his profession, viz. research and publication in association with a new scientific discovery. He does not want to acknowledge the company's role in providing him with this opportunity.

Another method used by companies in maintaining these ties of reciprocity is direct financial reimbursement. A number of company representatives described the nature of their financial arrangements with clinicians. Sometimes company representatives would pay individual physicians a "retainer." In exchange the physician would be available as a personal consultant to the executive, in essence giving the executive the right to call him or her frequently to ask for the latest news and information in that specialist's field. The amounts of money involved were not insignificant. One physician disclosed, in confidence, that the retainer received was on the order of $20,000 per year. This strategy tends to be used by the smaller equipment companies; the large companies are able to afford their own physicians, maintained permanently on staff. They are then able to consult their "in-house" physicians for the advice they need about new trends in medical innovation.

Of course, not all physicians approve of this kind of explicitly economic relationship. One physician related that he had been offered a retainer in exchange for "not associating with other companies." This offer was refused indignantly. But offers of cash can be made in more discrete fashion. For example, I asked a physician quite well known in a particular type of plasma exchange work how he had come to write a particular article published in a company sponsored "pseudo-medical" journal. His response was simple, "They asked me to do it and paid a considerable sum of money."

A more subtle way of transfering monetary value to clinicians is to sponsor their travel to legitimate scientific meetings, like the International Society for Artificial Organs or any of a number of similar professional associations. This practice is widespread. As discussed above, it facilitates the early spread of anecdotal information about a new technology directly from physician to physician. In one case a physician was sent to a European capital by the manufacturer to present data about the first use of a new technique. The company benefited from the exposure of ideas and the physician received a free trip, as well as professional exposure to his physician peers, something likely to benefit his career. Both sides gain from exchanges of this sort. The company benefits because the source of the information presented at the meeting is seen as neutral and scientific. (The physician

represented a well known research hospital.) And the technological imperative is supported by the rapid dissemination of new information.

Companies and clinicians exchange more than financial items. Sales representatives spend countless hours helping resolve mechanical difficulties that arise when clinicians use new equipment. Companies support medical research in many ways, including loans of expensive new machines, hoping that clinical trials will generate the data they need to prove these machines are effective.

I often observed representatives engaged in direct help with trials of new equipment. This help came in a number of forms. One type was basic scientific information combined with specific knowledge of the product under test. I overheard numerous technical discussions between manufacturers and clinicians about the molecular weights of various immunoglobulins and whether they could be removed efficiently by a particular device. I even heard salesmen avidly discussing recommendations about the ideal frequency for performing plasma exchange. The salesmen were often active participants in the actual TPE procedure -- turning the dials, suggesting changes, or helping with the recording of data

The building reciprocal relationships between salesmen (or in the early phases company engineers) and physicians are often quite intense. I observed cases where they spent long hours together working out the fine points in a new

piece of equipment. This is especially true if a product is actually undergoing initial clinical trials in a particular institution. A common practice is for companies to support the medical group using their product initially. This kind of relationship may be formal, set forth in an agreement governing eventual patent rights and similar legal issues.

Another basis for reciprocity can be seen in the explicit exchange of scientific data, which can only be provided by the clinicians with access to patients. These valuable data are provided to companies in exchange for equipment, machines, and other technical assistance. As one company executive stated, "We have to have good solid reliable scientific data that our equipment does what we say it will do." Supporting the collection of basic scientific data is problematic for the companies. If they are seen as too closely associated with a particular set of research data then the findings become automatically suspect in the collective mind of the scientific community. Medical companies are well aware of this potential contamination of data which they help generate either by supplying funds for research or by making available equipment or supplies. One company representative stated pragmatically, "if a guy [researcher] is identified as being on the corporate payroll, then immediately that ruins the image that the study was intended for." Another executive concurred, saying that he did not even like to have a small notice of company support printed in the acknowledgements of a paper.

Nonetheless, they must have the data, preferably from a specific physician (or hospital) within the scientific community whose name will command great respect. During the course of my research, I encountered numerous instances of companies supporting research in TPE. Specific companies were "known" (within the community of TPE researchers) to be associated with certain clinicians. The nature of support varied acording to the stage of development of the product in question. As TPE was expanding in application to other categories of disease, in the late seventies and early eighties, companies supported research with potential for expanding the use of TPE. For example, on hearing that a particular researcher was planning to investigate the use of TPE in treating kidney transplant rejection (at that time a new application of the technology), the company responded by offering to "lend" the researcher a machine. The physician explained this transaction as follows:

> [One] company has lent us a machine for a year, to use...in our study. After they heard we were starting a study they said, "Hmm - why don't you use our machine, and we'll help you do your study!" Fine, the more machines we have the easier it is to get folks on it.

The company stood to gain a great deal from this association because the doctor and hospital involved were well known and very established in the renal transplant field. Sponsoring this type of research project was a common activity of TPE manufacturers. One executive I interviewed had a large blackboard behind his desk which summarized the different

research projects the company was currently sponsoring, in this case nine projects in all. The actual financial support consisted of the use of a machine and the necessary disposable software products. In rare cases a company might also support the salary of a technician.

This lending of machines was a very common practice. I encountered it in many different medical settings. It was not always part of company sponsored research. A company occasionally might lend a machine to an important group of physicians just to have the reflected glory of saying their product was in use at hospital X or by physician y. The benefit for the physician is that he can then claim to have "the latest" technology at his disposal. In one of my field research sites a physician obtained a number of new model machines (on loan) in order to have the latest technology on display for a scientific course his institution was offering.

The participants in this exchange sequence were not unaware of the importance -- symbolic, social, and practical -- in what they were doing. Both sides recognized that the other actors had much to gain from their joint ventures. Although the company representatives were perhaps more aware of the importance of exchange, physicians were also well aware of the bonds of reciprocity that developed. For example, one physician was very clear that a company was providing him with free supplies in exchange for the scientific information he would then manufacture, using

their "gift." There was a clear presumption of an ongoing exchange relationship; the physician realized they were making an investment, as he said, "because if it [the new TPE device] gets off the ground...then their sales will go up...I don't think they're doing it for altruistic reasons."

When the salesman involved in the above transaction carried the new devices into the physician's office, he announced proudly, "I've brought you a present." The physicians proceeded with their part of the bargain and began clinical testing of the new device on patients. Once the testing was complete, I observed the salesman and the physicians pouring over the initial results, in the form of graphs and charts indicating the machine's efficiency at removing harmful products from the blood. The salesman commented that he was anxious to get these results back to the main office of his company. He stressed to the physicians present that this was an important step in obtaining further research equipment, stating, "When they see the results the circuit is complete."

Notes

1. There are, of course, exceptions to this general rule. One notable exception is the computed tomography (CT) scanner, which was developed without significant input from medicine. In the history of TPE equipment, a second generation machine was developed (primarily by engineers) which was enormously sophisticated but lacked immediate clinical applications. One physician called it, "a machine waiting for someone to find a use for it."

2. One reason that I cannot provide a quantitative assessment of the exact role played by equipment manufacturers in disseminating information about the clinical use of plasma exchange is because information of that specificity could only be obtained with an actual experimental design, comparing the rate of diffusion of a technology supported by private industry to a similar technology developed and marketed totally by a non-profit organization. And since the factors influencing the rate of growth of each technology are unique, the end result would be of questionable value.

3. This issue, industry support of meetings and publications, is of increasing concern within the medical community. An editorial in the Journal of the American Medical Association expresses grave doubts about the increasing tendency for industry to support biomedical publications and conferences (Soffer 1983). This concern is bound to increase as public support of research diminishes, causing further reliance on industry.

Chapter IV

Physicians and Patients:

Perspectives on a New Treament

> Physicians get neither name nor fame by pricking of wheals, or picking out thistles, or by laying of plasters to the scratch of a pin: every old woman can do this. But if they would have a name and a fame, if they will have it quickly, they must...do some great and desperate cures. Let them fetch one to life that was dead; let them recover one to his wits that was mad; let them make one that was born blind to see; or let them give ripe wits to a fool: these are notable cures, and he that can do thus, or doth thus first, he shall have the name and fame he desires; he may lay abed till noon.
>
> John Bunyan The Jerusalem Sinner Saved: or Good News for the Vilest of Men

At the center of the development of a new therapy are the innovating physicians who decide to use it and the patients who are first treated. The existence of sophisticated technical equipment and the marketing efforts of medical equipment companies just reviewed all set the stage for innovative treatment. I will now turn to the specific roles played by physicians and patients. I will demonstrate how two facets of the physician's role -- as researcher and clinician -- both support an imperative for making use of new treatments. Desperate patients are also key players, seconding the researchers' efforts by exercising demand for new therapies. Finally, I will describe how the physician's decisions about who and how to

treat, and the patient's response to therapy are, in part, socially negotiated. This process points up the constant tension between the ideology of rigorous scientific evaluation of new therapies and the social realities of caring for seriously ill patients.

Physicians

Although many factors are involved in decisions to use medical machinery, ultimately the most important is the physician. In both American and British medicine physicians have significant -- often exclusive -- authority to determine who will receive a particular type of medical care. Although this right may be eroding in the U.S. as fee-for-service medicine is supplanted by other organizational forms, it nonetheless remains strong. In Britain, too, in spite of the financial constraints of the N.H.S. the physician's role as key decision-maker continues. Preserving the autonomy of physicians was a major consideration in the negotiations leading up to the formation of the British health service (Willcocks 1967).

Physician authority derives from two sources. First, one of the defining characteristics of the physician role is that of keeper of a body of highly specialized and esoteric technical knowledge. Non-physicians, be they patients, administrators, or health policy experts, are not privy to this information and are legally excluded from making use of

medical equipment even if they should happen to possess the requisite knowledge. The ultimate decision about whether to recommend a treatment is left to the physician. Medical control over the use of technology has traditionally been completely self-regulated. This notion of control of esoteric information and skills is central to the definition of a "professional" set forth by sociologists like Freidson (1970). Hence, physicians maintain significant power based on their expert knowledge.

Second, again in both the American and British systems of medicine, physicians have traditionally exercised a significant degree of "cultural authority" over their patients. The term cultural authority is borrowed from Paul Starr (1982). This concept does not suggest that physicians force or coerce patients into cooperation with their suggested treatment regimens. The prestige of the medical profession does not derive exclusively from raw power. Rather, cultural authority "refers to the probability that particular definitions of reality and judgments of meaning and value will prevail as valid and true" (Starr 1982:13). To a large extent physicians define the very nature of the clinical encounter, from the initial identification of a disease process to the ultimate determination of whether a particular treatment was a success or a failure.

Cultural authority is augmented by structural power, which arises from physicians' ability to control the use of health care resources; doctors are the key economic decision

makers, responsible for most resource utilization decisions (Relman 1980). Health economists emphasize the physician's role in both generating the demand for new medical technologies and determining the supply. Physicians generate the demand for medical care because patients, for the most part, do not make independent decisions about their need for medical care, especially technologically based medical care. Although patients influence the process in many ways, as will be shown below, it is physicians who define the range of treatments available and determine who is eligible to receive them. Because of the dual nature of the control exercised by physicians -- deriving from both their structural position of power within the health care system and their cultural authority -- understanding how physicians perceive the nature of TPE and its potential benefits is crucial to an analysis of the innovation process in clinical medicine.

In the case of TPE, it became clear fairly early in my research that the meaning given to the enterprise of TPE by physicians was very different from that of other actors. Although patients, nurses, and industry representatives viewed their work as primarily oriented toward the idea of TPE as a <u>treatment</u> for individual patients, physicians were much more concerned with the notion of TPE as <u>basic research</u> in the biomedical sciences. At first glance it may not be clear why these two ways of looking at TPE are potentially contradictory. However there are significant implications

to viewing the research applications of a new technology as of primary importance. I will argue that treating the therapeutic dimensions of a new technology as an unplanned offshoot of basic disease investigation has great significance for the creation and maintenance of the technological imperative. Since a major "meaning" of TPE for physicians is as research rather than therapy, the desire to enlarge scientific knowledge serves as a kind of engine driving the expansion of a technology. This dynamic occurs in spite of serious economic constraints or structural obstacles to innovation, such as government regulatory efforts.

I do not, however, want the reader to think that motivation to treat patients and act in the role of physician (rather than scientist) is not a part of the technological imperative. Therapeutic goals are a strong force in their own right. As Fox and Swazey note in The Courage to Fail (1978) research physicians experience constant conflict and tension because their role encompasses the duties of both clinician and investigator. I shall describe below how both sides of this dual role are important to the technological imperative. The clinician is deeply motivated by the desperation of seriously ill patients. In reality both parts of the physician's role influence the technological imperative, although for very different reasons. For purposes of analysis it is necessary to separate artificially these two conjoined elements of the

physician's role -- that of healer and that of researcher -- in order to understand the important meanings and motivations deriving from each role.

TPE: Research or Therapy?

An indication of the importance of research in the meaning ascribed to TPE by physicians comes from examining the actual language clinical investigators use in discussing their work. One physician, involved in using TPE from a very early date in its development, said in a published review article: "Plasma exchange has recently been used in the investigation and treatment of immunologically mediated disease [emphasis added]" (Pinching 1978). Later in the same article the author described TPE as "a valuable clinical research and therapeutic tool" (ibid.), clearly revealing the dual meaning of TPE. The title of another article is even more explicit in defining TPE as a research tool. The physician called the paper, "Function of Circulating Antibody to Acetylcholine Receptor in Myasthenia Gravis: Investigation by Plasma Exchange."

Noteworthy in these illustrations is the clear indication that one "investigates" a disease using plasma exchange. TPE is not simply a therapy but a means to learn more about a disease process. A physician who supervised a large number of patients undergoing TPE described his major purpose as learning the cause of auto-antibody mediated disease. In both instances quoted above the research

application of TPE precedes the discussion of its therapeutic use. This ordering reflects the values of the physicians interviewed. When asked to discuss their involvement with TPE, physicians invariably began by talking about their research interests. Research is a key part of their thoughts about their work, even when patient treatment is an offshoot of the research activity. In fact, many physicians expressed displeasure that my interview schedule focused on TPE. This group of doctors kept trying to change the subject to their underlying research interests, such as immunologically mediated renal disease. One physician spent a good part of the interview drawing graphs and charts explaining the natural history of his particular disease. Another physician, commenting on my interest in TPE, stated, "you won't find universal plasma exchange men, but people interested in single problems...and not only therapeutic but scientific."

When visiting a TPE unit there are constant visual reminders of the primacy of research. A common scene, observed in hospitals throughout the world, is a physician researcher or technician waiting to collect diseased plasma from the patient in order to conduct basic research about the illness. Typically, a patient would come in for a treatment and be "hooked-up" to the machine. Hovering nearby, impatient for the treatment to begin, was the white lab-coated researcher with glass beaker in hand, waiting for the very first (and most concentrated) sample of plasma to

be removed from the patient. The more rare and interesting the patient's disorder, the more scientists were likely to be waiting and competing for plasma essential to their research activities. The diseased plasma of certain patients was so valuable that it was sold to commercial biological products firms at a substantial profit, sometimes offsetting the cost of therapy for the patient.

The use of patients' diseased plasma in investigating the pathophysiology of disease at the cellular (or molecular) level demonstrates an important dimension of the relationship between the scientific understanding of disease and treatment efforts. Therapeutic efforts may, in themselves, prove useful in elucidating the nature or cause of a disease or in furthering scientific understanding of a perplexing complex of symptoms. This relationship is illustrated by the history of leukemia. In the decade of the fifties, the clinical entity "leukemia" was a single disease, with a rapid course and uniformly high mortality rate. Following the discovery and initial use of chemotherapy, leukemia was gradually broken down into a large array of sub-diagnoses, based primarily on patient response to therapeutic trials of various chemotherapeutic agents. An informant who is a hematologist compared the early treatment of leukemia with the history of TPE. "Leukemia was one disease. Then they started [chemotherapy] -- some respond, some don't. Now you have 48 or 49 different classes of leukemia based on their response to

drugs." This researcher hoped for a similar improvement in our knowledge of the poorly-understood conditions being treated with TPE.

The use of TPE for three disorders, myasthenia gravis, hypercholesterolemia, and thrombotic thrombocytopenic purpura (TTP) demonstrates the relationship between treatment efforts and the search for disease etiology. As discussed in Chapter 2, when TPE was first used in connection with myasthenia gravis (a debilitating disease of extreme muscle weakness) the exact pathophysiology of the ailment remained unclear. Scientists had postulated the existence of an auto-antibody in the plasma which interfered with transmission of nerve impulses, hence causing muscle weakness. When the first few patients with myasthenia gravis actually became stronger after having plasma exchange, this fact in itself became an element in building the scientific case for documenting the etiology of the disease. The use of TPE with affected patients yielded large quantities of plasma, which were then injected into experimental animals (who subsequently developed symptoms similar to myasthenia), thus fulfilling Koch's postulates.

The use of TPE for familial hypercholesterolemia[1] is more complex. The disease itself is understood to be a genetically determined disorder resulting in extremely high levels of cholesterol in the blood. Patients with this disease die, often during childhood, of the adverse cardiac effects of high cholesterol. The use of TPE in this disease

elegantly illustrates the dual role of research and therapy in physicians' use of the new treatment. On the one hand, using TPE for these patients represents a desperate attempt to ward off early death among the unfortunate victims of this deadly genetic disease. On the other hand, physicians pursuing this work were also deeply committed to basic research on the relationship between blood lipids and heart disease. These researchers described their primary task as testing the "lipid hypothesis" about the etiology of coronary artery disease by making use of the "natural experiment" of familial hypercholesterolemia. The cholesterol rich plasma harvested from patients (who hoped for therapeutic benefit from the procedure) constituted the primary research material for the physician investigators. One of these doctors joked with a patient, "you're keeping a whole lab going with your products."

More recently, the use of TPE in treating TTP provides another illustration of how therapy itself may help "solve" the mysteries of a disease. TTP, a life-threatening condition of the blood coagulation system, is often successfully treated with TPE. And yet, as an editorial in the New England Journal of Medicine observes, "it is not yet clear why plasma transfusion and exchange, which have become the cornerstones of treatment, are beneficial" (Aster 1985:986). The editorialist speculates that the disease may turn out to have multiple causes. The implicit assumption is that therapeutic efforts may themselves help sort out the

true nature of TTP. He states, "It is to be hoped that studies aimed at defining the mechanism by which plasma exerts its apparently life-saving effects in some patients will lead to a fuller or perhaps even complete understanding of this remarkable syndrome" (ibid.).

Research is invariably a key part of physicians' thoughts about their work, even when patient treatment is an offshoot of the research activity. One doctor told me, "the division between research and therapy is not always clear or easy to determine." Another expressed the basic tension, stating, "It's [TPE] more a tool than a treatment." He immediately qualified his remark by adding, "really one is doing both."

The career structure of academic medicine, with its emphasis on new discovery, further supports this dynamic. Academic physicians are rewarded -- with prestige, promotions, and tenure -- based on their research record, not their accomplishments as clinicians or teachers. The significance, for physicians, of achieving basic scientific advances was often readily apparent in everyday activities. For clinical investigators the real meaning of their work is research. One weekend afternoon I observed a young physician conducting an emergency plasma exchange procedure on a woman seriously ill with rapidly progressive renal failure. The doctor was patiently trying to explain the rationale for the woman's treatment with TPE and certain immunosupressive drugs, viz. reducing the autoantibody that

was destroying her kidneys. The patient's husband said, "I understand all that, but what causes the autoantibody?" Without a pause the physician retorted, "If I could tell you that I would win the Nobel Prize!" This remark suggests the high stakes involved in devotion to scientific inquiry. Although concerned with the patient, he is also engaged in a quest for knowledge, attempting to "solve" another disease. Enthusiastic expression of the values of basic science was a common denominator in my interviews with physicians. One doctor stated, "[TPE] is opening a number of doors and paths toward clarifying disease, I find, and that's what's exciting -- no matter if you fail."

The expression of devotion to research goals at times took on a moral tone. One neurologist described his curiosity about basic disease processes as an obligation. He emphasized how important it was to keep asking questions, stating, "You may get answers other than those you asked." A nephrologist described his work with TPE in a similar vein. He stated quite passionately that you cannot just treat the patients, you must study the results so "progress" can be made. Success, such as his earlier work with TPE for a certain type of kidney disease, which resulted in "radical improvement," causes you to look at what you've done. "[Success] poses a question which you have to answer [emphasis added]."

Most physicians are cognizant of this overlap between research and therapy, realizing that the two activities are constantly muddled together in the real world of everyday practice. The primacy of research goals over treatment, however, supports a technological imperative in medicine.

The Ideology of Clinical Trials. Physician's collective choice of research as the primary meaning of their work with TPE is, of course, consistent with the basic values of twentieth century western medicine. As Margaret Lock (1986) has observed, the metaphor of "scientific excellence" is omnipresent in medical discourse. If taken strictly at face value one would assume that every aspect of medical practice was governed by strict application of scientific principles. Reality is much more complex. The goals of scientific medicine (as formulated most clearly in the physician's role as researcher) often come in conflict with the goals of clinical medicine, such as compassion and concern for the welfare of the individual patient. In the case under study, the metaphor of scientific excellence (and the meaning of TPE as research, not therapy) is expressed through a preoccupation with rigorous testing of TPE by means of the controlled clinical trial. Hence the use of TPE as a treatment also falls under the rules of scientific experimentation. Patients treated with TPE were often entered into clinical trials of the new technique for a particular disease. Treating patients as part of a controlled trial (rather than haphazardly) is the epitome of

scientific excellence in clinical medicine. Although frequently breached, this rule is powerful and has a central place in the practice of modern medicine.

A clinical trial is a method of evaluating the efficacy of a new therapy in a rigorous, scientific way. It is specifically designed to get beyond the subjectivity of the individual clinican's evaluation of his own patient's response to treatment. Although there are many varieties of clinical trials a key feature of a good trial is the existence of a control group of patients who receive either no therapy or a different therapy. It is very important that there be no difference between patients selected for treatment and those selected as controls. Assignment must be random. Occasionally "historical" controls are used, that is, a new therapy is compared with the response of patients before a new treatment was introduced. The ideal clinical trial is double-blinded, meaning that neither the patient nor the physician evaluating the treatment is aware of whether the patient received the new therapy or was part of the control group. In the case of TPE, the ideal clinical trial requires the use of "sham" plasmapheresis and the evaluation of patients by physicians who did not know if the patients had received treatment. To eliminate every possible source of bias, the ideal trial also must be "multi-centered:" physicians at a number of hospitals or clinics must use a standardized procedure to test a large number of patients.

When speaking with physician informants about how a new technology is first evaluated and eventually disseminated into medical practice the word most often encountered is "clinical trial." In medical rhetoric, the concept of the formal, controlled clinical trial is the sine quo non of medical acceptibility for any new procedure, including drugs, diagnostic tests, and surgical procedures. When I asked physicians to discuss the "state of the art" with regard to TPE they universally responded in terms of clinical trials -- whether they had been completed or not, the difficulties of mounting good trials, the rigor with they were performed, and the likely outcome of trials currently underway. In keeping with the values of good science, the use of TPE for any disease theoretically must "pass" the rigors of a clinical trial in order to gain acceptance as a standard therapy.

As an interview technique I reviewed a list of specific diseases for which TPE had been utilized, asking each physician whether they considered the use of TPE "standard" or "experimental" for that condition. Physician informants uniformly responded to the question by discussing whether or not clinical trials had been performed or whether mounting such as trial was justifiable. A physician expressed scepticism about whether TPE for a particular condition was standard therapy by saying, "I haven't seen any really good controlled trials with five years of follow-up." Other typical comments were: "I think you need another randomized

study," or, "There certainly needs to be a controlled trial." In one case where a major multi-center trial was underway the physicians responded optimistically, "We'll have the answer within a year." Faith in clinical trials was often expressed with a religious fervor. "It's never too late to do a controlled trial...[Treatment] is purely a hypothesis; it's a new machine. The theory behind it is attractive, but somebody has to do some controlled trials."

The good clinical trial is discussed by physicians as the conceptual opposite of the "anecdotal report." Anecdotal reports consist of informal trials of new treatments performed in an "off the cuff" manner. A physician who treated a seriously ill patient with a new technique would then communicate the results to colleagues in one of three ways: through direct person to person networks, in the form of case reports or letters submitted to professional journals, or in brief presentations at professional meetings. Within the ideology of clinical trials anecdotal reports are considered useful and a necessary first step in innovation. However, they ultimately must be superceded by rigorous clinical trials. The ideal progression is from anecdotal reports of a few isolated cases, to preliminary uncontrolled trials (generally meaning without a control group) with a few patients in a single medical center, to large scale multi-centered randomized controlled clinical trials. These implicit rules, however, are often breached because of the

stresses caused by the physicians' experiences as clinicians treating seriously ill patients.

Physicians as Healers: the "Desperation Reaction"

A comprehensive account of the physician's role requires that the picture of the TPE doctor as clinical researcher be counterbalanced by a description of physician as healer. Although often subordinate, the healer role exerts a powerful influence on the technological imperative. Faced with critically ill patients, physicians often respond with what I shall call, a "desperation reaction" phenomenon. Kenneth Warner, a health policy analyst and economist, first used the phrase desperation reaction to account for the very rapid increase in the use of chemotherapy for leukemia after its introduction in the 1950s and 1960s. He explained the rapid diffusion of the new treatment as a function of the desperation experienced by physicians who treat these patients (Warner 1975). With a rapidly fatal disease they were willing to grasp at any possible therapy. The desperation reaction phenomenon provides further understanding of the meaning physicians derive from their work. Physicians are acutely aware of the very ill patients who provide the material for their research. The perception of patient desperation becomes a justification for action, which may require breaking the rules of pure science described above. The desperation reaction also helps explain physicians' overwhelming

predilection to employ an available treatment, often with unclear knowledge of its effectiveness, when confronted with a patient in a dire medical situation. Fox and Swazey report that Belding Scribner's first attempts to construct an arterial-venous shunt for long term dialysis was motivated by the death of a particular patient (1978:202).

I asked one physician whether he had been considering the idea of therapeutic plasma exchange as a treatment when he first employed it. He responded:

> Oh absolutely not. I can be quite clear about that. I can say that this was simply a move of desperation in one particular case. It wasn't part of a planned approach. We didn't sit down and say, we need a new treatment for lupus, why don't we get 15 patients and try plasmapheresis? ...we had experience of the technique from quite other fields and we thought, "let's just throw it in in her case. And because it was dramatically effective we decided then to get [together a series of patients].

Another physician who worked with SLE patients described a similar scenario:

> [A doctor] rang me up and said, "I hear you're interested in SLE. Well, I've got this terrible patient who's dying -- will you do something about her?" And she came over here -- incredibly ill, virtually dying. And the next morning, after one plasma exchange, she was serving tea on the ward, she was so well. It was so dramatic...it was just like penicillin curing peumonia.

These quotations from innovating clinicians reveal two important points. First, an attempt to try a new therapy is often motivated by the critical condition of a patient. It is extremely difficult for western trained physicians to refrain from at least attempting to treat. A common rationale for trying TPE was "when there's nothing left to try" or in "patients who have disease that's totally refractory to standard therapy, where there is no other treatment and the progression is very, you know, very fulminant, very disabling and/or potentially fatal." Thus the desperation experienced by physicians as they stand by and watch patients go "down hill" is a potent force in stimulating treatment efforts.

Second, the enthusiasm and excitement generated by these initial treatment efforts is also quite clearly heard in the statements above. A physician described his reactions to treating the disease TTP:

> TTP is a highly fatal disease...In the past few years, for the first time since I've been a hematologist, patients aren't dying of TTP any more. They all used to die of TTP.

The disinterested values of pure science are difficult to maintain in the dramatic environment of desperate patients. Pushed by the responsibilites inherent in the clinician role, physicians occasionally violate the rules of science in response to the precarious situations of their patients, primarily by being willing to try therapies that have no

proof of success, or by sometimes treating their patients outside of approved clinical trials.

The "First Patient Phenomenon." Discussions with pioneers in TPE work revealed a particular variant of the desperation reaction, which I will call the "first patient phenomenon." This force, which relates to the feelings of desperation discussed above, also mitigates the ideal of scientific discipline represented by an elegant clinical trial. By "first patient phenomenon" I mean the enthusiasm generated by a randomly occuring positive response to a new therapy in the very first, or first few desperately ill patients treated with a new technique. In the ideal clinical trial setting the scientifically neutral physician would automatically discount results obtained in a very few patients. He or she should be especially suspicious of a single dramatic success. In the situation of early work with TPE, however, the experience physicians gained from single (dramatic) successes proved to have significance for their later behavior and their general enthusiasm for TPE as a treatment method.

The "folklore" of modern scientific medicine contains a number of verbally transmitted homilies that deal with this issue. A common statement is that a clinical researcher or physician spends the rest of his career trying to discover (and replicate) the reasons for an early success. Clearly, a dramatic success exerts a potent psychological force on the research physician, providing a capital stock of

"success" which can provide the motivation for later hard work and the unavoidable failures that are part of clinical research.

During the development of TPE a number of early workers maintained interest and motivation because of phenomenal successes with their first patients. The dramatic responses in patients with SLE and TTP described above are good examples. In the case of the first American group to use TPE for myasthenia gravis the first patient treated responded far better (as it turned out) than was characteristic of later patients. Having been severely debilitated by the muscle weakness associated with the disease, the patient progressed rapidly, over the course of a few treatments, regaining sufficient strength to resume playing the piano (the patient had been a serious pianist). Attention from the media reinforced the spectacular nature of the improvement. Newspaper photos appeared of the patient swimming in a pool. The word "cure" was heard for the first time in discussions about a disease that is notoriously hard to treat.

Based on this highly favorable initial response, the physicians involved eagerly proceeded to treat additional patients with myasthenia. Although the response in many of the later patients was less dramatic, the experience of the first successful patient buoyed the team's enthusiasm and encouraged them to proceed with therapeutic trials.

A contrasting history can be seen in the case of another group working in the field of renal disease. This group, in England, was responsible for the innovation of using TPE in treating certain autoimmune renal conditions. However, about two years before their first successful effort, an earlier patient treated by the group failed to respond to TPE and progressed to further renal failure. After this initial failure it took two full years before the team elected to try the procedure again, in marked contrast to the reports of other groups who happened upon success in their early patients.

Further evidence of the importance of the first patient or patients came in interview data with staff members. In many cases, the clinicians involved tended to remember their experiences in terms of dramatic events associated with particular patients. A nurse commented that she remembered an event clearly because "it was the night Jerry died." It became clear that experience with individual patients helped establish the meaning of the new treatment for the participants.

In their formal discussions of their work and portrayals of the research process physicians claim to be uninterested in any single treatment outcome because of the demands of scientific discipline. This discipline demands that one make the assumption that the results of any single treatment event are most probably inconclusive; assumptions based on a single event are likely to be erroneous.

However, the successful treatment of a single patient may take on an importance far beyond that produced by its immediate impact on the happy patient and his clinician. The data generated by treating the first patient becomes ammunition in the contest for scientific expertise and priority of discovery. Successful events are rapidly communicated via formal and informal networks among physicians and researchers. As discussed above, these informal communication networks may be partially stimulated and supported by another interested party -- the medical equipment industry. Transmission of isolated case reports is a very common activity of company representatives.

Medical careers are not based on the work of physicians who carefully and patiently disprove new treatment modalities. A bias toward positive results is inherent in the system of rewards within medicine. A number of physician informants expressed frustration at the difficulty they experienced when trying to get negative results published. In theory (and ideology), negative results in a well designed clinical trial are of equal value and importance as positive results. Nonetheless, negative results are not as highly valued within the profession and are not as valuable as a means of advancing one's career.

Patients, too, are more interested in positive results, since they are often desperate for a cure. The next section of this chapter examines their role.

Patients

An investigation of both physicians and patients is central to understanding the social context of the technological imperative. An analysis of the patients' role provides a necessary complement to the previous discussion of physicians. Patients, the ultimate object of the process of innovation in clinical medicine, at times play very active, and at other times very passive, roles. As part of a therapeutic dyad consisting of innovating physician and willing patient they are crucial to progress in medicine. From the patients' point of view, TPE is a treatment and represents hope for their own well-being. The scientific advances hoped for by physicians are peripheral to them. As one patient said, "the fact that it's research is someone else's concern; for me it's treatment."

In the case of TPE, the patients' role is crucial to understanding the technological imperative for two distinct reasons. First, the behavior and attitudes of patients help create the "desperation reaction" described above. In response to their debilitating and life threatening illnesses they generate the desperation, and in many cases also supply the enthusiasm, that motivates the physicians working on TPE. I will review the nature of patients' response to treatment with TPE, including a description of "patient demand" for treatment. Second, the reaction of patients to TPE indicates the importance of the "cultural

fit" of a new technology if it is to succeed readily. Patients' response to illness and their efforts to receive treatment are shaped by basic cultural values and belief systems. By describing the "emic" or patient view of TPE I will demonstrate how the fit of emic explanations of TPE by patients, the meaning they gave to their treatment, facilitated the development of the technology. Media coverage, which reflected these cultural beliefs, encouraged patient demand for treatment, and had a direct effect on TPE's rapid expansion in the late 1970s. Special disease interest groups (like the Muscular Dystrophy Association) provided both publicity and funding for early research.

Patient Reactions to the Machine and Experience of TPE

Patient response to treatment with therapeutic plasma exchange is complex and multi-layered, combining elements of terror and enthusiasm. In discussing patient response it is necessary to mention one important issue. The patients receiving TPE suffer from a wide array of illnesses, ranging from debilitating chronic conditions to immediately life-threatening diseases. A patient with acute kidney failure can be expected to react quite differently than a patient with chronic arthritis of many years duration. To use Strauss' term, the individual "trajectories" of the illnesses treated with TPE are very different and responses to therapy are thus partially mediated by response to the underlying condition. It is difficult to separate the

patients' response to their underlying illness from their response to the TPE treatment itself. Nonetheless, there are similarities in the way patients respond to the treatment which seem to be unrelated to their disease process and directly related to the experience of treatment with TPE.

Patient response to the direct experience of being connected to the cell separator machine has two distinct features: fear and awe. Almost all patients approach the machine for the first time with trepidation. One patient said, "The first time I was scared stiff, petrified, I shook like a lily." Others reported being "terrified" or "extremely frightened." The exact source of the fear is not clear but appears to come from the experience of watching one's own blood being removed and manipulated. The fear of the machine itself is in addition to an underlying terror caused by knowledge of the disease process. A few physicians reported having difficulty recruiting subjects for research studies because of the "fear factor." However, desperation most often overcomes fear.

This initial fear is accentuated by the physicial discomfort of being connected to the machine, which requires the insertion of very large needles or catheters into the patient's veins. For most patients this discomfort fades after the treatment begins; for other patients vein problems become a continuing "nightmare" and color their response to the treatment as a whole. (These problems are described in

chapter V). A typical response is, "The worst part is the needles," or, "I feel like a pin cushion." For the majority of patients the treatment becomes fairly manageable once the initial terror is surmounted through continuing experience with the machine. The discomfort at needle insertion, however, continues.

During the actual exchange process most patients report very few sensations, stating that they feel nothing at all. As one patient stated, "once the line is in it's nothing, really." Another common reaction (for a clinically stable patient) is boredom; veteran patients were likely to fall asleep during TPE. The exception to this is side effects due to reactions to specific anticoagulants or symptoms related to a rapidly changing blood volume. These, for the most part, can be controlled by a skillful operator. One patient who received TPE on a chronic basis aptly described his adaptation to the procedure. "It's like eating or sleeping -- having a plasma exchange on a Monday; [it's] integrated into my lifestyle." Many patients become actively involved in their own treatment, monitoring the procedure by constantly watching the machine and the technician's performance.

Despite this eventual "adaptation" to a new experience the inherently dramatic nature of the treatment is a feature of TPE experienced by all patients. Many patients mentioned their reaction to watching their own blood circulating through the machine. One described this as a "funny

sensation." And most were impressed by the sheer volume of equipment, tubes, and personnel. It would be difficult to fail to respond to the inherent drama of the scene. One patient joked, "When does the music start...I'm all wired up for sound!" Patients tend to overestimate the complexity of the machine. One English patient had a wildly inflated idea of the machine's monetary value, believing that it must cost at least 500,000 pounds (the reality is closer to 15 thousand). The dramatic nature of TPE as a therapy creates a particular ambience, a mood ripe with expectation and the promise of spectacular results.

When asked to describe patient response to TPE physicians also mentioned the dramatic nature of the treatment. There is a universal concern about this among clinical researchers. They fear a possible placebo effect resulting from the inherent drama of the treatment as opposed to its actual effectiveness. One physician summed up the potentially dramatic effect of TPE on the patient as follows:

> Well, plasma exchange is the ultimate Walter Mitty like experience, isn't it? I mean a patient's lying there in bed with this machine going [round and round]. Do you know the movie The Secret Life of Walter Mitty? Remember the machine that goes toponka, toponka, toponka? It's all a sort of medical fanatasy...but this time it's true. I mean, it's the most marvelous procedure you can imagine -- this machine and attendants moving levers back and forth...

Although not all physician respondents were this articulate in discussing the impact of TPE on patients, most were aware of its great dramatic appeal. One doctor stated plainly, "pheresis is fun!" Another said, "on the whole we've found everybody receptive and rather excited about having it [TPE] done...They feel that it's very dramatic and that they're getting a lot of attention, having modern twentieth century technology applied to them." As we shall see below, this background state of generalized excitement is crucial to understanding how patients' response to therapy may be socially negotiated.

Setting aside the problem of patient response to the machine itself and the general context of receiving TPE it is also useful to examine how patients evaluated their individual response to the treatment. That is, did they feel specific improvement, and, if so, in what ways? Patients' evaluation of their own progress is, of course, directly related to the nature of their underlying condition. Response is mediated by the magnitude of the threat to health and well-being. Keeping this qualifying fact in mind, the general response of patients to treatment with TPE is overwhelming enthusiasm, occasionally true even for patients who do not experience much subjective improvement in their symptoms after receiving TPE.

A large subset of TPE patients feel that they have experienced considerable improvement as a result of their treatment. The most enthusiastic statements came from

patients who had been seriously disabled by their illness. One person with myasthenia gravis made the following response to a question at the end of our interview when I asked if she had anything to add. She said, "Perhaps you should have asked how it has changed my life. [And the answer would be] dramatically, drastically. Not only physically but psychologically and every way. I'm a different person." This kind of response was characteristic. One patient described the entire process as a "miracle." Another said, "It's keeping me alive; that's how I look at it." This level of excitement is not unexpected from a myasthenic patient, because improvement in this disease can be quite dramatic, especially at the very beginning. One patient said, "After the first one [TPE treatment] I was able to lift my arms and do my own hair for the first time in seven years." But the excitement is not limited to patients who might actually experience an immediate subjective change. A patient who received TPE to <u>prevent</u> increased kidney failure during an exacerbation of SLE was equally enthusiastic. She reported, "I feel great. I have a new life...I could jump out the window and go home." These examples show how willing patients are to attribute their improvement to the machine, rather than to other aspects of their therapy, such as drugs. It is much more dramatic to be connected up to the cell separator than to take a simple pill. Even though plasma exchange is often performed in conjunction with powerful pharmacologic

immunosuppression patients tend to attribute their improvement to the more dramatic aspects of their care, neglecting the role of drugs.

Patients who are unaware of any perceptible physical change are sometimes able to follow the changes that are measurable in the blood, accepting these as a marker of progress. In reality, because of the complexities of immune function, blood levels of harmful proteins may be unrelated to the clinical manifestations of a disease. For many of these patients, relief comes simply from the fact that something is being done, that there is an objective goal in their care. These patients became resigned to continued therapy. One man said, "I must like it...There's no alternative for me."

Patients who have no objective signs of improvement are sometimes more cautious and realistic about success. One woman stated, "I honestly don't know if it's made any difference or not." More sophisticated patients realize the full complexity of evaluating clinical progress in a chronic illness. One man thought that he felt "great," but, "It may well be my mind rather than my body."

If anyone provides more cautious optimism it is the nurse technicians operating the equipment. Perhaps because they have the least emotional investment in the success of the therapy their assessment of patient response tends to be much more conservative. Nurses are often unable to perceive the improvement patients report after having had treatment.

One multiple sclerosis patient described improvement in glowing adjectives, claiming to have had "a complete metamorphosis," now a "changed person," at a "high plateau." The nurse who treated her reported, "There's one M.S. [multiple sclerosis] patient in particular who claims she's had results and felt much better after her exchanges. I've never really noticed any results..." Physicians also voice scepticism about patient perceptions of improvement but their own personal investment in the treatment's success or failure makes it more difficult for them to discredit enthusiastic reports of patient improvement.

A nurse summarized the many pressures on these patients to experiment with new therapies:

> Patients are at the end of their rope...[They] have nowhere to go...There is seemingly no other therapy at this point. They're very enthusiastic. They'd come in the middle of the night, or they'd stand on their head during the procedure or they'd do anything. They're desperate. And they're going to have a good response to this procedure if it kills them....They're so psyched for it.

TPE as Blood Washing: Culture and Explanatory Models

Medical anthropologists have long noted the need for "fit" between the cultural beliefs and values of a sick person and the methods of treatment employed by a healer. A person who believes that his symptoms are caused by spirit possession is unlikely to consult a conventionally trained psychotherapist. Cultural fit between patients and healers must exist on two levels: participants in healing must share

basic concepts of disease and proposed treatments must blend in well with preexisting concepts of therapy. In the example cited above, the patient and client share neither the basic belief that the illness is caused by an evil spirit nor beliefs about what would constitute appropriate therapy. A totally new mode of healing might eventually gain widespread acceptance purely on the basis of dramatic effectiveness. The near universal acceptance of antibiotics in the developing world is a clear example. But initial acceptance and enthusiasm are increased if the therapy "makes sense" to the prospective clients in terms that are culturally specific. Because of the increasingly complex nature of modern medicine this is not a simple goal. There are often as many basic differences in beliefs between Western doctors and their patients as exist in cross cultural health settings, when healer and patient are from different national or ethnic backgrounds.

An interesting feature of TPE as a treatment modality is its "fit" with basic cultural values which equate concepts of cleanliness and purity with ideas of good health and the healing process. Plasma exchange "makes sense" to us on a number of levels. First, it fits in well with long-standing western ideas of "bad blood" as an important cause of ill health. Problems with the blood were important in explaining many types of diseases. Syphilis is perhaps the best example. Second, there is also a strong pattern of association between disease and filth, or unsightliness.

(This may relate to the disfigurement caused by a number of infectious diseases.) Lepers were considered "unclean." And finally, many Western folk remedies involve notions of either cleansing or purging. Use of enemas, leeches, and forms of blood-letting all share the underlying rationale of ridding the body of noxious subtances (or restoring a proper balance). Often healing ceremonies include a symbolic washing ceremony, or occur at springs or fountains. The most significant New Testament example is the Pool of Bethesda in Jerusalem, which was believed to have healing powers (John 5: 2-4). And baptism, of course, "cleanses" new Christians of their original sin.

Because of this shared cultural background, patients were able to "understand" the rationale for using plasma exchange by resorting to a metaphoric comparison of the process of TPE with the notion of cleansing. Patients were frequently unable to understand the complex nature of antibodies or other proteins circulating in their blood. However, the notion of removing a noxious substance had almost universal explanatory power. Both American and English patients (and not only those lacking in scientific sophistication) referred to TPE as "cleaning the blood" or made use of other cleansing metaphors.

The following is a characteristic response when a TPE patient was asked to explain how his treatment worked:

> They take off the red cells and clean them up. You know, the old yellow stuff [is taken off] and the new clean blood is mixed

> in. It's all pure going back into me...all new and clean; it must do some good musn't it?

Another patient described the process:

> It's like having a big clean-out...It's like having a bath. When you get out you feel all tingly and fresh.

Similar language was used by many of my patient informants describing the procedure. Some talked about "purifying the blood" or having a "blood change." A constant feature was the tendency to refer to the removed plasma in pejorative terms, i.e., "impure" or filled with "baddies." Conversely, the replacement plasma was spoken of in highly positive terms, as "fresh," "clean," "pure," associated with new life. One patient was convinced that since the donors for the replacement plasma were likely to be younger people, the plasma itself was bound to have a "rejuvenating effect."

These treatment metaphors were reinforced in a number of ways. Most important, there was direct visual reinforcement; the old plasma tended to look cloudy and dark compared to the plasma replacement fluid which was generally clear and lighter in color (see figure 4 in chapter I). For the most part, the substances removed, such as antibodies or immune complexes, were not directly visible in the patients' plasma. For some patients, however, the substance removed from their blood, for example cholesterol, is quite visible in the removed plasma. Thus the cleaning explanation makes

especially good sense for this group of patients but is not limited to them.

The use of metaphoric descriptions of TPE as a cleansing process was not found exclusively among patients. Physicians and nursing staff often reinforced patient beliefs by using similar language when talking casually about TPE. For example, it was not unusual when listening to a physician talking about TPE with a patient to hear the physician use the phrase "having your blood washed." Different TPE treatment units developed different short-hand phrases to describe the procedure, often encorporating the cleansing metaphor. Nurses reinforced the idea that the old plasma was bad as they discussed the procedure with patients. I overheard one nurse say, as she pointed to the plasma removal bag, "That's where the grotty stuff is." Similar explanations came from other sources. A company representative described TPE to a patient as "like an oil change [in a car]".

Of course it is impossible to determine the exact origin of this explanatory model. Is it strictly the patients' explanation or did patients acquire these linguistic formulas from physicians attempting to explain the procedure in easy to understand lay language? The answer would be difficult to determine and is irrelevant to the model's power in explaining TPE. Ultimately it doesn't matter where the exact language came from, the important point is that it helps create meaning, and a culturally

shared meaning, in the minds of both patients and staff performing the treatment.

Coverage of TPE in the media also exploited the metaphor. The titles of articles in the popular press reflect the cultural relevance of the idea of TPE as cleansing. One article was titled, "Blood Purge" (1979) and another "Cleansing the Blood" (Edelson 1982). A third included the caption "washing out antibodies" (Clark 1978). Even an article in the staid New York Times was subtitled, "Separating 'Bad Blood' from Good" (Altman 1982).

It is also important to keep in mind that this explanatory model is not mutually exclusive with more "scientific" explanations. Although the complexities of the immune system are such that talking simply about removing antibody has little scientific veracity, there is no doubt that the TPE procedure accomplishes the removal of theoretically pathologic material from the blood. Thus the scientific models of TPE easily coexist with the more popular model based on cleansing.

Many patients incorporate both views into their thinking about the treatment. It was not unusual for a patient to combine the two elements, speaking in mixed metaphors. One patient said, "the anti-GBM antibody resided mainly in the plasma and so what they used to do was remove the plasma and replace it with fresh, clean, plasma..." [emphasis added]. Another patient was able to give a very complete, technical account of the pathophysiology of his

underlying disease, talking specifically about destruction of the myelin sheath surrounding his nerve cells. However, when discussing the new plasma he described it as "clean." This fit between the two kinds of explanations adds to the overall appeal of TPE as a therapy. A patient summed up his views on TPE by stating, "The treatment makes sense to me on a logical level...It's logical, sensible, reasonable."

Clearly, the notion of cleansing, especially when accomplished by a remarkable-looking machine, has considerable symbolic value in the context of western culture. In addition to the cleansing metaphor it is important to recognize the symbolic importance of a treatment encorporating the manipulation of a person's blood. Blood is a relatively easy concept for most lay people to understand. Since everyone has seen and felt blood, it is not as remote an entity as the pancreas, pituitary gland, or lymphatic system. Blood also has a central position in the array of symbols in Judeo/Christian cosmology. It is representative of a person's essence and very being. One nurse described this belief in the almost sacred status of blood. "People think their life is in their blood and part of their life or personality is gone [removed with the blood]." She attributed this to "Biblical ideas equating the soul, the heart, and the blood." And the idea of "new" blood is closely associated in the Christian religions with ideas of new life and regeneration. The communion wine (the miraculously transformed blood of

Christ) imparts new life to the believer. Reformed sinners are, "washed in the blood of the Lamb."

I believe that the cultural fit between the modern concept of TPE and these ideas of treatment based on cleansing helps to account for the rapid acceptance of TPE as a treatment modality. Many of my informants expressed similar views. One physician said,

> The whole idea is something that, maybe in a macabre sort of way, appeals to patients...They get their blood taken out through this machine and somehow the things that are making them sick are going to be removed. Sort of like a modern version of removing the evil humors.

In and of itself this notion of cultural fit would be incapable of explaining the rapid acceptance of TPE by patients and physicians alike. Combined with other factors, both structural and cultural, it adds to our understanding of the technological imperative at work in the early stages of TPE's development.

Patient Demand for Treatment

In many instances patients are not merely passive recipients of a new therapy but rather become active protagonists in the "drama" of new medical discoveries. While investigating the early use of TPE I discovered many examples of patients receiving therapy after exercising considerable pressure on physicians to treat them, often outside the bounds of established clinical trials. I interviewed patients who had travelled widely around the

country seeking out treatment with TPE. A patient from a San Francisco hospital had journeyed to both Stanford University Medical Center and the Mayo Clinic in Rochester, Minnesota. A second patient, whom I encountered in Minnesota, received TPE first in Los Angeles. A discussion of "patient demand" for therapy provides the patients' perspective on the "desperation reaction" decribed above for physicians. Desperate patients demand therapy from their physicians.

One patient's search for an answer to his debilitating multiple sclerosis illustrates the importance of patient activism in gaining access to therapy. This man, from the rural area of a western state, found out about TPE on his own:

> I saw one little thing in an M.S. [Multiple Sclerosis Society] flyer that says, plasma exchange. I didn't know anything about it. So I looked at it and I looked at it and I called up my doctor in Smithville, Dr. Andrews. And he didn't know anything about it either. So he called the [state] medical school.

After gathering information, this man called a physician at a large urban hospital.

> I called him the 1st of June and talked to him on the phone...He didn't know whether I should come or not, you know. So then I told him my situation, I said, well, I've got to do something. I can't just sit around here and wait...this is damn foolish. So he said, fly on down, and I said, well, I'll come as soon as I can make arrangements.

He eventually received a course of TPE for his multiple sclerosis after overcoming numerous difficulties, including financial problems. A physician summed up the situation of similar patients:

> And always, for things like cancer, rheumatoid arthritis, M.S., there will be patients who are desperate, at the end of their tether, and will try anything... They'll swallow stuff that's known not to work, and known to have harmful side effects...Because they're desperate.

This doctor went on to say that physicians have an obligation to protect patients from this sense of desperation and from potentially harmful treatments. However, this obligation is complicated by physicians' dual roles as clinicians and researchers. Physicians may wish to protect their patients from harm, but it is precisely those patients desperate enough to try "anything" who become partners in medical research.

The Role of the Media. Descriptions of god-like physicians making brilliant discoveries are favorite themes in the lay press. These cultural stereotypes are often exploited by the media in their presentations about new medical discoveries. Medawar and Medawar attribute the problem to lack of understanding of how science really operates:

> Laymen do not realize the width of the gap between conception and execution in science, because they have been misled by a particular kind of fiction in which a young medical scientist, with a dedicated expression on his face, tiptoes

> purposefully out of the ward to devise, or perhaps even to discover, some new serum or nostrum he has just thought of. It is the width of this gap that makes possible the interposition of wiser counsels and restraining hands between far-fetched ideas and the attempt to put them into effect (1977:162).

However, the media often attempt to jump this gap by reporting even the earliest glimmerings of a cure, especially if the disease is serious or life-threatening. Our cultural preoccupations make these stories newsworthy. A successful "formula" in such a story included a catchy title, often capitalizing on the cleansing metaphor, plus a photo of the patient -- preferably attached to the machine to increase dramatic interest -- with the physician "inventor" in attendance. A number of stories describing the technology as a major breakthrough in medical research appeared in the early years of TPE's development. Articles appeared in major newspapers (Altman 1982, Positive Research 1983, New Treatment 1983, Hamilton, 1981, Robertson 1978, Petit 1979) and magazines (Clark 1978, Blood Purge 1979, Edelson 1982, Zimmerman 1980, Langone 1981). These articles often had a direct impact on physicians providing care to patients. One informant described being "deluged with calls" after publication of a report on TPE for rheumatoid arthritis in Time (Blood Purge 1979). Numerous physicians and nurses reported receiving phone calls after the piece appeared. Following another article, an English physician received calls from America in the middle of the night.

Clearly, media coverage promotes patient efforts to gain access to new therapies before they have been evaluated.

A good example of patient demand for access to new treatments following media discussion occured early in TPE's development. A physician well known in medical circles for experimental work with TPE in systemic lupus erythematosus (SLE) was the subject of a short article in the Ladies Home Journal (Zimmerman 1980). The article was written by a reporter after he attended a scientific meeting where the physician gave a lecture; the reporter never contacted the physician directly. This physician was stunned to receive hundreds of responses to a magazine article that was only a few paragraphs long. He allowed me to examine the large collection of correspondence he had received from patients and their families after publication of the article. The letters came from all over the United States. Some were labeled "urgent" with exhortations for a prompt reply. Many prospective patients offered to come long distances in order to receive the new therapy. In addition to the requests for inclusion in this doctor's research program, the letters asked for either additional information or referrals to other physicians.

Selected quotations from the letters reveal desperation in the face of chronic illness and excitement at the prospect of a new-found cure. One woman wrote:

> My family and I were very thrilled when we read an article in a magazine about your discovery of plasmapheresis for the

> treatment of SLE. My daughter [name withheld] had her first attack in 1974. She wonders if plasmapheresis could help her or is it too late for her? God bless your endeavors.

Other writers described multiple failed attempts at therapy, all "to no avail."

> I have taken so many drugs, been pricked, probed and experimented with for almost six years. I'm tired of it, but the pain is taking over now. I don't know if you can help but I had to try. This may be my answer...Right now I am under the care of a kidney specialist but he is running out of answers.

Despite past experience with failure many patients were encouraged by the media explanation of the new therapy and wished to try it. A husband wrote about his wife. "She needs help desperately. Is it possible for her to undergo your procedure Plasmapheresis?" Another wrote, "I would appreciate any information that could be given on how to become a part of the reserch [sic] program."

The intensity of these responses indicates both the despondency of patients with chronic illness and their potential power in demanding access to new treatments during "experimental" stages of development. It is very difficult for patients to understand why they can not receive a new treatment that is written up in the popular press or discussed on television.[2]

After TPE's first use for myasthenia gravis in the late 1970s, the new treatment was featured on the Muscular Dystrophy Association (MDA) "Telethon," a very popular U.S. television event hosted by the American media personality

Jerry Lewis. Films of patients, including "before" and "after" scenes, were emotionally powerfully and successful in raising funds: the explicit function of the telethon. However media events such as this serve a less visible function as well, viz. alerting potential patients to the possibility of a new "cure." Immediately following the Telethon, one physician reported receiving 70 letters per day. As described above, this pattern was repeated around the U.S. after each major media event or article.

In the case of plasma exchange, one significant difference between America and England was in the area of patient demand for treatment. I rarely came across instances of patients receiving TPE in England because they had requested it or lobbied for it. Indeed, most of the English patients I encountered had not even heard of the technique before receiving it.[3] In America, by contrast, I encountered many patients who had more direct influence over the course of their treatment, including patients such as those mentioned above who had read about the new treatment and aggressively fought to receive it.

In England the lack of patient demand is at least partially due to the very different organization of medical care. Referrals to hospitals and speciality clinics are made almost exclusively through a patient's local general practitioner. Direct access to specialty care -- which is generally available in America through self-referral to physicians -- is not possible in England under the N.H.S.

Another feature of the English system is a less "demanding" patient. This opinion was corroborated by many of my informants. English patients certainly do not view themselves as active consumers of medical care, a common stance among American patients. They tend to express gratitude for the care they do receive, plus confidence in their physicians, or if not confidence at least resolute acceptance that the doctor knows best. When questioned about patient pressure for treatment, many English physicians expressed horror at the thought of a patient initiating the idea of treatment with TPE.

Finally, different views of "medical ethics" (really etiquette in this context) make it more difficult for English patients to obtain direct knowledge of physicians working with new treatments. In contrast to America, it is considered highly questionable for a physician to have his name publicized in association with a report about a new drug or therapy. A physician who breaches this informal code of conduct opens himself up to censure from colleagues.

Disease Interest Groups. In addition to the lay media, another important source of patients' knowledge of new techniques -- and thus increased patient demand -- is the "disease interest group." These voluntary organizations, exemplififed by groups such as the Multiple Sclerosis Society, the Muscular Dystrophy Association, and the American Cancer Society, provide an organizational focus for patients' efforts to fight the ravages of their diseases.[4]

Found widely in both the U.S. and U.K., these groups were influential in the growth of TPE in a number of ways. First, they generated patient demand for treatment through their function of supplying patient members with up-to-the-minute information about new therapies. It was not unusual to encounter a patient who had first learned about TPE through such an organization, like the man with multiple sclerosis described earlier.

In addition to speeding the flow of information early in innovation, the societies also served as a direct influence on the development of TPE by providing funding for early research activities as well as some direct services. When TPE was first applied as a therapy for autoimmune disease many considered it an "off the wall" idea. Hence research funding from conventional sources (like federal grants) was practically impossible to obtain. According to my physician informants, on a number of occasions various disease interest groups provided monetary support for research. The MDA supported early research in myasthenia gravis and funded an international conference to disseminate early findings among clinicians and scientists. The Kroc Foundation (funded by the founder of McDonalds Restaurants) supported some of the early work in multiple sclerosis. Because donating capitol equipment is a dramatic and visible gesture, these organizations would sometimes donate a TPE machine to a hospital, thus subtly coercing the organization

-- even a financially strapped N.H.S. hospital -- to contribute the funds necessary for supplies and personnel.

These organizations also support patients in their efforts to obtain therapy. One disease interest group sponsored a house across the street from an innovating clinician's hospital. Out of town patients were invited to stay in the house free of charge while receiving prolonged courses of therapy with TPE. The disease interest groups are subject to the same pressures as physicians. Although they try to reflect scientific values of disinterest and rigorous evaluation of new treatments, they are, nonetheless susceptible to the considerable pressue for new therapies generated by their members. The basic tension between scientific interest and patient demand is accentuated by the disease interest groups.

The Negotiation of Therapeutic Response

Fox (1959) recognized three decades ago that patients and physicians often form partnerships in the process of medical discovery, with patients volunteering for dangerous new treatments or experimental drugs and physicians pursuing goals of basic research. The many forces enumerated above -- the mutual desire for a successful outcome, the desperation experienced by patient and clinician alike, and the powerful research goals of physicians -- put enormous pressure on the process of evaluating new therapies. Often patients experience great demands to demonstrate that they have had a

"correct" response. A good response is a way to repay physicians and other health care workers for the time and energy devoted to their care. And after investing considerable personal resources -- including physical discomfort, time and emotional energy -- to an innovative treatment method, patients are primed for a dramatic response to therapy. When one factors in the spectacular nature of TPE and its fit with pre-existing ideas of therapy, it is clear that the stage is set for dramatic improvements.

The actual social interaction in the TPE treatment unit often "trained" the patient to make a correct response to therapy. There was enormous pressure on patients to get better or at least report improvement. I observed numerous examples of physicians giving patients cues as to how they should respond. When a woman patient reported no change in her condition after her first plasma exchange, her physician responded, "Well, we don't see any response in our patients until they've had four or more treatments." She was thus informed of the correct timetable. They were also given encouragment to show progress. I watched a physician doing a neurological exam to evaluate a patient's improvement. After requesting that the patient squeeze his hand, the physician asked, "is that as good as you can do?" Thus patients who failed to improve were failures, putting additional pressure on them to "conform" and report progress. Patients also talked frequently with each other,

for example while waiting for treatment, thus further refining their knowledge of what constituted an ideal response.

The control physicians exert over patients contributes to the social negotiation of patients' response. A number of nurses noted that patients would only complain to them, always remaining positive when the doctor -- who controlled access to further therapy -- was present.

> Rita noted that even if a patient has been lying in the bed bitching to the nurses, when Dr. Daniels comes in to the unit, they stop bitching. Rita said that she thinks patients are afraid of him...they don't want to displease him because he has the power to stop their treatment...Rita then demonstrated for me how Dr. Daniels would look at a patient, rub their skin, and tell the patient that their skin seemed softer and that they were better. Rita's comment was, "I though scientists were supposed to be objective...I don't see any difference" (fieldnotes).

The scientific values of the physicians come into direct conflict with their responsibilities as clinicians. Often the values of science prevail.

> Dr. Ward described an incident that had happened that morning. They had seen a patient who wasn't a candidate for the clinical trial. Dr. Ward told the patient that she could not be in the trial and could not have TPE. He described her as very upset, crying, her husband was almost crying, too. Ward Described this as a "tragic situation." But, "you have to be hard-nosed or science won't get done" (fieldnotes).

These decisions are exceedingly difficult. On another occasion I observed this same physician make the opposite decision and treat a patient in spite of the fact that she did not meet the criteria of a certain experimental protocol. All innovating physicians experience the tension produced by their dual role as scientist and clinician.

Even when clinical trials are conducted they do not always lead to clear, unequivocal results. Clinicians must make treatment decisions daily in the face of considerable uncertainty; that is the nature of clinical practice. Thus, for both physicians and patients powerful pressures, first to make use of new therapies and then to evaluate those treatments positively, are of paramount importance in the technological imperative.

Notes

1. Specifically for homozygotes with type IIa disease.

2. A recent example of the collective power of patients in shaping the treatment practices of physicians is seen in the handling of the AIDS epidemic. In this situation, unique because many of the patients formed a solid political group based on a shared sexual identity, patients exerted considerable power by demanding access to new experimental therapies and refusing to cooperate with standard clinical trials which denied universal access to new treatments.

3. However, the small size of my sample of patients precludes a definitive statement about the differences between American and British patients.

4. The prototype of these organizations is the National Foundation for Infantile Paralysis (later the March of Dimes) established in 1938 to fight polio. This group pioneered the techniques of mass fund raising and support for basic research which are commonplace today.

Chapter V

THE ROUTINIZATION OF TECHNOLOGY USE: THE SOCIAL CREATION OF A "STANDARD" TREATMENT

> Routinization, regularization, repitition, lie at the basis of social life itself.
>
> Jack Goody

In previous chapters I have described the scientific history of TPE, the relationships between medical equipment manufacturers and innovating medical researchers, and the forces influencing physicians and patients to endorse new therapies enthusiastically. This is vital information; we cannot hope to understand the operation of the technological imperative in medical practice without this knowledge. However, none of this information sheds light on the crucial question of how TPE (or any new therapy) actually becomes imbued with a new "meaning," how it loses its experimental tone and begins to be understood by those participating in its development as a standard therapy. In this chapter I explain this changed meaning in terms of the social processes of the individual TPE treatment unit. I heuristically remove the treatment unit from the web of social, political, and economic forces which form its breadest context in order to focus on social interaction.

It is crucial to note that I am describing a social phenomenon which occurs separately from the strictly scientific, medical evaluations of efficacy being conducted by TPE users. Routinization is occuring as clinical trials are carried out; in actuality the two processes are intertwined. However, a heuristic separation is central to my analysis because new medical technologies do not become accepted as standard therapy simply because they are scientifically proven to work. An enormous number of commonly used procedures have become routine without ever having been proven effective. Blood-letting and cupping provide good examples in western medical history, as does the prescription of antibiotics for the common cold.

In this chapter I begin by discussing the theoretical importance of the routinization argument, dealing with the issue of how meaning is "constructed" in a social setting. Next I provide a careful micro-level analysis of the process of routinization in TPE treatment units, contrasting the routine with the experimental setting. I then discuss the social characteristics of routinization, including actual ward rituals, and the changing division of labor and altered social relations on the units. I focus special attention on the role of the nurse in "managing trouble" as it occurs, thus allowing the treatment ritual to proceed. I conclude by discussing the transmission of medical knowledge to a new generation of workers. The wider organizational context of

routinization is discussed briefly to frame the major argument.

The Routinization of Technology Use

In medicine a new therapy begins as an unusual, perhaps dramatic, but certainly out of the ordinary event. This is true whether the therapy is a new medication, a complicated surgical procedure, or an impressive machine-based technology. Although administering a new tablet is quite different from orchestrating a new cardiac surgery technique, they share the basic characteristic of novelty. The use of a new therapy upsets the everyday routines of clinical practice. Like test tube babies or the artificial heart, they are front page news.

Over time, however, this upset must resolve. The news of subsequent heart implants is buried in later newspaper pages and gradually recedes from public attention and notice, attracting no attention. Medical procedures which are not abandoned in the earliest stages of use eventually proceed to a state of "ordinariness." Their use is no longer perceived by hospital staff and patient as unique and new. They become the standard of care.

The core of my argument is that the meaning of new biomedical technology changes as participants become habituated to its use. Through a social process which I will call simply "routinization," the meaning a technology holds

for its participants becomes redefined. Routinization, of course, lies "at the very basis of social life itself" (Goody 1977:28). Social life would be impossible without the familiar patterns of the routine. "...Habitualization makes it unnecessary for each situation to be defined anew, step by step" (Berger and Luckman 1966:53-54). Since illness is by its very nature chaotic and unpredictable the fact that social settings in medicine tend to be highly routinized is not surprising.

I believe that it is through a process of social routinization that this changed meaning takes place. An initial "exerimental" designation gives way to a new interpretation, that of "standard therapy." The meaning of the technology for the participants, either experiment or standard, is derived from the social setting itself. An experimental situation is drastically different from the everyday hospital routine.

As Barley (1988) shows, the use of sophisticated new imaging devices in medicine demonstrates the importance of the social context in comprehending the effects of technology. Although CT scanners clearly cause change in the social organization of the radiology departments in which they are employed, the scanners' impact is felt only through the constructed understanding of the equipment which is developed by the users as they struggle with a novel technique. The meaning of a new technology is not automatic, but evolves gradually. In the case of

therapeutic plasma exchange, I argue that one key facet of this meaning -- the placing of the machine along an axis of experimental versus standard therapy -- occurs as participants in the use of the technology struggle with its application and gradually tame the machine through a process of routinizing its use in everyday practice. Originally, the CT scanner's "adoption by a local hospital [entailed] a sudden rent in the tissue of day to day experience" (Barley, ibid.). Before too long, however, the machine users had developed strategies to keep up at least "the appearance of normal operations" (ibid.). A similar process occurs as TPE is used with greater frequency.

Contrasting Views: "Experimental" vs. "Routine" Treatment Settings

In the early, experimental stage of its use, a new technology may seem cumbersome and even bizarre. One of the inventors of the I.B.M./N.C.I. cell separator (discussed in Chapter II) described the first use of his new machine with human subjects.

> I can remember with great fondness the original studies in man. I remember how we prepared the instrument using hand-assembled plastic tubing sets made in our own laboratory. After everything was sterilised, we wheeled the entire assembly from the laboratory area into the hospital and right to the patient's bedside. We made a strange sight wheeling that huge machine with various bottles hanging from brackets through the hospital wards (Freireich 1975:xxxiv).

During fieldwork I was able to observe a "natural experiment," the introduction and early clinical trials of a new type of TPE equipment. Although it accomplished the same task as the earlier model, this equipment was based on a different principle: filtration of the blood rather than centrifugation. As I observed this equipment in use it immediately became apparent that something out of the ordinary was happening. An examination of the first use of this new procedure provides an illustration of the experimental treatment setting.

First of all, the "newness" of the machine was celebrated by a constant stream of visitors; each person who entered the treatment room focused immediate visual attention on the machine itself:

> They always asked technical questions and were given an elaborate explanation. The visitors seemed intrigued with the technology. One physician came in, asked a question, and received a detailed description of the size of the pores in the filter membrane (fieldnotes).

This picture of a circle of white-coated figures gathered around the machine, attracted as to a fire on a cold night, was repeated over and over in the course of my observations. Scenes such as these are graphic representations of the fascination with technology inherent in Western medicine. Second, many of these visitors were physicians. In my experiences with the use of TPE in everyday treatment settings, physicians were rarely present as the therapy was being administered. By contrast, with

the new machine it was physicians who were most intimately involved with both setting up and running the novel device.

The physician primarily involved, Dr. Parker (a pseudonym), was constantly in attendance. The new machine was to be used daily for three days, including the weekend, when no nursing assistance was available. A patient with an unusual and damaging blood protein was the subject. The tone of the procedure was one of moment by moment uncertainty and hesitation, beginning with setting up. Dr. Parker had to negotiate with a nurse from the kidney dialysis department (experienced in the extracorporeal manipulation of blood) in order to get help in setting up the system.

> A number of trips had to be made back and forth to the dialysis unit, which was a distance away...[and] upstairs to the lab for filters and notebooks. They kept needing additional little bits of equipment that they had forgotten or didn't know they would need (fieldnotes).

After a struggle that lasted for a number of hours (and was repeated to some extent each day the machine was used) the treatment got under way.

This general level of confusion continued throughout the treatment. Every decision point was problematic and required additional work and negotiation. Dr. Parker was on hands and knees with the nursing staff (or when they were not present, with the anthropologist) piecing together bits of equipment and drawing up medication in syringes. Also present throughout was a representative of the manufacturer

of the new machine. The representative removed his jacket and gave "hands-on" assistance with the equipment. He helped collect samples of the patient's blood every few minutes in order to gather data on the machine's efficiency in removing the suspect protein. He loaned the medical team a special infusion pump to make the procedure easier and made numerous telephone calls to gather needed information on technical questions, such as the proper amount of anti-coagulant medication needed. Dr. Parker attempted to reduce the tension level in the unit by joking, "This could be done by one person if they knew what they were doing."

Eventually the team managed to complete the series of treatments in spite of major complications during one procedure when the patient's blood clotted in the filter. In summarizing the three day's treatment I noted:

> Dr. Parker kept repeating throughout that he didn't know what he was doing. The treatment room was in a constant state of chaos, with staff members laughing, IV poles falling to the ground and physicians running in and out of the room. How the patient managed to remain calm is a mystery. When the procedures were finished the room looked like a deserted battle field. There were empty boxes everywhere, the bed was covered with blood and there was spilled plasma all over the floor (fieldnotes).

The social scene was the complete opposite of the calm and orderliness characteristic of a "routine" TPE procedure. You had only to walk into the room to discern that something out of the ordinary was going on.

The contrasting images of a "routinized" treatment setting are strikingly different. The most powerful visual image of routinization is a picture of the plasma exchange nurse sitting calmly at the machine controls which have only half of her attention, the other half devoted to the morning newspaper. All the needed supplies are available; the equipment is set up and ready to go. The nurse has spent over an hour carefully preparing the machine and other equipment before the patient arrives. This orderly atmosphere was summed up by a patient who said, "It's almost an assembly line." Another veteran patient who had been receiving treatment for a number of years noted the great differences between the TPE unit "in the old days" and currently. Whereas previously she had felt like "an oddity" while receiving treatment, she now described her TPE therapy as "almost like a tablet." By describing her TPE therapy as feeling as routine as swallowing an aspirin for a headache, this patient graphically illustrates the changed tone present on the unit.

Although every unit has busy and chaotic days when crisis follows upon crisis, especially when acutely ill patients are treated, the overall tone of the TPE unit that is well established is one of calm and orderliness. The "assembly line" feeling is pervasive. Patients come and go, supplies are ordered, routine blood tests are carried out, all managed efficiently by TPE nurses. Nurses dominate the setting. Their interaction with the equipment itself is

matter-of-fact, embedded in the everyday hospital routines rather than set apart as in the scene described above when Dr. Parker was in charge. The following observations are exemplary: "Edith read the Guardian and did paperwork during the exchange...The nurse heated her lunch in the microwave and ate while seated at the machine controls" (fieldnotes).

But this seemingly calm exterior can be deceptive. In order to maintain an appearance of the routine in the face of the realities of clinical practice in medicine (that is, the constant problems of applying a technology to particular human beings), a major activity of the nurse on a TPE unit was that of "managing trouble." It is important to note that the underlying chaos does not disappear completely as a new therapy gradually loses its experimental designation. Rather, by managing trouble the nurse shields the physician investigator from all but the most serious kinds of aggravation (or "aggro" as the English nurses called it). The nurse makes sure that the healing rites of TPE are always performed in the "correct" fashion.

Although an exact estimate of the frequency of untoward events is impossible, information from my own observational data plus records of TPE procedures kept by some treatment units indicate that they are an everyday occurence. Numerous fieldnote entries include an example of a nurse coping with a disaster or smoothing over a procedural difficulty. In one unit over a two week period I noted that one out of three treatments (approximately one

per day) was complicated by some difficulty. Although problems with vascular access were the most common, other difficulties include failed transport arrangements for patients, machine failures, or shortage of supplies, including plasma replacements. Some problems are predictable in that they occur regularly (even if this is often not acknowledged by the staff). Other problems are more unique, such as an entire shipment of plasma freezing -- and thus becoming unuseable -- during a January blizzard in the American midwest. The following example is illustrative, describing a procedure that was troublesome from the beginning when staff had difficulty getting access to the patient's veins.

> From here on things got even worse. There was a serious problem with the machine and blood leaked all over. It spurted all over the nurses, the machine itself and the floor; it was a terrible mess. A physician looked in the room incredulously, made a face, and left. There was blood everywhere...Eventually the nurses were able to get control of the situation and clamp off tubes, etc. They then dissolved in almost uncontrollable laughter (fieldnotes).

This scene was reenacted over and over: sometimes air would mysteriously enter the system, sometimes the patient's blood would clot in the centrifuge bowl, occasionally the blood flow from the patient would be so slow that the procedure would drag on for hours longer than expected. Nurses were constantly engaged with controlling the effects of untoward events.

Social Relations and the Division of Labor

On the surface the social milieus of the TPE treatment episodes I have described appear alike; confusion and disorganization seem the order of the day. Yet as one examines the social relationships among key actors these similarities disappear. Significant differences exist in the actual division of labor among TPE participants as well as in the hierarchical ordering of relationships. The changing roles of physicians, nurses, patients, and equipment manufacturers are revealing. These differences are crucial in interpreting each actor's understanding of the meaning of the TPE therapy. Of particular importance is the meaning of the therapy for physicians because of their dominant position in making decisions about the use of TPE.

For the physicians, even actual clinical encounters with patients and troublesome machines sustain the meaning of TPE as research. While the patients and technicians remain in the chaos of the experimental treatment setting, the physician is able to escape to the world of "the lab" and "data." Even in the "chaotic" experimental treatment situation described above the end result for the physician, at work in the lab a few weeks later, is far removed from the scene described. When this physician was interviewed he enthusiastically displayed the data obtained from the treatment. The actual experience of treating the patient had been turned into a series of graphs and charts showing

the machine's performance and the changes in levels of substances in the patient's plasma measured against clinical improvement. The entire event was neatly recorded and graphically represented, reduced to a few pieces of paper and in the process "transformed." The data, representing the fruits of research, remain long after the patient has gone home and the scene of the treatment has returned to normal. The data become the meaningful reality. For the physician, routinization occurs as clinical encounters are turned into research results. The imperative to make use of new machines derives, at least in part, from the equipment's data-generating capabilities.

Perhaps the most important change which occurs during routinization is the change in who actually performs the TPE procedure. During the experimental, uncertain stage of development physicians are in constant attendance, struggling with the new procedure and working alongside the other staff. A pioneering TPE patient told me, "Dr. Daniels used to sit by the machine with a book trying to figure out what to do next." In fact, most of the physicians who were pioneers in developing TPE were expert technicians, often conducting all treatments unaided. Nursing staff familiar only with the routinized stage of TPE's development expressed amazement that physicians had once done all the work themselves.[1] The nurses' incredulous reactions speak to the fact that in the routinized treatment setting actions and patterns appear inevitable.

By contrast, the later, non-experimental stages of TPE's development are dominated by nurses. Notable was the physician fleeing from the room as trouble began in the scene described above. One nurse claimed the physician she worked with had never been in the plasma exchange room. Others complained of the lack of interest of physicians in the routinized treatment setting, stating that they were no longer helpful or willing to explain things. When the machine is new all eyes focus upon it, whereas in the later stages a request for help is met with the physician's uninterested reply, "It's not my patient." Thus, important signs of routinization are the changes in the actors' level of involvement and in who actually performs the procedure.

Another sign of increasing routinization can be seen in the type of relationship which exists between physicians and nurses. Early on, in the experimental, non-routinized phase of TPE's development, nurses and physicians act as partners in the research endeavor. Tasks are shared, not rigidly divided. A nurse might appear as the co-author of a scientific paper. As time passes, however, these egalitarian relationships are transformed into the more traditional nurse/doctor relationship, hierarchical in nature. In this phase the physician simply "orders" the procedure which is then carried out by the nursing staff. Trouble, which is shared mutually in the experimental phase, becomes in the later stage an annoyance to be handled by the nurses. It is almost as if the experimental tone of the

early phase allows a violation of the traditional superordinate/subordinate relationship. With increasing routinization the barriers to egalitarian cooperation go back up. No longer research partners working within the same uncertain treatment setting, the actors are now clearly identifiable as nurses who skillfully carry out a procedure (and manage trouble) and physicians who simply issue orders. Strauss and his co-workers also found changes in work relationships among professionals in their study of the use of medical equipment. They report that, "When the technology is quite new, especially when a new unit is being set up that embodies novel technology, then there is more likelihood of a blurring in the division of labor" (1985:157).

Other key actors, primarily patients and equipment manufacturers, are also involved in the transformation of roles and responsibilities which occurs as a treatment becomes routinized. Patients, by exercising demand for new therapies, play a role in creating the "standard therapy" meaning of TPE as it develops in individual treatment units (see Chapter IV.) In highly experimental settings patients are much more likely to be treated as partners in the research endeavor rather than as passive recipients of treatment. When the patients' TPE procedure tended toward the new or unusual their treatment by hospital staff members was much more casual and informal, more collegial. The patients were known as individuals, often called by first

names. Their social distance from staff members was negligible. Indeed, some clinicians recalled their early use of the procedure in terms of specific patients and their treatment. The patients who had been involved in important "firsts" were remembered in great detail. A new therapy was recalled as, "the night that Mary almost died." Likewise the patients are very much involved in and aware of the research being conducted by their doctors. The patient "subject" in the experimental scene described earlier asked many questions which were answered seriously by the physicians. Fox found a similar relationship between pioneering patients and physicians in the early years of experimentation with kidney transplantation and related therapies (1959). She describes patients being treated by their physicians almost as if they were professional equals, calling them "patient-colleagues" (Fox 1959:89).

As the patient's social relationships with staff alter there also occurs a change in the patient's involvement in the actual TPE procedure. As routinization progresses they develop standardized ways of participating in the treatment itself. As they became familiar with the procedure for doing TPE, patients (who were not dangerously ill) began to play a role in monitoring the TPE equipment. Their role in watching the equipment occured primarily at "dangerous" moments in the treatment process.

One of these moments occurs when it is necessary to add a new bottle of plasma replacement fluid as the previous bottle is emptied. If not timed properly air can enter the system, creating the potential for a life-threatening bolus of air to the patient or a major delay in the treatment. After "learning" the machine's functions some patients created a role for themselves by monitoring the level of fluid remaining in the bottle or bag. The patient would watch the bottle carefully and then signal the nurse or technician when it was time to hang a new bottle. This was often done while marking the progress of the treatment by talking about which "bottle" you were on. Hanging the last bottle meant the treatment was almost over.

Another dangerous moment occurs at the very end of treatment (with one variety of TPE machine). It is necessary to return the patient's own blood from the centrifuge bowl as well as the blood remaining in the elaborate series of connecting tubing. One method of doing this is to flush the blood back to the patient by allowing air to enter the tubing from the machine side to force the blood back to the patient. This is an inherently dangerous procedure because of the risk of inadvertently infusing a large air embolus. Because of the danger it is essential that the tubing be clamped before the air nears the patient's vein. The nurse or technician usually stands at the patient's side holding a large pair of clamps. In routinized treatment settings, I observed patients take part

in this procedure by carefully scrutinizing the exact position of the air in the tubing and signalling to the nurse when to clamp the tubing off. This patient initiated routine is accompanied by a great deal of stylized joking behavior, reflecting the high level of tension present at this critical moment in the treatment. A staff member joked that if a patient "misbehaved" the nurse caring for the patient should "give him the air." The jokes disguise the tension felt by both patients and staff. They become part of the ritual of ending a treatment. The process of patients' developing roles in the actual technical procedures of TPE is an important part of routinization.

Similarly, the role of the medical equipment manufacturer is very different as routinization progresses. As described above, in experimental settings it was not uncommon to see the company representative, with shirt sleeves rolled up, working alongside the professionals, solving problems, taking samples from the machine or assisting with calculations. The company representative present during the early stages of development is likely to function as an equal partner, actively working with the clinicians to solve an engineering difficulty. Role relationships are highly reciprocal at this point, with each side providing needed input into machine design and specifications (see chapter III). In the developmental stages of TPE, social relationships between physicians and representatives were quite egalitarian; first names were

often used and, most significantly, representatives had easy access to the clinicians. Company representatives jokingly referred to this phase of development as the "cocktail napkin design" period, alluding to designs sketched out over drinks in a pub or restaurant near the hospital. All parties needed each other; the exchange of ideas, data, equipment, and technical support sustained the relationship.

However, as with the easy relationship between nurses and physicians which is characteristic of the first stages of machine development, the nature of the relationship between clinicians and company representatives is also transformed over time. The reciprocity (based on mutual need) which typifies the experimental stage gives way to a more rigid and hierarchical set of social relationships. The social distance between physicians and manufacturers increases; company phone calls are not returned and representatives are shunted off to lower level hospital functionaries, such as purchasing agents or technical staff. As the machine is used more frequently, social barriers based on the established differences in the hierarchical position of representatives and clinical investigators return. At this time a likely pose for the company representative was patiently (at least in appearance) waiting outside the physician's office for a moment in which to extoll some new feature of the company's equipment. At this point the representative was likely to be mistaken for a "detail man" from a drug company, giving

out free samples and engaging in classic business marketing techniques. By this stage of development the TPE machine is an accepted part of the hospital environment, described by one physician as, "part of the furniture."

The Organizational Context of Routinization

The organizational context of TPE beyond the individual treatment unit, including the hospitals where TPE units were located as well as the overall health care system, did not impede the routinization process. In fact, special features of bureaucratic organizations are helpful in the routinization process. Once a special staff has been assembled, procedures developed, and resources devoted to a new technical procedure, it develops institutional momentum. Generally this happens before the new technology has been fully evaluated. The organization responds to the increased "need" to perform the new procedure.

Finding personnel is a challenging task in the experimental stage. In the TPE units I visited at first nurses were "pulled" from their work in other areas, such as the blood bank or dialysis, in order to assist with plasma exchange. Low status physicians (registrars in the U.K., fellows or house staff in the U.S.) often did plasma exchange in their spare time, frequently staying late into the night. As the technology expands the demand becomes too great for these temporary arrangements to continue.

Different kinds of hospitals and organizations developed different solutions to these stresses. The desire of particular departments or types of professionals to expand their power and influence within the hospital sometimes resulted in a more rapid creation of an institutional base for the new technology. The role of hospital blood banks is the most interesting example. Because of the original use of cell separators in harvesting blood components, these machines were often located within hospital blood banks. Traditionally, physicians in charge of these units, called "blood bankers," have not enjoyed high status or prestige within the hospital. This is primarily because they are engaged in providing a service to the rest of the hospital. Often the blood banks were controlled by high prestige surgeons -- the major users of blood resources. Association with a new therapeutic (as opposed to service-related) technology greatly increased the local power and influence of the blood bankers.

With the advent of TPE as a new therapy for autoimmune disorders, clinicians in hospital departments such as neurology, rheumatology or nephrology were forced to turn to their colleagues in the blood bank for access to the machines necessary to perform TPE. This created strain within some hospitals. One hospital blood banker showed a slide of a castle-like fortress with a moat while giving a presentation at a scientific meeting. There had been a huge increase in demand for therapeutic plasma exchange

procedures in his insitution. He commented, "We have been completely surrounded by clinicians demanding that we treat their patients." The role of blood bankers as "gate-keepers" to the new technology could theoretically have slowed the process of innovation. They spoke frequently, for example, of the need to treat patients only within the context of a controlled trial so that the "data" would not be lost.

However, once the procedure was being performed regularly (and routinely) in their own units, it became extremely difficult for blood bank physicians to exercise a triage function over TPE's spread to new categories of disease. In order to maintain their increased prestige within the institution they had to perform the procedures requested by their collegues. One blood banker said, "Yes, everyone who has a theraputic plasma exchange [in our hospital] has to have a consultation with me." However, he emphasized, "I don't usually refuse." They knew that their refusal would only lead to their colleague's eventually buying their own machines, a situation that happened in some locations where physicians in control of cell separation equipment attempted to control the rapid expansion of TPE for un-tested uses.

Factors beyond the bounds of the individual TPE treatment unit or hospital are also relevant. In the early stages of TPE's development many factors in the general organization of health care in both America and the U.K.

facilitated its rapid growth, allowing routinization to proceed unhampered. The primary role of physician control over clinical decision-making has already been mentioned (see Chapter IV). Another crucial element, particularly in the U.S., was the lack of serious economic or regulatory restraints to the routinization process. When TPE was first used as a therapeutic modality, there were no restrictions placed on it. Although by definition American insurance companies do not reimburse for "experimental" procedures, in reality they payed for the bulk of early therapeutic plasma exchange procedures. Informants described this process as simple, saying that the right reimbursement "codes" were already in the "computer." Using plasma replacement was an accepted part of existing therapy, as were the traditional uses of plasmapheresis detailed in Chapter II. The right codes were punched in and hospitals were reimbursed for the procedures. It took considerable time for third party payors to recognize that something new and unusual was occuring.

The new therapy also occured in a time period when the regulatory environment for new medical equipment in the U.S. was not very well developed. Certificate of Need requirements for new technology -- a policy instituted in the 1970s in an effort to control costs -- had no effect on TPE because the initial capital investment required to initiate a plasma exchange program was well below the amount that required prior approval from local review boards. In

1976 Congress passed the Medical Device Act which gave the Food and Drug Administration (FDA) the authority to regulate new medical equipment. However, since cell separator machines were already in existence, their use was "grandfathered" in; the device act had no impact on the initial growth surge of TPE. As my manufacturer informants emphasized, when the Device Act was passed the FDA had no engineers on its staff, limiting its ability to evaluate new technologies immediately.

Concern about cost was not a major restraint to the development of TPE in the U.S. Under cost-based reimbursement there was no disincentive for the use of an expensive new technology. In fact, the opposite was the case. Technologically-based procedures have historically been reimbursed at very high levels in the U.S., levels that well exceed the actual cost of providing the service. As Showstack, Schroeder, and Steinberg comment, "...it appears that the charges for technologic procedures reflect a high value for technology in and of itself" (1981:507). By the time federal agencies like the Health Care Financing Administration became concerned about the cost of TPE its use was widely disseminated throughout the world.

It is likely that the new prospective payment systems for reimbursing health care in the U.S. may change this dynamic (Anderson and Steinberg 1984). However, even in situations of economic scarcity the technological imperative may be poweful. In the U.K., physicians were quite creative

in circumventing problems created by lack of resources to conduct TPE. One physician described how he purchased a cell separator by submitting ten separate purchase orders in order to avoid an N.H.S. procedure for vetting capital expenditures. Overall, the environmemt of TPE, whether reflecting organizational forces within or outside the hospital, did little to restrain the process of routinization.

The Development of Ward Rituals

At the heart of the routinization process is the creation and maintenance of treatment rituals. Traditional anthropological explorations of ritual have focused on the religious/magical referrents of collective ceremonies (Moore and Myerhoff 1977). By definition, rituals are viewed as separate from their "technological consequences" (Hellman 1984:123). Although discussing the place of ritual in the everyday world of medical work may seem incongruous, in reality the distance between ritual and technical task may not be great. In modern medical practice, the division between ritual and technical aspects of healing is not absolute; the two are often interwoven (Ibid.:134). Turner reminds us that, "In tribal and archaic societies what people do in ritual is often described by terms which we might translate as 'work'...the ritual round in tribal

societies is embedded in the total round of activities..." (1977:39).

The concept of "secular ritual" has been employed in the analysis of many non-religious settings (Moore and Myerhoff 1977, Gusfield and Michalowicz 1984). Some commentators have objected to this broadened scope of the concept of "ritual," claiming that extending it to the description of everyday, secular activities makes it so all inclusive as to become meaningless (Goody 1977). I use the concept here because it helps to point out the importance of purely social elements of behavior in a highly technical setting.

The minute by minute technical tasks involved in carrying out a TPE procedure are the substance from which the rituals of a "standard" medical procedure are created. An accepted function of ritual is "traditionalizing new material" (Moore and Myerhoff 1977). The development of ward rituals in TPE treatment units contributes to the changed meaning of the therapy; these rituals create order and a sense of certainty where none had existed before. I observed two types of rituals in operation: the actual <u>tasks</u> of carrying out the TPE procedure were turned into highly structured series of actions, repeated in exactly the same manner each time a treatment was carried out. Likewise, the <u>social interaction</u> surrounding the treatment developed ritualistic features; activities and verbal exchanges between patients and staff were highly patterned. The key

elements of the treatment process which were subject to ritual formation were the tasks of setting up the equipment and getting the patient "on" the machine, actually carrying out the repetitive tasks associated with conducting the plasma exchange, and finally, removing the patient from the machine and restoring the patient to "normalcy."

The existence of idiosyncratic treatment rituals became evident in the course of comparing TPE treatment across different settings. There were innumerable variations, both major and minor, in the way the procedure was carried out. What was constant was the dogmatic way in which the procedure was always done in the same way in a particular unit. Some variation can be accounted for by the use of different models or types of equipment. However, even when the same machine was used in different units there was variation in the configuration of the I.V. tubing, the type of replacement fluids used, the way records were kept, and the way the patient was monitored. In one unit, for example, all the bottles of replacement fluid were carefully prepared (with medications added) and placed on a windowsill before the patient arrived for treatment. This procedure was invariably followed even though it occasionally meant the waste of hundreds of dollars worth of plasma if the treatment had to be cancelled. One might assume that these highly standardized routines were made necessary by technical requirements of the procedure itself. However, the significant variations found among different treatment

units and the rigorous adherence to routines suggest that something beyond the pragmatic was in operation.

A curious "starting up" ritual had evolved in one unit. In this highly routinized setting the physicians were only present at the very start of a procedure, when they were called to perform the venipuncture and connect the patient to the machine. After gaining access to the patient's vein the physician would wait until the machine had been "primed" with normal saline solution before doing the final connecting. A by product of the priming procedure was the accumulation of excess saline in a waste bag. In this unit, after completing the task of hooking the patient up to the machine, the physician would invariably pick up the waste bag filled with saline and toss it across the room, attempting to make a successful "basket" into the sink. When questioned about this curious behavior -- which they sometimes even half-jokingly refered to as a "ritual"-- one physician laughed and stated that it was necessary to make a good throw in order to guarantee a successful, speedy procedure. Renee Fox described similar "magical" routines in the early treatment of kidney disease patients (1959:111).

Other starting-up rituals evolved around the difficulties of connecting the patient to the machine, since, as discussed above, vascular access is often problematic. Asking the patient to soak his or her arm in a bucket of hot water immediately before treatment was a well

established procedure. Although theoretically based on physiological principles, e.g. heat will cause veins to dilate, I did not see any observable benefit from this procedure other than allowing the participants to feel that they were doing everything possible to get through the difficult task of hooking the patient up to the machine. The complexities of gaining access to patients' veins, or "connecting work," are disucssed by Strauss, et al. (1985). This aspect of medical and nursing work is suffused with enormous uncertainty (and consequent anxiety on the part of fearful patients). Hence it is a particularly ripe setting for the creation of rituals to minimize uncertainty and gain the illusion of control.

Another unit had develped a particular "ending" ritual. As the last bottle of replacement fluid was administered, the nurse would send someone to the kitchen to make the patient a cup of tea. As the treatment was ending the patients would be served tea and biscuits as they recovered and rested quietly before going back to normal activities. The cup of tea marked an important transition: the TPE recipient moved from the status of patient, utterly dependent on the machine and staff to fulfill his every want, to an independent status, able to freely move around the unit, no longer under the direct control of the staff.

The middle period of the TPE treatment, which ranged in length from two to over four hours, was also subject to highly patterned behavior and the creation of rituals. Many

of the activities required of the staff in operating the equipment were highly repetitive, so some of the need for regularization was pragmatic. These types of activities included gathering and recording information about the patient's condition and the machine's functioning. However, other behavior was also subject to routinization. In some units, the verbal exchanges between patients and staff were highly patterned. For example, in one treatment setting there would invariably be an elaborate discussion, with comments from all present, about how many TPE treatments a patient had undergone. A patient would comment, "Today is my 105th plasma exchange." This statement would be seconded by a staff member who would exclaim that the patient had undergone an impressive number of procedures. Similarly, in another unit the patient and staff would always begin a treatment by making an informal wager about the exact time the treatment would end, a subject of some importance because if a procedure was speedy it usually meant that it was painless and free of technical trouble, also that the patient and staff could leave the hospital.

As mentioned above, the elaborate joking behavior I noted in TPE units seemed almost ritualistic at times. Jokes were used to reduce anxiety at problematic moments, such as during machine malfunctions. When the machine a patient was connected to began making unusual noises the nurse said (while laughing), "This machine is going to have a heart attack -- hopefully after you're off."

Rituals in medicine serve many useful functions (Hellman 1984:123-140; Bosk 1980). "Rituals may disguise realities, portray fictions, save face, and convince all parties that matters are in order and in their own control" (Myerhoff 1977:217). TPE treatment rituals, those actions which elaborate and embellish the technical task of plasma exchange, first normalize and then stabalize the meaning of TPE as an accepted, taken for granted therapy. Performing the TPE treatment in a particular fashion, in the same way over and over again, fulfills some vital ritual functions. Perhaps of most importance, the treatment rituals I have described function to reduce the omnipresent uncertainty of clinical encounters.

With the high degree of clinical uncertainty inherent in the work of medicine and nursing, the need to create a situation of "normal operations," as Barley (1988) has described it, is acute. The disorder and lack of routine characteristic of the experimental setting cannot be tolerated for long; the social aberrations of the experimental setting, for example the temporary dissolution of normal hierarchical relationships, must be resolved. As routine procedures are developed and treatment rituals evolve, a new social cohesiveness forms among the staff. The inevitability of the new treatment, and the commitment of the staff to continue treating this patient, is celebrated by the ritualized discussion of the large numbers of procedures which the patient has undergone. In spite of

the high level of excitement generated by the use of new therapies, over the long term it creates too much anxiety and disorder for patients and staff alike to be constantly faced with situations for which predetermined actions do not exist. Treatment rituals develop to fill this void and help create a climate of certainty.

When a new therapy is used key questions remain unanswered: Is it safe? Will there be unexpected side effects? Will the machine perform as expected? And, of primary importance, will the treatment ameliorate the patient's disease process? Procedural routines and rituals reduce this uncertainty. They disguise the reality that the patient's condition might not be treatable with any known method, and that the therapy is only a chance which may or may not work. Likewise, the rituals of treatment allow the professionals to believe that they are in control of the patient's debilitating disease, that they have some power and can take some action against its ravaging effects. Patients' fears of the procedure are minimized if the treatment is performed in a competent and crisply efficient manner by professionals who carry out their tasks with authority and seeming security. The "starting up" rituals described above address this uncertainty directly. These actions are like exhortations to "protect" the participants -- patient and staff alike -- from the potential misfortunes of treatment. The "ending" ritual symbolizes the patient's

safe transition away from the danger of the machine and back to ordinary life.

As discussed above, the nurse's role as manager of clinical trouble is crucial to the process of routinization. As ward rituals develop and solidify into everyday events, the nurse, fulfilling the role of "ritual specialist," is of paramount importance. It is the nursing staff who manage and guard these ward routines, making sure that they are carried out in the "correct" fashion and passing on the idiosyncratic ritual knowledge of the TPE unit to newly hired staff. After their central involvement during the experimental stage, physicians disappear into the background. As physician investigators search for the next new therapy, nurses run the unit, manage trouble, and carry out the therapeutic rituals of TPE.

Transmission of Knowledge

Once a treatment ritual is established, an important step in its eventual routinization is its transmission to a new "generation" of health care workers. The meaning of a new routine "thickens" or "hardens...in the process of transmission to the new generation" (Berger and Luckman 1966:59). The process of teaching the TPE treatment rituals to a new generation of physicians speeds the acceptance of the technology as standard therapy. As Berger and Luckman remark, "...to put it crudely, if one says, 'This is how

things are done,' often enough one believes it oneself" (1966:60).

In peasant or tribal societies the transmission of culture takes place gradually, over many years, as a child is initiated into the many roles expected of an adult. The locus of socialization is generally the family, extended family, tribe, or other group. In the world of a medical ward or treatment unit, socialization takes place remarkably quickly. In American clinical medicine every July marks the initiation of a new generation of recruits who must be quickly taught the ward culture if they are to function effectively. Although the turnover of nurses on a typical treatment unit is neither so regular or frequent, new staff members must often be trained or oriented to the specific procedures of the ward. The end result of these rapid staff turnovers is that new procedures and treatments can become institutionalized remarkably rapidly. The meaning of an experimental practice can quickly solidify into an accepted therapy.

A procedure which seems dangerous and innovative to an intern may be perceived totally differently as he teaches the new technique to his subordinates a year or two later. The younger physicians I interviewed in TPE treatment units, those not involved in the initial period of innovation, reflected these changed perceptions. Having never been exposed to the sources of social ambiguity characteristic of

the experimental treatment setting, they tended to accept the procedure as a fait accompli.[2]

The altered social relations of the experimental phase of a new technology are seen in the patterns of transmission of information about the technique. In the early stages of development the innovating physicians themselves are responsible for orienting other staff members, including nurses and technicians. This training is generally haphazard, occuring while treatment is attempted.

In the routinized stage of a new technique, nurses teach other nurses the elaborate treatment procedures and rituals which have developed. Procedures are learned almost by rote, down to the most mundane detail of record-keeping or setting up equipment. This careful attention to detail may have an important practical function. While educating new staff members nurses purposefully emphasize the careful and perfect execution of detailed treatment protocols in order to minimize the possibility of error.[3]

At the same time, new physicians are unlikely to be trained formally in the technical details of TPE. Once a procedure is routine, it becomes an exclusive province of nursing. Although physicians remain technically responsible for the overall procedure (and continue to carry out certain tasks, such as inserting catheters into veins) their knowledge of how the procedure works may be negligible.

In summary, evidence of routinization is disclosed by the varying social relationships found in "experimental" versus "standard" uses of the technology and in the creation and maintenance of treatment rituals. These new routines are sustained by nurses, who act as ritual specialists and preserve the unit's knowledge. Once a new technology begins to be used routinely, powerful bureaucratic forces sustain its use. The routinization process is further supported by physicians' overriding interest in the research applications of the technology and the desperation for new therapies experienced by both patients and their clinicians (as discussed in Chapter IV). The implications of these processes, and the changed meaning of the technology, are the subject of the final chapter.

Notes

1. Judith Swazey (personal communication) reports that a later generation of dialysis physicians were surprised when told that their seniors had stayed in the hospital all night, piecing together equipment and actually dialyzing patients themselves.

2. On the other hand, the new generation of physicians is less emotionally invested in the procedure. Hence it is often the newcomers, taught the procedure as a matter of everyday routine practice, who are able to see the procedure's flaws. This dynamic eventually leads to a new round of clinical innovation.

3. I am grateful to dialysis expert Susan Hopper for this observation.

Chapter VI

Conclusion

The Technological Imperative in Medical Practice: Implications for Health Policy and Bioethics

> Science and technology revolutionize our lives, but memory, tradition and myth frame our response.
> Arthur M. Schlesinger, Jr.

This discussion of the social and cultural features of therapeutic plasma exchange can be viewed as a logical extension of previous work by medical anthropologists. Understanding the relevance of clients' values and social beliefs was a central concern of anthropologists working in international public health in the decades following World War II (Foster 1976:13). Helping ease the introduction of new technologies was the usual focus of their work. In this dissertation, I have taken these traditional concerns and applied them to the heart of Western biomedicine: advanced medical technology. Examining the social and cultural features at the core of our own medical system is in some ways more challenging than studying other cultures, because it forces the observer to delve deeply into the nature of basic Western assumptions about the primacy of technology and the scientific method. However, accepting this challenge is essential if anthropologists are to make a

meaningful contribution to the wide array of problems facing our health care system today (Clark 1985).

Many of the problems of modern health care stem from the growth of technology. Numerous authors have suggested the relevance of social science methods in exploring the complex meanings of medical technology, particularly in the area of bioethics (Clark 1984, Davis and Aroskar 1978:281-301, Fox 1976). The profound questions of moral meaning raised by techniques which force us to reevaluate the nature of life itself are particularly well suited to anthropological analysis. Ambivalence about technology is widespread and deeply rooted. There is much fear and suspicion of these modern miracles, at the same time that their use creates intense interest. As Callahan notes, the public desires access to innovative techniques yet, at the same time, refuses to pay the enormous price tag their use entails (1988). The questions raised by technology generate daunting health policy concerns, necessitating complex trade-offs.

This case study of TPE reveals the importance of social and cultural analysis in understanding the operation of a technological imperative in Western medical practice. The imperative to employ TPE was shown by the rapid increase in the use of the procedure in the late 1970s. The history of TPE demonstrates the many powerful forces which helped generate enthusiasm for a new therapeutic approach to serious autoimmune disease. The stimulus provided by the

for-profit medical equipment industry was significant, providing technical support, speeding the communication of information about the new technique in its earliest state, and eventually contributing to the routinization of TPE's use by health care workers. The many pressures experienced by seriously ill patients -- pressure to lobby aggressively for new therapies and then to respond appropriately -- furthered the rapid expansion of TPE. Physicians, honoring their research interests as well as responding to their desperate patients, gave the new technique increased momentum by writing articles, purchasing equipment, and treating ever larger number of patients.

Even as these events were happening, many physicians expressed scepticism about the ultimate usefulness of TPE and worried that its use was expanding far too rapidly. In an editorial about TPE in the New England Journal of Medicine one physician pioneer commented:

> Today's physicians are often inclined to be doers rather than thinkers, and if modern technology appears to offer a dramatic mechanical approach to the management of a dangerous disease, there will be a great temptation to hurry into action, perhaps before the evidence has been adequately weighed (Verrier Jones 1977:1173).

The fact that the potential dangers of the technological imperative are so well understood, and yet often elude control, indicates their force. Active resistance is an enormous burden which can be shouldered only with institutional support, generally accorded only to those in prestigious research institutions.

The many forces summarized above set the stage for the process of routinization. The activities of companies, physicians, nurses, media respresentatives, disease interest groups, and patients all encourage routinization. Once these forces intersect, the scene changes -- and a new meaning of the technology emerges.

A Moral Imperative for Treatment

The technological imperative is sustained by inherently social forces which result in a new meaning for TPE: the meaning of standard therapy. New routines are created, treatment rituals develop, and physicians continue their focus on research. The most interesting question is the relationship between the changed meaning of a new therapy and the nature of medical decision-making by individual physicians for patients who might benefit from a new machine. Or, how does the technological imperative become transformed into a moral imperative to provide a new therapy? The notion of an imperative implies constrained choice. I would argue that a moral imperative to provide

treatment is experienced by physicians when they are faced with a decision about whether to prescribe a therapy which has begun to "feel" routine. The moral tone derives from the sense of social certainty experienced by health professionals working with a technology whose use has become routinized. Once the use of a procedure is perceived as a standard of care, its use becomes a moral, as well as a technical, obligation.

When a therapy clearly belongs in the experimental zone -- and everything about the treatment situation reveals this to the staff -- there is no obligation to provide it. Yet when a new procedure has crossed over the mysterious boundary into the territory of a standard therapy, it cannot be denied. As the use of TPE became ever more routinized, the clinicians I observed would break their own rules of scientific excellence, often providing treatment to patients not part of established controlled trials or in the face of contradictory evidence.

As with TPE, a new treatment may or may not be efficacious; it might be risky. The moral imperative for treatment overrides these concerns. It becomes unthinkable for the physicians not to perform the treatment. The social inevitability of therapy takes on a moral tone; the experience of a technological imperative becomes a moral imperative for action. Once a new therapy is available it becomes extremely difficult, if not impossible, to forego its use. One physician remarked that denying a patient TPE

(for purely scientific ends such as a trial) seemed like a "Buchenwald approach to medicine." Experimental procedures, those which upset the everyday hospital routine, are not morally indicated. Their use is not mandated. It remains optional, at least until a later stage of development when the social forces of the technological imperative have resulted in a changed meaning.

Hence, the creation of a moral imperative is a social process, the end result of the routinization and consequent acceptance of a new medical technology. The moral meaning of a technology, its perception as a standard therapy, is embedded in and expressed through changes in social organization. I do not mean to suggest that the ongoing scientific evaluation of new medical technologies is unimportant. Rather, I believe that scientific "facts" about efficacy are informed by a careful reading of the social milieu in which treatment takes place. The evaluation of a new technique as a standard therapy derives from a complicated "reading" of the social setting in which it is used and not simply from an asssesment of the results.

The key element in this analysis is the suggestion that even in a highly rational, scientific setting the meaning of actions and events evolves, at least in part, from the underlying social and cultural organization. The meaning of a new technology as standard therapy crystallizes, over time, from many sources: scientific studies of effectiveness, assessments of economic costs and benefits,

and political considerations all have their place. Although often ignored by policy analysts, an understanding of the social context of technological innovation can inform our knowledge of the meaning of new technologies. There are a number of significant practical ramifications of the analysis presented here. The power of the technological imperative in medical practice, particularly the strong tendency for routinization to speed the change in meaning of a new therapy from experimental to standard therapy, has broad implications for the fields of health policy and bioethics. A recent major report on the future health policy agenda in the United States underscored the importance of these issues:

> New technologies are often used prior to a full and clear understanding of the financial and social consequences involved, but it is usually not long before cost-benefit questions and ethical issues arise. Scientific discoveries and the complex issues that accompany them will no doubt continue into the next decade and the next century (Boyle 1987: 1200).

Implications for Health Policy: Technology Assessment

The inexorable social and cultural forces underlying the technological imperative have implications for ongoing debates about the appropriate use of technology. The speed with which expensive, new therapies can gain the label of standard therapy is of major concern in the area of technology assessment. How best to guide and control the

growth of medical technology is debated extensively in the health policy arena in both the U.S. and the U.K. (Banta et al. 1983; Council for Science and Society 1982; Jennett 1984; McKinlay 1982). Formal technology assessment programs are increasingly called for as a means of controlling the use of dangerous or marginally effective new technologies (Institute of Medicine 1985). One assumption behind the idea of conducting rigorous evaluations of new technologies early in their development is that new machines or techniques which are inefficacious or unsafe can be easily eliminated from the clinician's technical repertoire. Ironically, as this dissertation reveals, the very process generally considered necessary to evaluate new therapies in a rigorous and scientific way, that is, the use of randomized controlled clinical trials conducted in a number of medical centers, itself contributes to the social process of routinization. It should be fairly obvious that the act of setting up clinical trials can (and often does) begin the process of routinization. Once a new machine is in use, even if in a limited way, it is very difficult to change course and stop using the machine. Its use becomes entrenched.

Plans to control the rapid proliferation of marginally effective, expensive technologies by resorting to "better science" -- usually meaning more elaborate clinical trials -- are seriously flawed because they ignore (or discount) the social forces which support the technological imperative.

In some cases, for example in lobotomy, historical analysis reveals that the evidence of the new treatment's lack of effectiveness was available very early (Valenstein 1986). Unfortunately, this did not hinder the wide use of lobotomy in treating mental disorders. The procedure was not abandoned until it was supplanted by another new therapy -- chlorpromazine, the first psychoactive drug. Valenstein cautions that the social and political forces responsible for the wide acceptance of lobotomy have not vanished with the technique, but are "part of the bone and marrow of the practice of...medicine" (1986:291).

In the case of TPE there is also evidence of uncritical acceptance of early reports of treatment success. Searching for an explanation of this phenomenon, one recent analysis suggests that the problem of overly enthusiastic endorsements of new technologies could be solved if editors of scientific journals would be more circumspect about publishing conclusions that go beyond the scientific evidence presented (Shapiro and Shapiro 1987). Although laudable, calls for more rigorous science ignore the fact that many of the influences on the meaning of a new technology are outside the realm of scientific "facts." Also ignored is the reality that the ultimate decisions about appropriate use of medical technologies are social and political -- as with U.S. government funding of treatment for end-stage renal disease (Plough 1986) -- and not strictly medical or scientific.

Most of the recent political debate about technology use in health care has revolved around issues of economic cost. The adoption of a new technique as a standard therapy has a significant and direct impact on the overall cost of health services. Most American insurance companies and government programs provide reimbursement for health services based on the status of the service. A procedure which is considered to be the standard of care must generally be reimbursed while experimental procedures are specifically excluded. Hence the meaning of a new treatment, its perception as experimental or standard therapy, has serious economic consequences. Who determines this meaning? Often, a panel of experts is assembled. The expert physicians called upon to evaluate the status of a new technology, generally those using the new technique themselves, are in an inherent position of conflict of interest and highly likely to perceive the equipment as essential (McKinlay 1981). Using a new therapy contributes to its acceptance as a necessary part of routine treatment. An understanding of these physicians' involvement in the social process of routinization might lead to improved decision making about reimbursement.

Other policy makers have suggested that correcting the economic bias within the American medical system -- a system which provides significant financial rewards to specialists who use technology -- will solve the problem. That correction is certainly prudent and essential. However, by

themselves financial manipulations of the reimbursement system will not solve the problem of the inherently social forces supporting technology use.

Technology assessment programs deal with issues of safety as well as cost and efficacy. The same social forces which affect physicians' perceptions of a treatment's efficacy also influence beliefs about safety. As its use becomes part of everyday hospital routine, users become indifferent to the technology's inherent risk. A technology whose use is highly routinized is increasingly perceived as safe, even though the inherent adverse effects of the technique change only marginally as a team gains experience with a new procedure. Often an irreducible risk of bleeding, infection, or other serious complications remains, but the meaning of the risks is transformed from untoward and dangerous to expected and manageable. Thus transformed, they can be ignored, occasionally leading to tragic events, as when the danger from the space shuttle Challenger's "O" rings was ignored for so long that the process of ignoring it became routine, and critical safeguards were overruled in the launch procedure.

An additional policy concern (one with ethical overtones as well) is the need to choose between competing demands for limited resources. There is general agreement that the dramatic advances in sophisticated diagnostic and therapeutic technology have added to the overall cost of medical care. More difficult is the question of whether

these costs are justified by an accompanying improvement in health status. It is not always clear that this is the case. McKeown, among others, argues persuasively that the common perception of modern clinical medicine as the cause of improvements in the overall health of the population is erroneous (1979). There is undoubtedly a point of diminishing returns on investment in expensive equipment that benefits only a small proportion of the population. This is especially true if resources are shifted from public health measures in order to finance technological advances. Should governments sponsor artificial heart implants in preference to research into the etiology of coronary artery disease?

Cost and allocation issues are of relevance in both the U.S. and the U.K. Decisions about the appropriate balance of high technology versus other services must be made regardless of the means of financing health care. It may be politically less feasible to say "no" to specific medical advances in the U.S. than in the U.K. (Miller and Miller 1986). Nonetheless, I would argue that a technological imperative operates in both systems. The social processes of routinization and physician emphasis on research occur on both sides of the Atlantic, although the effects are, of course, modified by the health systems as a whole, with primary care services receiving greater priority within the National Health Service (Ibid.). Political and economic

conditions may limit the pace -- but not the overall trends of the technological imperative.

Implications for Bioethics: A Challenge to Patient Autonomy

The second major implication of the routinization of technology use is in the realm of personal autonomy in health care decision-making. The technological imperative experienced by health care providers, alive with moral meaning, has the potential to wrest control of decisions about the use of technology from patients themselves. The patient's voice may not be heard, as Plough (1981) demonstrates for end-stage renal disease. The field of bioethics has emerged over the past fifteen years in tandem with the belief that respect for patients' wishes, even when difficult to realize, is of paramount importance (President's Commission 1982). Many of the clinical problems confronted in the late sixties and early seventies -- problems which contributed to the growth of bioethics as a discipline -- centered around when and under what circumstances an individual patient could make his own, independent decisions about medical care. The growth of a legal doctrine supporting the right of patients to provide "informed consent" for treatment has paralled developments in bioethics in the U.S.

This large body of legal and ethical thinking has failed to grapple with the fact that, by and large, the clinical reality within which patients make their decisions about care is defined by providers. On a pragmatic level, patients are privy only to information provided by health care professionals. They have very few independent sources of information or means of interpreting the complex events involved in their care. But of much more significance than merely withholding or failing to disclose relevant "facts" about a case is the provider's ability to create those facts. As Arney and Bergen (1984) have noted, the meaning of health and illness, life and death, have come increasingly under the sway of a "medicalized" definition. In the case of decisions about technology, the meaning of what constitutes "standard therapy" vs. an "experimental" treatment is created by the physicians themselves. It is a highly subjective assessment, not based exclusively on scientific facts gained by evaluation of the safety and efficacy of new techniques. As I have demonstrated, the standard therapy meaning comes, at least partially, from a "reading" of the social milieu of treatment settings, from the experience of altered social relations and treatment rituals.

The implication is that patients make decisions about whether to receive medical therapies based on an assessment of the technology's state of development that may be, if not seriously flawed, at least biased by the operation of a

technological imperative. The forces of social routinization which push new therapies forward along the experiment/standard therapy continuum appear inexorable. Patients themselves contribute to this dynamic by demanding immediate access to new therapies. Supported by the activist orientation of western physicians, the centrality of research goals, the power of the medical equipment industry, and reimbursement policies biased toward the use of equipment-embodied technologies, the decision to use a new procedure like TPE seems inescapable. In the process, true patient autonomy is usurped. It may well be true, as Jonsen has suggested, that there is "an inverse relation between scientific, technologic medicine and freedom of therapeutic choice" (1975:126). It is ironic that the seeming increases in options created by widespread information about new technologies through the media and disease interest goups may, in fact, inhibit choice. Patients are now free to demand access to therapies which in reality are highly experimental but are made to appear routine.

I began this dissertation with a sense of astonishment that a medical "miracle" like the implantation of an artificial heart could so quickly be perceived as a routine, taken for granted therapy. The exploration of therapeutic plasma exchange has revealed some of the social complexities which must be unravelled to understand medicine's technological imperative. To conclude, I return to the

apparent contradiction of analyzing scientific medicine with the same tools one would employ in describing a healing ritual in a social setting very different from a modern hospital. Since high technology medicine seems to be a direct embodiment of scientific knowledge, we wish to believe that the application of these new machines to patients is objectively determined, comprehensible to all. This case study of TPE reveals that even in the seemingly rational world of medical science one cannot ignore the social realm -- encompassing the highly subjective experience of participants in medical innovation. A full understanding of the relentless advance of medical technology requires knowledge of the social world in which medical machinery is developed and used. As routinization occurs and a new meaning for a medical technique solidifies, policy options narrow. Without a broad understanding of the social and cultural roots of the technological imperative we will be unable to make fully informed decisions about the appropriate use of technology or comprehend the constricted choices for patients that this imperative implies. Our understanding of the technological imperative in medical practice is enhanced by the recognition that the meaning of a new therapy is, in large part, a social construction.

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Appendix A

STATUS OF TPE IN THE 1980s

Since the early period of intense excitement about the possibilities of TPE and the subsequent rapid increase in its use, the clinical situation has changed. Not surprisingly, recent articles in the medical literature lost the enthusiastic tone of early case reports. Enthusiasm dampened when it proved difficult to replicate early successes in the more rigorous setting of carefully controlled clinical trials. A period of cooling off after initial excitement is an unavoidable, and expected, part of innovation in medicine. The physicians involved in clinical research are not unaware of this pattern. Speaking of TPE for neurological diseases, one physician recently commented, "The exuberance of adolescence has been replaced with the cautious assessment of middle age" (Tindall 1985:114).

In reading more recent review articles about TPE it is difficult to believe that the authors are discussing the same technique they so enthusiastically reported only a few years ago. In some cases the later cautious assessments come from researchers who (writing case reports and speaking often at plasma exchange conferences) had been avid promoters of the technique in the 1970s. Although a fair amount of new scientific information has been accumulated in

the past ten years, few of these findings have been startling or unequivocal. Many questions remain and it is these questions which concern reviewers, who use titles such as "A Time for Reassessment: Plasmapheresis at Maturity" (Tindall 1985) and "Plasmapheresis: Therapeutic or Experimental Procedure?" (Dau 1984). The summary opinion was expressed by Shumak and Rock in a major review in the New England Journal of Medicine. They emphasized the need for more research and concluded that "...the indications for therapeutic plasma exchange remain unclear" (1984:762). Recent authors also bring up the issue of the economic impact of TPE on the health care system as a whole (Linker 1983) as well as safety concerns, including the more than fifty reported deaths which are attributed to TPE (American Medical Association 1985).

In my interpretation, the tone of the medical literature has altered even though the basic information on which judgments are based has changed only slightly. Some clinical trials have been published but they are often difficult to interpret. For example, trials involving rheumatoid arthritis show some improvement, but it remains unclear if the same amount of improvement could be brought about through less expensive means, such as bedrest. The nature of these changing assessments demonstrates how the evaluation of a technology is suffused with social elements which interact with the process of conducting formal

evaluations, such as clinical trials and reviews of adverse effects.

The current, more cautious perspective on the use of TPE which I have described sounds at odds with the picture of overwhelming enthusiasm for the procedure which is characteristic of the early phase of innovation. This seeming contradiction only reflects the rapid pace of change. It is important to keep in mind that the arguments presented here about the social context of the technological imperative apply only to this early phase of TPE's development, the upswing portion of the curve when a new technology is in the early phases of clinical use. The social forces which define the latter stage, the stage of critical reflection and disillusionment, have not been examined. These would require a separate, complex study.

Appendix B

INTERVIEW SCHEDULES

Patient Interview Schedule*

1. What is your experience with plasmapheresis?
2. Why was plasma exchange used in your treatment?
3. How did plasmapheresis affect the course of your disease?
4. What was it like to be hooked-up to the cell separator machine?
5. Are you going to have any further exchanges?
6. Do you remember how the decision to use plasmapheresis in your case was made?
7. Who first talked with you about having an exchange?
8. Did you discuss the decision with anyone else, any family, friends, doctors, or nurses?
9. Had you heard of plasma exchange before you were treated? (If yes,) from what source?
10. Had you read about it before you were treated? After your exchanges?
11. Have you recommended plasmapheresis to anyone else?
12. Was your treatment part of a research protocol? (If yes,) what were the doctors trying to find out? How did you feel about being part of a research project?

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* In this and in all the following interview schedules specific questions and terminology may have been altered during the course of the interview to make a particular question better suited to an individual informant. Also, the schedules were used primarily as general guides to discussion; additional questions and probes were invariably inserted. Finally, each interview began with a brief description of the project for the informant and a discussion of the informed consent document.

13. How are plasmapheresis treatments funded in the unit where you were treated? (For American patients,) does ordinary health insurance cover this treatment?

14. Have you ever been in contact with organizations that fund research on your illness, such as _____ (Muscular Dystrophy Association, etc.)?

15. Based on your experience as a patient, how do you think plasma exchange services should be provided in the future?
Specifically, how should funding for plasmapheresis research and treatment be arranged?

16. What questions have I forgotten to ask?

Nurse/Technician Interview Schedule

1. How have you personally been involved in the use of plasmapheresis as therapy? When did you begin this work?
   How were you trained in the use of the equipment?

2. What kinds of diseases have you treated? Which physicians do you work with most closely? What percentage of your work is therapeutic (as opposed to collection of blood products from normal donors)?

3. Have there been changes in your unit since the advent of therapeutic plasma exchange? What has happened?

4. Based on your experience, what is the typical patient response to plasmapheresis? (Specific follow up probes for this question included: type of improvement, level of enthusiasm, dependency reactions, pressure for treatment.)

5. What type of equipment is used in your unit?

6. What has been your experience with the representatives of the companies who manufacture plasma exchange equipment?
   Do you talk with them often? How would you rate the service they provide?

7. What is your view of the current "state of the art" of therapeutic plasma exchange? Do you consider it to be an experimental treatment? How do you rate the level of "risk" in performing plasmapheresis?

8. What do you think are the possibilities for plasmapheresis in the future? Have you thought about the cost of the treatment?

9. Do you belong to any organizations of health professionals interested in plasma exchange? Have you attended any conferences or meetings?

10. What questions have I neglected to ask that you feel are important?

Company Representative Interview Schedule

1. What is your position with the company? What exactly do you do?

2. How have you been involved in the development of therapeutic plasma exchange? How has your company been involved?

3. How was the original plasmapheresis equipment developed? (Asked of participants involved in machine development.)

4. In what ways has your company supported the therapeutic use of plasma exchange?

5. What role do medical equipment manufacturers play in the process of innovation in clinical medicine?

6. How has your company been affected by the changing application of cell separation equipment?

7. How is clinical investigation supported? How is work with specific clinicians set up and clinical trials arranged?

8. How do you evaluate the potential of a therapeutic innovation? Specifically, what issues do you consider when you evaluate the potential of a new piece of equipment or idea?

9. How do government regulations affect your work?

10. In your opinion, what should be the ideal relationship among clinicians, manufacturers, and government regulatory bodies?

11. What is your view of the current "state of the art" of plasma exchange as a therapy? Do you consider it to be an experimental therapy? For which diseases? (Informant here asked to respond to a list of diseases.)

12. What do you think are the future possibilities in the use of plasma exchange? What is going to happen?

13. What criticisms do you have of how plasma exchange has developed over the last five years?

14. What important questions have I neglected to ask?