RESEARCH METHODS IN SURGERY

Edited by WALTER F. BALLINGER II, M.D.

WITH 25 CONTRIBUTING AUTHORS

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Associate Professor of Surgery, Jefferson Medical College;
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Philadelphia

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FOREWORD

In this book concerned with surgical research, the philosophy and technique of research in many different fields are described. In addition, the obtaining of assistance to accomplish this research is discussed, including financial and technical help, laboratory space, and instrumentation.

I think this volume should be valuable to young surgeons embarking on an academic career of teaching and research. The hours spent in reading it should save them weeks and months of learning by the trial-and-error method. Perhaps all learning is eventually by trial and error, but a surgeon does not need to cut a laryngeal nerve in learning to perform a thyroidectomy or the common duct in performing his first cholecystectomy or the spermatic cord in learning how to perform an inguinal herniorrhaphy. By perusing this book the reader should be able to avoid the errors common to the beginner. The book is packed with useful knowledge in many fields of surgical investigation.

When Research Methods in Surgery was conceived, the surgeons invited to write chapters were, for the most part, not full professors or heads of departments. As the book approaches publication, I find that many of the authors are now full professors and that at least one has become a department head. The authors chosen by the Editor appear to be rapidly moving up the academic ladder.

I congratulate all the authors of this book for their contributions. I congratulate especially Walter F. Ballinger II, who conceived it, wrote a number of chapters, and, as Editor, had the energy, industry, and patience to carry through to completion this significant contribution to the education of young surgical investigators.

John H. Gibbon, Jr.

PREFACE

There are more people engaged in surgical research today than ever before, and their numbers will probably increase with the years. Most will not stay in the laboratory but will quite properly become clinicians. A few will remain in investigative surgery in a full-time capacity. Many, it is hoped, will continue the polygamous relationship of the residency years and embrace teaching, clinical surgery, administration, and original research, forming that curiously happy amalgam which makes up academic surgery today.

The complexity of research has increased, as has the number of researchers. The young investigator is faced with a multiplicity of techniques, each with its own difficulties and inherent errors. Basic rules for planning and conducting research stem from logical concepts recognized centuries ago, and are too little appreciated by the novice. All investigators make mistakes; this one has had his share. In retrospect, however, it can be seen that many were avoidable, and it was to this purpose that this book was conceived.

Most of the space here is given to the description of those basic techniques in surgical research which the authors felt most useful and productive. Each author was chosen because of the excellence of his experimental work. Advances in methodology and the development of newer, more precise, and more adaptable equipment have been described. Between the time of the preparation of the manuscript and the publication of the volume, there have been many significant contributions in the literature that could not be included. In preparing such a book as this, time is remorseless; it is impossible to be completely up to date. Nevertheless, the basic techniques fundamental to the performance of research in the areas discussed here are well outlined and will continue to be useful.

As Editor of this book, I have acted simply as one who draws upon the experience of others. To each of the authors, I express my sincere gratitude for his contribution. The suggestions, criticism, and encouragement received from Fred Belliveau of Little, Brown and Company were of great aid in the formulation of the text. I also thank Esther Montgomery, Ph.D., and Mrs. Marilyn Elias for their valuable help in reviewing, editing, and preparing the final manuscripts.

The foreword by John H. Gibbon, Jr., M.D., is a source of particular pleasure to me. His investigations in the surgical laboratory leading to the development of a heart-lung machine and its successful clinical use provide a brilliant example of the application of sound methods, persistence, and the wisdom to apply newer techniques to the solution of a problem. To him, I offer my special thanks.

Philadelphia W. F. B.

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SURGICAL RESEARCH AS A DISCIPLINE

WALTER F. BALLINGER II, M.D.

The word discipline has many meanings, including a "rule or system of rules affecting conduct or action" and a "course of training which corrects, molds or strengthens."(8) Thus the word may refer both to method and to the training to acquire experience in method. A third definition, considered somewhat archaic, is "a branch of knowledge" and this most closely approximates the sense in which the word is used in the title of this chapter. Cervantes wrote that it is one thing to praise discipline, and another to submit to it. He was, of course, referring to still another meaning of the word. One cannot help wondering how many praise the discipline (in Cervantes' sense) of surgical research without really understanding it and how many submit to it as a temporary evil, a period of servitude among the animals, the completion of which merely contributes toward qualification of the individual for the American Board of Surgery examinations.

A laboratory — surgical or otherwise — is a place where ideas are tried out. It is important to recognize the order; the idea comes first. The validity or lack of validity of an idea is ascertained by experiment. A good experiment is conducted under carefully planned conditions which comprise the experimental design or the experimental model. Independence and individualism in a researcher are to be encouraged, but it is wise to recognize that the general rules of experimental procedure have been gleaned from trial and error. They are only suggested rules, but experience has shown them to be most helpful for productive research, most protective in avoiding well-known pitfalls, and most likely to allow accumulation of valid data.

Thus the idea comes first, and the laboratory is used for confirmation, modification, or refutation. This does not mean that good ideas do not arise in the laboratory; many of them do. During the conduct of experiments designed to test one idea, other ideas are generated, often with overwhelming rapidity. Some are valuable, others are worthless. Part of one's own self-imposed discipline concerns the difficult decision whether to follow the original plan or to deviate in the direction of a new idea or "hot lead." Too many ideas at one time can clutter and render ineffective the original experimental design.

The relation of the surgical laboratory to the academic milieu is important. A medical school and its affiliated hospitals exist in order that students may learn medicine and that the science of medicine may be advanced. In the former process, the students examine patients in the hospital, where they observe the many facets of illness and practice the diagnostic and therapeutic methods which they have been taught in the classroom. Furthermore, it is hoped that they begin to appreciate the

subtle art of the physician-patient relationship. According to Alfred North Whitehead, "the task of a university is to weld together imagination and experience."(9) He observed that the two functions of education and research meet in an academic environment. Whitehead compared knowledge with a dead fish; neither keeps very long. Research is an intellectual adventure, and it is this adventurous curiosity that should stimulate the student of medicine to investigative work. It is to be hoped that the thrill of discovery makes the acquisition of knowledge a preoccupation with increasing numbers of students. Glenn has described favorably a program of required student research at Yale.(5) He was particularly impressed by the intimate relationship and mutual respect which developed between faculty advisers and students in their joint attack upon a research problem.

A lack of creativity among surgeons has been commented upon by George T. Moore.(7) He believes that the environment provided by surgical training is unfavorable for creative endeavor, since the resident feels great need to develop clinical skills and to become a master technician. Thus, a period devoted to the pursuit of investigative problems becomes almost impossible. By the time the resident finishes his training and obtains his certification in surgery, the pressures to become financially independent and to attain stature in the community are enormous and usually preclude rekindling the spark of curiosity and the allotment of time to the surgical laboratory. Although gradual increases in salaries have lessened these pressures in recent years, they have not been obliterated.

Nevertheless, this may be a process of natural selection, since a man with sufficient intellectual curiosity and purpose who wishes to attempt an investigation will often find the means to do so. The fault in our training program probably lies in not pursuing more of a middle path. Obligatory research at any level is a poor approach. On the other hand, too many roadblocks are placed in the path of the potential investigator at the early stages. More emphasis might be placed upon opportunity for research during student days, especially if some portions of the medical-school curriculum could be dispensed with in order to allow a worthwhile amount of time for laboratory work. Young and creative minds could then be turned to problems with lack of bias accrued from years of didactic teaching and with less social pressure to enjoy the financial rewards of full-time private practice.

Francis D. Moore commented in 1958 that research "born in the minds of young men... has been responsible for the eminence of American university surgery today."(6) Curiosity should be present in superabundance in young surgeons, and the subject has intrigued many established investigators. According to George T. Moore, for maximum creativity, the habit of imaginative thinking should be established as early as possible.(7) He believes that most important contributions to science probably are achieved at relatively young ages. Gibbon stated, "To educate oneself, one must want to do so."(3) He noted that the continuing presence of the unknown is the best stimulus to curiosity. Walter B. Cannon dismissed the subject with a certain finality that brooked no argument; although Paradise was lost, the Tree of Knowledge was gained.(2)

Gibbon later defined the qualities of the man who would be best equipped to solve some of the problems confronting us as surgeons.(4) Scrupulous honesty with himself and others was listed first, followed by patience, persistence, and industry. However, he observed that there are many men with these qualities who have no desire to do research and therefore would never become investigators. He suggested that "the best way for a person to discover whether he is interested in research is for him to spend a period of time, seldom less than a year, working under supervision in the laboratory. During this trial period he will discover

whether research appeals to him or not; his supervisor will also quickly learn whether the beginner is a 'self-starter.' The man with potentialities as an investigator will see problems that need solution and will outline methods of approaching these problems. The methods he proposes may be inadequate because of his experience but the fact that he recognizes the incompleteness of his knowledge in a certain area and that he formulates an attack upon the problem indicates that he is a potential investigator. On the other hand, the individual who spends the year intelligently and faithfully carrying out the suggestions of his supervisor, adding little or nothing of his own to the solution of the problems under consideration is not the man to continue to do research...both he and his mentor will have a good idea at the end of that period as to whether he has the capacity for research. If he has not, the time will have not been misspent, because the year's experience will enable him to be a more critical reader of surgical literature during the rest of his professional life."

In a delightfully illustrated monograph, Of Research People, Burch stated that the difficulties in selecting young men for research could be compared to those of a child with a bottle of ink: "a serious problem — and the final outcome as unpredictable."(1)

Three distinct types of young investigators are found in the surgical residency. In the first category, I include those who spend time in the laboratory simply because they were assigned there and consider the experience only as a necessary evil toward completion of the residency and qualification for the American Board of Surgery examinations. These men often exhibit no more enthusiasm and curiosity during the clinical portion of their residency. In the second group are the men who honestly believe that a year spent in the surgical laboratory is a good preparation for their chosen career. There are two subdivisions within this large group. There are those who know that surgical research is a "good thing" simply because this concept had been drummed into them during medical school and the early years of their postgraduate training. The larger subgroup, I believe, enter the research laboratory with an open mind, making an honest attempt to discover whether surgical research is interesting to them. They are best assigned to an existing research program in order to learn techniques, and they often contribute significantly to that project. They should be encouraged to develop ideas of their own when practicable. The final group is by far the smallest. It is almost always possible to predict which residents will fit into this group on the basis of past performance. They are the men who look forward to laboratory experience with intense enthusiasm, who frequently have participated in research in one form or another during their student days, and who enter the laboratory with an idea or ideas already worked out in principle. These men usually find the laboratory an exciting complement to an already absorbing career in clinical surgery. They are not content to read about new developments in surgery but desire to participate in their beginnings. These are the investigators who are most productive in their early years.

All biologic research may best be described as applied research; certainly, there is no basic surgical research. Surgical research, if another name need be given, may be called a type of applied physiology. Biochemists and biophysicists work in surgical-research laboratories but they are not surgeons. Surgical investigators utilize biochemistry, biophysics, mathematics, and electronics. The researcher may flirt with problems of radiation physics; he will not become an expert radiologist or physicist because of his flirtation and for this he may be criticized. Francis D. Moore has cautioned against surgical research's becoming too basic and writes of "the very urgent and elegant work of applied science." He describes

the surgical investigator as "a bridge tender, channeling knowledge from biological science to the patient's bedside and back again. He traces his origin from both ends of the bridge. He is thus a bastard and is called this by everybody. Those at one end of the bridge say he is not a very good scientist and those at the other say that he does not spend enough time in the operating room. If only he is willing to live with this abuse, he can continue to do his job effectively."

An essential quality of the complete researcher in either pure or applied science is individualism. He who recognizes a problem, thinks about it, and proposes an idea for its solution must, almost by definition, be capable of independent thinking. Cannon has described two groups of scientists; guessers and accumulators.(2) The guessers propose and solve, the accumulators find dozens of other ways to reach the same conclusion or apply the basic principle to a dozen other entities. The accumulators are probably better suited to the team approach in research, an approach which I prefer to call "fragmented" as far as the individual is concerned. This does not imply that all surgical investigators should be locked individually in closets with a single piece of equipment. It does imply that a project can be attacked by one responsible individual with as much technical help as is required. I do believe that four competent surgical investigators locked in four separate closets would probably do a better job with solving a particular problem than the four together in one room. Nevertheless, the trend has been toward the team approach in recent years. If this could be limited to different groups working on different facets of a large problem in different locations, each group with separate responsibility and free to pursue sidepaths when advisable, then the team approach has real merit. However, a large group of responsible investigators working on one problem under one roof tends to become chaotic in research.

Thus, we find that surgical research can be a discipline in its many meanings: it is a period of training which improves the investigator within the framework of his specialty, which helps him to think clearly and critically, and which stimulates his curiosity; it is a method of conduct in which ideas are carefully tested using generally acceptable rules; and finally, it includes a rapidly expanding body of knowledge which continuously contributes to the mainstream of clinical surgical practice. An integral relationship exists between surgical research and clinical surgery. Much has been written about the impossibility of being both a good investigator and a good clinician. In my opinion, there is an unhealthy detachment if a clinical surgeon has never been exposed to surgical research and an equally unhealthy detachment if a surgical investigator becomes separated from clinical surgery.

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