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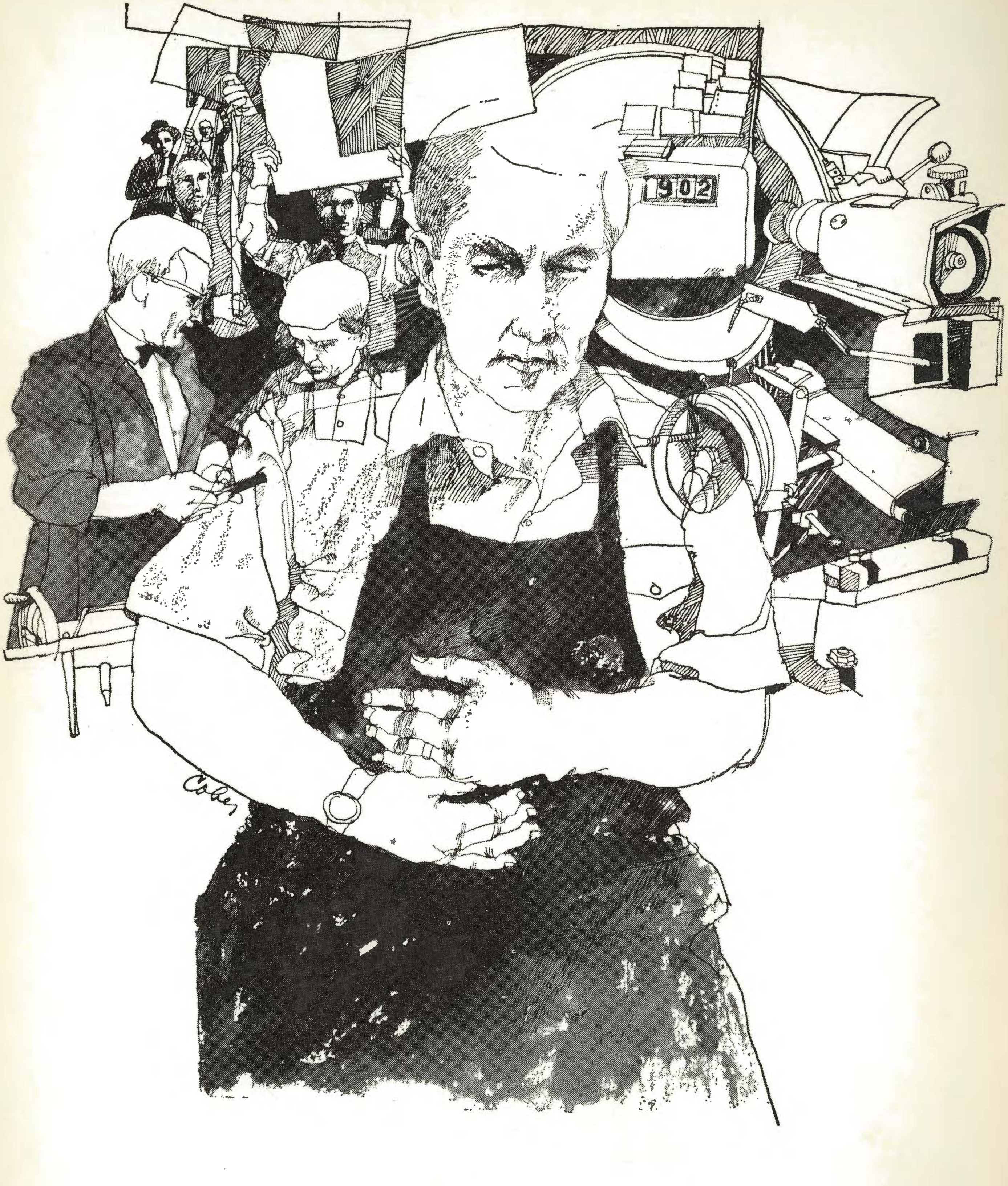
MEDICAL COLLEGE OF VIRGINIA QUARTERLY

WINTER 1966

COMPUTERS IN MEDICINE



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MEDICAL COLLEGE OF VIRGINIA QUARTERLY

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CONTENTS

The MEDICAL COLLEGE OF VIRGINIA QUARTERLY is designed primarily for the postgraduate education of physicians. The QUARTERLY will publish results of original research in basic and clinical sciences, and report on seminars and symposiums held at the College. Contributions from outside the MCV faculty are invited.

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The Future Effect of the Computer and the Research Scientist on Medical Practice

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The title of this presentation is concerned with the future effect of the computer and research scientist on medical practice. I will try to avoid the pitfalls of prediction outlined by Dr. Mount,* namely that if one predicts the immediate future he will be too optimistic, and if he predicts 10 years or so in the future he will be too pessimistic. So I will not put any time limits on my comments.

Quantitation of Medicine

Perhaps the greatest contribution to medical research and practice of the computer and the methodologies surrounding it has been the introduction of a quantitative attitude into medicine. Let us examine quantitation for a moment. In order to begin, let me explain my concept of biometry. Biometry may be defined as the study of the application of quantitative scientific methods to biological phenomena. Today biometry is represented by five overlapping, but yet separately organized, disciplines: biostatistics including demography and public health statistics, biomathematics, biophysics, bioengineering and biomedical computer sciences. Although these separate disciplines utilize somewhat different approaches to problems, they all make use of a knowledge of mathematics. Not everyone will agree with the use of the word biometry in this general sense, but since the five disciplines mentioned above overlap in their interests, a single term to describe their entirety is useful.

With the increasing emphasis on quantitation in biology, biometry can be expected to play an important role in the future of medicine by leading in the development of methods to accomplish such quantitation. However, we must remember that quantitation, per se, is not the goal of biometry. Rather, quantitation is a means to increase our understanding of biological phenomena with resultant improvement in our ability to care for the ill. What does quantitation actually accomplish, or in other words, why quantitize? There are basically three reasons.

1. It increases our ability to be precise in describing biological processes. By precision, I mean, in effect, reproducibility. It is easier to reproduce quantitative measurements than subjective ones. In part, this is because subjective impressions change as one learns, which is desirable, but it reduces reproducibility.

2. It increases sensitivity, that is the ability to discriminate between two objects or processes that are different. This is due in part to having greater resolution of the measurement scale.

3. It makes information collected earlier easier to interpret and in general makes the information

* Dr. Joseph Mount, of the IBM Research and Development Center in Houston, had spoken earlier on "A Model of the Heart."

This paper and the two that follow were transcribed from presentations at the Nineteenth Annual Stoneburner Symposium on "Computers in Medicine," March 31—April 1, 1966, Richmond. I am grateful to S. J. Kilpatrick, Jr., Ph.D., chairman of the department of biometry, for editing the transcripts. —Ed.

MCV QUARTERLY 2(4): 234-237, 1966

more useful. As an example, compare the relative values of an electrocardiogram as compared to a physician's written description of an electrocardiogram to another physician.

In any move to quantitate, we must be sure that we are measuring something worth measuring, that is, that we are in fact measuring an entity for which we desire information. The concept of quantitation is receiving much scientific attention today. The problem of what to measure, and how to measure it, are two of the greatest challenges facing medicine. It is essential to identify those qualities whose measurements will yield information sufficient for decision making. Let me give you an example; how does one measure the effect of treatments in mental disorders? What are the criteria to be used in arriving at a decision as to whether the patient has benefited from the therapy? These are considerations for which there is not now a mutually acceptable answer, although various criteria have been put forth. One reason for this is our lack of sound basic principles, expressed in a quantitative sense, of the functioning of the emotional aspects of man. The first step in implementing a computer application is to gain good quantitative information to build upon. In some systems, mathematical models of that system suggest variables that need to be measured. For example, Dr. Mount has pointed out that given a model for the electrical activity of the heart, the question arises as to where measurements should be obtained to get the optimum amount of information. The fact that he started with 130 leads gives some idea of the amount of experimentation that must take place before the computer system is finalized. In others, empirical results from large epidemiological studies will provide the clue. And in still others the discerning eye of good clinicians will suggest an answer. After some item has been suggested, it becomes necessary to determine how to measure it, that is, the technological requirements to accomplish this measurement. This is where the biological engineers have been and will continue to be important. This includes a group of people called human engineers who are interested in problems of how best to get information from and to human beings.

Study of Variability and Its Causes

However, once a decision has been made as to what to measure and how to measure it, we must then determine the properties of this measurement. That is, how is this measurement distributed in healthy persons and in disease states. What sorts of factors influence this measurement, and in particular, what sorts of technical considerations influence it? Are these technical biases constant over the full range of measurement? We are beginning to consider measurements made in man as dynamic rather than static quantities. We have started to examine the variability of quantities such as the serum cholesterol and the electrocardiogram during the day to day routine activities of a person as well as during unusual physical and emotional stresses being placed upon the individual. The concept of intra-individual variation as opposed to inter-individual variation is receiving more and more attention. Hampton and co-workers (1966) have found, for example, that the plasma fibrinogen levels in patients with documented myocardial infarction as compared to a series of matched controls without previous myocardial infarction or other signs or symptoms of coronary artery disease differed very little in their mean levels, and in their subject-to-subject variation. However, if one makes the determination of the plasma fibrinogen over time and adjusts these data for those factors known to influence the serum fibrinogen such as infection, it turns out that the intrasubject variability of the serum fibrinogen is much greater, as a matter of fact, five times greater on the average than it is in the matched controls. The exact significance of this finding is not yet known. Other workers are examining the variability of serum cholesterol, of the electrocardiogram and of other variables in man. The study of such variability over various time spans has presented difficulties in experimental design and in the analysis of the resulting data. We are currently studying more effective ways to measure variability from non-independent observations as well as more effective experimental designs.

A more detailed study of the factors influencing the values of such measurements is extremely important, that is, the influence of the environment upon biological processes. We are now able to look at interrelationships of several factors and of their influence on measurements, and can thereby better evaluate the meaning of the particular observation. Various workers are critically examining the concepts of normality and of the distribution of measurements in a healthy or normal state. The concept of *optimal value* has been put forth by L. E. Lamb (unpublished manuscript), that is, those values which are most highly associated with the state of continued good health.

What are the sources of information concerning the distribution of measurements in various states and the expected variability of such measurements? Of course the time-honored sources are the studies specifically designed to obtain this information. Design of such studies must be rather flexible, in the sense that they do not impose unrealistic rigidity, and they must be broad in the scope of their considerations.

A second major source of such information has been made possible by the computer. This is the routine screening of individuals for particular measurements by use of automated multi-test laboratories. Dr. Morris Collen has applied computer technology to the periodic health examination by using the results of multiple screening techniques, and a specially designed and constructed facility. This system has been described in some detail elsewhere (Collen, 1966), but basically it consists of patients passing through some 20 stations where a procedure such as chest x-ray, electrocardigram, etc., are performed. Information from these procedures is entered into punch cards and then into the computer, which prints out a report constituting advice as to any additional procedures which should be done prior to the next examination. This advice is based upon decision rules, previously established by internists, based upon specific test results. A second approach has been that of routine MMPI evaluation, such as has been reported by the Mayo Clinic (Pearson et al., 1965). Both such systems will be useful for the acquisition of data concerning the problems of particular items of measurement and the interrelationship of such measurements.

The third source of such data should come from the increasing use of physiological monitoring. Physiological monitoring seems to be a workable system for yielding a valuable continuous evaluation of the status of the patient during surgery, intensive care, and the performance of diagnostic and therapeutic procedures, and should be useful in long-term monitoring of subjects performing various tasks in various environments. Of course, the astronauts provide perhaps the best example of monitoring of subjects in unusual environments, but similar information is needed about those of us who are earthbound and going about our usual tasks. We need to know both the short and long term behavior of various physiological parameters. By monitoring patients receiving medication, it should be possible to obtain more dynamic information concerning response to therapy. In this way we can study the influence of various factors upon the behavior of variables and can then hopefully evaluate the relative value of such measurements as parameters of therapeutic effect. This is not an easy task, nor is it one that is currently as effective as it will be. Many important and competent people are working in the area of physiological monitoring, and I look forward to the time when this provides us, not only with a source of dynamic information, but great assistance in the clinical care of patients as well. Such a system should provide us with up-to-date meaningful information, upon which realistic decisions can be made.

Other sources of basic quantitative information should come from computer processing of images. Although the work in this area is still primitive, information about size and spatial relationships should be forthcoming in the future from this source. Still another method for obtaining information especially about the natural history and therapeutic aspects of disease should be the automation of the flow of information within a hospital. It is my feeling that such a system holds great promise for increased efficiency in patient care as well as a valuable source of management, patient care and disease process information.

Much information is currently being gathered, and more will be in the future. What are we going to do with this information? How are we going to disseminate it so that it can be readily available to persons requiring it? Hopefully, current research in information retrieval techniques will lead us to a system for the systematic organization of medical information. Such an organization should accomplish two things. It should in the first place provide for easy retrieval of desired information and secondly it should point out our information deficits. Various approaches to the systematic organization of medical knowledge have been put forth. The National Library of Medicine makes use of a very detailed system for organizing published knowledge. Whether any scheme now on the scene is totally effective remains to be seen. However, the point is that various workers are now investigating ways to organize our knowledge so that it is retrievable, so that it can be brought up to date, and so that it becomes useful. Such information should conceivably be available in an immediately retrievable form for maximal usefulness.

Computer Assisted Instruction

Up to now we have been discussing ways in which information should be gathered and stored. Now let us address ourselves to the problem of disseminating the information, that is the problem of education of medical students and house staff officers, and the continuing education of practicing physicians and scientists. This is an area in which some of the most exciting work is now being done involving computers, that is, utilizing the computer as an instructional aid in the imparting of medical knowledge to people. We have been interested in this approach to the teaching of medical information for some time and unfortunately do not yet have a working system.* However, other workers, particularly Feurzeig and co-workers (1964) and Entwisle and Entwisle (1963), have reported working systems in the teaching of differential diagnoses. Basically what they do is to have the computer simulate a patient, have the student sit at the

* Since this presentation, we have developed a working system which will be described in Harless, W. G. The implementation of a computer-assisted instruction program in a medical center environment. *J. Med. Educ.* (in press).

computer or at a console, and the student asks the computer questions much as he would ask questions of a patient or of a clinical laboratory. One method even has built into it delays, so that if you ask for a blood culture, you do not get the results immediately. The point is that the student is asking the questions and the computer is giving him the information that he needs. It will provide answers to specific questions and it can be set up to answer any question, within limits, that a student asks, even though the question does not pertain to the particular patient being simulated. This is one approach to the problem of computer-assisted instruction. In the future the computer will be used not only in this fashion, but also will have available to it visual and auditory aids. For example, it will turn on a tape recorder so that the student can listen to heart sounds and flash slides so that he can look at biopsies, blood smears, or electrocardiograms. The modern digital computer can communicate with students in a conversational mode, and courses can be developed for computer-aided instruction without requiring a student to learn a special code, computer programming, or other technology. It should be pointed out that it is not the purpose of this form of instruction to replace human instructors, but rather to assist them in their task. As a matter of fact, it should actually improve their teaching, since the computer can maintain records on the progress of students including information as to student deficiencies, so that the instructor can be aware at all times of how effective his teaching has been. This should allow for a more dynamic teaching, in that the material being presented to the students can be altered to fit the needs of the particular students receiving the instructions.

Modern computers can respond within micro-seconds to student questions and can accomodate several students virtually simultaneously. Therefore, student experiences can be multiplied greatly with only a small increase in time. The primary advantages of such instruction are that it allows each student to progress at his own rate, it provides feedback information to the instructor so that he can provide the kind of instruction that is needed, and permits students to use it at times convenient to them. This latter consideration could, of course, be advantageous to the student by more effective utilization of his available time. This form of instruction is still in early developmental stages, but it should be an effective method for the future.

Conclusion

The computer is here. It has become a part of medicine. We have talked for a day and a half now about some of the applications of computers in medicine, and of the future of at least some of these applications. There is a language problem in communicating with computers, but certainly the future is going to see a medical language, comparable to the scientific language Fortran, built to enable physicians to communicate with the computer. The real advancements in computer application depend at least in part upon active use by physicians of computers.

In closing, let me summarize by saying that I feel that the major effects of current research will be to:

1. provide more quantitative information concerning man's physiology especially as it is affected by his environment;
2. provide a classification, storage, and retrieval system for the collected information; and
3. provide more effective means for continuing medical education.

It should be emphasized that modern medical research should provide us with the information necessary for physicians to make meaningful decisions concerning the care of their patients, and after all good patient care is the goal of all of medicine.

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Applications of Computers to Medicine

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The purpose of this paper is to present an over-view of current applications of computers to problems in medicine and not to discuss any specific application in detail. This discussion will be concerned only with digital computers.

The modern digital computer is not very old. As a matter of fact, digital computers as we know them date from approximately 1949. Yet in this short span of time they have contributed to almost every sphere of man's activities. Computers have been applied to medical problems since about 1956, and have played an important role in increasing both the depth and breadth of medical research and practice.

It seems to me that computers have had two major impacts in medicine. *First* they have provided a focus for a true multidisciplinary approach to medical problems. Computer scientists and computer centers have contributed to this in part by their own research programs which have served to stimulate physicians and scientists to make use of computers and computer methodologies. Furthermore, the capabilities of computers has stimulated the joining together of medical scientists and physical or mathematical scientists to solve a medical problem. *Secondly,* the need for computers to have well defined problems has required physicians and scientists to better define their problems and to be more critical concerning the precision of their data and the design of their experiments. The ability of the computer to handle multivariate problems and to effectively work with the interrelationships of variables has made it possible to get more information from critical experiments than had been possible previously.

It is difficult to point to any single major contribution due solely to the use of computers. However, Dr. Shannon (1965) in his introduction to Dr. Waxman's book has pointed out that computers contributed materially to the work of Drs. Watson and Crick in elucidating the structure of nucleic acids. The effect of computers on medical activities has been subtle but nonetheless impressive.

Statistics

Since medicine is an empirical science, it seems only reasonable to begin our discussion of computer applications with the impact of computers on medical statistics and epidemiology. Let us examine some of the general experiences. Computers have had several major impacts on medical statistics. First, they have permitted statisticians to effectively summarize masses of data in informative ways. Clearly, masses of data by themselves are not necessarily informative, but when collected systematically with a good design, can be useful, especially in clinical medicine and in

MCV QUARTERLY 2(4): 238-241, 1966

public health. Furthermore, computers have permitted multivariate statistical methods developed some thirty years ago to become practical statistical tools for analyzing more realistic medical experiments. This potentiality is fraught with dangers because of the rather severe limitations of these methods from an interpretive point of view, but computers have made research into multivariate statistical methodologies practical and useful. The third major impact is related to the first two in that data arising from complex and/or unconventional experimental designs can now be analyzed more effectively. This has again permitted statisticians to assist in the design of more realistic experiments. Finally, statisticians are now able to more effectively study their own methodologies and thereby evaluate and hopefully strengthen their tools.

Epidemiology

Epidemiology and epidemiological studies have long provided the major share of clinical medical knowledge especially as it relates to etiology, natural history, and preventive and therapeutic aspects of disease. In recent years, epidemiologists have changed their focus from infectious to chronic diseases, especially lung cancer and coronary artery disease. The problems of study posed by such diseases are challenging. The usual approach has been multivariable and has involved large numbers of subjects. Therefore, one major aspect of the work of the chronic disease epidemiologist has to be the understanding of the properties of the quantities which he is measuring and the influence of each of these quantities upon the values of each of the others. It is very doubtful that the information gained from such studies would be available without the accessibility of computers to summarize collected data and their relationships to disease. The amount of data gathered in even a modestly sized epidemiological study is formidable, but the editing, storage and logic capabilities of digital computers have led to greater accuracy, faster reporting of findings and new approaches to the analysis of such data.

Mathematical Models

Computer techniques have made mathematical analysis of biological phenomena feasible. Of particular importance are mathematical models of biological systems. Dr. Eugene Ackerman (manuscript in press), a biomathematician at the Mayo Clinic, has set forth two goals for such models: description or characterization of the biological system and improvement in the understanding of the mechanisms of the system. Successful models of several biological systems have been developed including the electrophysiology of the heart (Bayley and Berry, 1964) and the body fluids and electrolytes (Maloney, 1966).

Radiation Therapy

Another application of mathematical methods to medical problems is in the realm of radiation therapy. By deriving mathematical expressions for the dose distribution within a beam or around a source, it has been possible to compute radiation doses to particular tissues and thereby to select that treatment plan which will result in the most effective dose to the desired area of the body. Work in this area has been largely due to Shalek (Shalek and Fletcher, 1962) and Adams (Adams and Meurk, 1964) with implanted radium needles and to Sterling and Perry (1962) with external beams. Evaluation of the success of these approaches must await a more complete statistical evaluation of survival data, but it certainly seems reasonable that some such method will be more successful than is otherwise available.

Analogue Applications

Analysis of bioelectric signals has been one of the more fruitful areas of computer applications to medicine. However, this success has not been without much work and frustration. The ability to work with such signals requires good data collection and recording instrumentation which will not mask the desired signal with artifact. Furthermore, since these signals are continuous relative to time, it is necessary to convert them into discrete numerical values if a digital computer is to be utilized in the analysis. This is accomplished by use of a device known as an analog-to-digital or A to D converter. Our knowledge of analog-to-digital conversion techniques is increasing and this should contribute to our ability to work with these signals. However, these data acquisition procedures have resulted in huge volumes of data, and new techniques for handling such volumes have been required. Results of such work on the electrocardiogram have been particularly interesting and this has been discussed by Pipberger (Pipberger and Stallmann, 1964). The electroencephalogram has also been studied in detail as have other biological signals.

Patient Monitoring

The ability to acquire and process bioelectric signals has given rise to still another application of computers, that of monitoring physiological events. In this application, the computer is an integral part of an experiment in that it serves to continuously monitor the input data and to process such data while the experiment is going on. This allows for modification of the conditions of the experiment on the basis of analysis of the data from earlier parts of the experiment. In this way, the computer plays an active role in the conduct of the experiment. Two terms are frequently used in physiological monitoring: "on-line" and "real-time." On-line indicates that the data source is connected directly to the computer, that is without intervening recording of the data. Real-time indicates a computational configuration in which the values of time varying parameters are generated at their actual rate. Both of these characteristics are necessary for an effective monitoring setup. It should also be pointed out that on-line monitoring systems permit the study of intact physiological specimens and thereby of the control systems responsible for maintenance of equilibrium. Work of this sort has been pioneered by Stark (1964), Macy (1964) and others. More recently, physiological monitoring techniques have been utilized clinically by Wilber and Derrick (1965) to monitor patients during surgical anesthesia, by Weil (1965) to monitor during circulatory shock and by others. Boyd (1965) has set forth four functions of a physiological monitoring system. These are: acquisition of data, recording and output of data, logical manipulation of data and provision of warning devices in the event variations exceed preset limits. Data acquisition is dependent upon the availability of sensors that are relatively artifact free, do not interfere with the physiological system under study and have a long useful life. Biological engineers have been responsible for the development of the instrumentation required for monitoring activities including the development of improved sensors. The future promises many advances in the physician's ability to care for the ill by use of monitoring instruments and techniques.

Publications

The current flood of medical literature poses one of the greatest challenges in history to medical workers. With the amount of literature currently available, it is rapidly becoming virtually impossible to screen all of it to find and read the articles of greatest interest. One solution to this problem has been developed by the National Library of Medicine (Karel, Austin, and Cummings, 1965) in the form of a computer system known as MEDLARS (Medical Literature Analysis and Retrieval System). In this system the content of the medical literature is analyzed and assigned descriptive words which summarize its content. This information can then be systematically searched for all references described by specific descriptive terms, and a list of all such references prepared.

Computer Diagnosis

One application of computers which has received a great deal of publicity and which has stirred up much controversy has been that of computer diagnosis. Part of the reason for the controversy has arisen from differences in the expectation of what a diagnosis should be. Ideally, I suppose, we would like a computer to be able to make the correct diagnosis or diagnoses from a minimum amount of easily obtainable information. At the present time, this is not feasible for many diseases. This is due, in part, to our lack of understanding concerning the relationships of specific items of information to specific diseases. If, on the other hand, one wishes the computer only to assist him in arriving at a diagnosis, then this is possible with a few diseases. However, effective use of these procedures requires the physician to know in advance that the patient has one of the diseases included in the developed system. Probably the best known work in diagnosis is that of Dr. Homer Warner with congenital heart disease (Warner et al., 1961). His procedure utilizing Bayes' Theorem has proved successful if the physician provides good information. It is unlikely that the computer will play a major role in disease diagnostic efforts for some time to come, but studies of its usefulness should continue so that we can better define its role.

Pattern Recognition

Thus far, I have discussed only a few computer applications to medicine. These applications have utilized information in three forms: numbers (for the statistical and mathematical applications), electrical signals as with the electrocardiogram and English words in the library applications. However, information in still another form, visual images, has been approached by the computer scientist. It should be stressed that all of these forms of information must be translated or converted into discrete entities such as numbers or letters before they can be processed by digital computers, however, representation of the information by such discrete quantities should not materially alter the information content. Computer processing of the information contained in visual images has primarily revolved about chromosome identification (Mendelsohn et al., 1965) and work with chest x-rays (Becker et al., 1964; Meyers et al., 1963). Work thus far accomplished has demonstrated the feasibility of applying computers to this form of information.

Medical Records

Automation of the flow of information within a hospital is currently receiving much interest. Hopefully, such automation would decrease the time required to transmit information, provide better means for maintaining the accuracy of such information and in general improve the efficiency of the hospital operation. This application is beset by many problems, but it does seem that a computer oriented system for hospital information flow may accomplish these ends.

Conclusion

This has been a brief glimpse at some of the applications of computers in medicine. This is an exciting time for all of us involved in medical problems since the availability of computers and computing methodologies has presented us with an opportunity to expand our abilities to be creative. It is not an easy road but it promises to be productive. Those of us interested in biomedical computing have learned a great deal in the last few years and we still have much to learn, but the future looks bright for increasing our knowledge of medicine to improve our care of the ill and our ability to maintain the healthy.

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Effects of Computers on Patient Care

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In reviewing the specific topics of this lecture series, I was immediately struck by the fact that if computers have any impact on the practice of medicine, the organization and administration of hospitals and health care facilities, or on general medical research, it must follow that computers will have an effect on patient care. After all, patient care is essentially the output of a system which has medicine, research, and administration as its inputs. If, through the use of computers, any one of these inputs can be aided, a beneficial effect on patient care should result. You have heard thus far that there are many outstanding benefits which can be achieved through the use of computers in the practice of medicine as well as in general medical research.

Development of Hospital Systems Analysis

I am sure that by now you are all aware of the marked current interest in the use of electronic data processing, operations research methodology, and many industrial engineering techniques in hospitals. However, I believe that a little historical development would help to set the stage for my discussion today, as it might focus your attention on what I consider to be some of today's problems. You will probably be amazed to learn that one of the first persons interested in designing better patient-care systems was none other than the founder of the concept of motion study and one of the fathers of the scientific management movement, Dr. Frank B. Gilbreth. He made extensive studies of management in many hospitals throughout this country and in Europe. In addition, he conducted many method studies in operating rooms in hospitals in this country. In 1916, in a paper presented to the AMA, Gilbreth stated "In studying these many hospitals, we find conditions, as a rule, much worse from a managerial standpoint than in the average factory, and some hospitals are so bad that they should actually be closed immediately." Remembering the conditions that existed in the factory system in the early 1900's, you will probably get the full impact of Gilbreth's criticism. He went on to point out that there were no reasons that present management and systems in hospitals could not be revolutionized; that the waste in transference of skill in surgery could not be eliminated; and that the methods proven in industry could not be applied to the hospital. A little spark of interest was triggered by Gilbreth's discussion when Pool and Bancroft (1917) described a system study of a surgical service in which many concepts of today's operating suites were discussed and presented. It was over 20 years before Lawrence and Berry (1938) made the next appeal for the use of industrial motion study principles in the operating room.

It was still to be several more years before any real activity was to take place. Surprisingly enough, the nursing profession began to champion the cause of designing better patient-care systems. Two nurses at the University of Minnesota School of Nursing were interested enough to attend classes in motion and time study at the University's School of Engineering. They began to put into practice some of the principles that they had learned (Dodds, Petry, and Koepke, 1940). About the same time, Dr. Ralph Barnes, a pioneer industrial engineer, carried out several studies at the University of Iowa College of Dentistry (Speidel and Barnes, 1942), and Dr. Lillian Gilbreth (1945) made another appeal to hospital administrators, which was essentially the same as her husband had made 30 years before.

However, it took World War II with the shortage of nursing personnel in the post-war years, the sharply rising costs of patient care, and the changes in the pattern of patient care to really awaken the hospital world. About the same time the operations research star began to rise, as the use of the computer made possible solutions to mathematical problems which could not have been solved previously. The slow awakening of hospitals to modern management methods took place over 35 years after the initial discussions about the patient-care system by Frank Gilbreth.

Computerization of Clinical Data

Now if we consider scientific management a revolutionary movement, you might ask what difference does it make *when* we jump

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on the bandwagon, just as long as we jump. There is a difference, and this is one of the two significant points that I would like to leave with you today. It is exceptionally difficult to jump on a rapidly moving vehicle without first accelerating to an equal speed. Industry has had over 40 years to adjust to the gradual changes which create the proper environment and a receptive attitude for the use of new management technology, such as computers.

Unfortunately, many hospitals today view the use of computers as a panacea. In one respect, nothing can be further from the truth in the patient-care system. Simply replacing the current information system by computers may result only in an amplification of the speed by which "garbage" is processed. The effect that this type of approach has on patient care may well be a negative one. Hospitals must first accelerate to the pace of the bandwagon.

In order for computer applications to have the most beneficial effect on patient care, all patient-care systems must be carefully studied and evaluated. Let me define what I consider a patient-care system. A patient-care system would include the physical activities required to carry out a function or goal, together with the accompanying information systems that are related to those physical activities.

As I have said, all patient-care systems must be carefully studied and evaluated. In effect, I am imploring you to eliminate the "garbage" and the "noise" initially. In order to do so, the patient-care system must be studied carefully, and system decisions must be based primarily on the patient as the center of activity, and not the computer. In many cases, the physician's order supplies the goals to be met by the patient care system. These goals must be carried out within the context of the entire hospital operation. Although I may have implied that the physician's order may be considered a goal or a set of functions to be achieved, I *do not* imply that the method for achieving these goals is restricted. For example, coming to Richmond may be considered to be an explicit goal, but you know that there are many methods of transportation and many routes to follow that would satisfy this goal. Thus, in a hospital system, for example, requiring a specific medication T.I.D. is one thing, but deciding how the prescribed drug is to reach the correct patient at the specified time is something completely different. The careful study and design of which I speak requires a consideration of the possible alternatives and a selection of the one most feasible to carry out the specific function in question. Hospitals have been quite remiss in carrying out this type of activity.

Design of Hospital Computer Systems

I might add that restudy and reevaluation is also a necessary component of system studies to keep up with the many changes in medical technology that are introduced into the patient-care system. This same approach or philosophy must permeate the indirect care systems as well as the direct care systems.

This atmosphere of study and design is a spiraling one. It is similar to the variance between fire-fighting and fire-prevention. Most people associated with hospital management find themselves constantly problem solving or in a fire-fighting situation. They have little time for planning or fire prevention, and the less time they spend in fire prevention, the more fires they will have to stamp out. This usually continues as a downward spiral.

The concept of proper design of a patient-care system can be an upward spiral as opposed to a downward spiral. If one first takes the time to properly design a patient-care system or a component of a patient-care system, the number of difficulties or problems will be fewer, thereby providing more time to spend in design.

The study and design of hospital systems is, of course, no easy matter, nor one that can take place overnight. The use of computers as an information processing medium must be included as a part of the system studies, if greatest effectivity is to be achieved. The capacity for computer performance is great, but it is always dependent upon the imagination and the sophistication of its man-made programs.

Current Uses of Computers

The effect that computers have on patient care will depend on their mode of operation. Computers may be called upon to process information "after the fact" or after required action has been taken, or they may operate in real time or "on line" with the events as they are taking place. Most of the computer applications existing in hospitals today are of the former type. They have been focused on business office or fiscal affairs and on certain medical statistics. These types of computer operations are essentially after-the-fact manipulations of stored information. It should be pointed out that many of these applications are exactly the same as their industrial counterparts, and the transformation of industrial programming was easily accomplished, since the industrial system, in many cases, had been reevaluated and redesigned with the eventual use of computers in mind. We find such applications as accounts receivable, accounts payable, hospital payrolls, patient ledgers, and general ledgers. The use of computers in these applications has facilitated the hospital administrator's business-office operation, and has provided for greater accuracy in patient billing and, hopefully, for reduced operating costs. To the extent that these activities were achieved, patient care in a general sense was improved.

The computer evaluation of certain medical statistics provide information that perhaps was not previously available. A good example of this is the service offered by the Commission on Professional and Hospital Activities. Hospital case history data is processed to compile routine statistics on discharged patients, as well as to index cases by diagnosis, operative procedure, physician, etc. Comparisons of data which can be made could result in improved patient care. For example, one could evaluate the length of stay of patients with the same diagnosis, and possibly infer a more successful treatment modus operandi. Computer storage of large masses of data, such as those found in the medical record, patient index, physician index, disease and operative index, etc., will be of great benefit in the development of computer-aided diagnosis and eventually in improved patient care. However, these applications to a certain extent are still in the research stage, and their implications to patient care really remain to be seen.

The most exciting and probably the most beneficial effect on patient care will be achieved in the use of the computer in clinical activities within the hospital in real time. In these applications, data is being continuously fed into the system, and processed results are continuously available. This feature is especially important to the hospital, as hospitals are faced with extremely difficult problems of logistics. These problems are magnified due to the communications required by the very large number of departmental interrelationships and more importantly, the system perturbations caused by wildly fluctuating demand for services and facilities.

A computer operating in real time is well-equipped to consider both of these peculiarities. It can not only take them into consideration but can rapidly respond to them. The problem of communications begins with the physician's order and permeates the entire system, as various services are brought to bear in the treatment of the patient. In the first place, the correct transmission of the physician's request to all the agencies will be a step forward in improving patient care. In addition, as Dr. Brandt pointed out, computers can receive directly many of the physiological measurements about the patient picked up by monitoring devices. They can provide programmed responses such as alarms when out-of-control conditions develop.

One should go through all of the departments of the hospital to really see how this type of computer application would affect the performance of each and every service area. In short, I would suggest that if you would visualize the accurate transmission of information and the immediate feedback of results facilitated by computers coupled with properly designed physical performance systems, you would see an image of the dynamic hospital system of tomorrow.

In my opinion, the most beneficial impact of computers on patient care rests primarily in the better control made possible by the use of the computer. This control in essence provides medical care as prescribed by the physician with the minimum amount of error and delay. The problem of how to prescribe the care is the physicians' problem. The hospital patient care system must take the instructions which the physician provides and operate on that input in such a way as to develop outputs which accurately reflect the mission of the hospital.

Summary

In conclusion, the computer alone is not enough to provide the best possible patient care. Every hospital must be introspective about each patient-care system so that the performance aspects of the systems are meaningful and efficient. Couple the best methods of performance with the information processing and control capabilities offered by the computer, and one can envision a smoothly functioning patient-care complex in which the wild perturbations one sees in today's hospital operation are minimized. However, medical care finds itself in an awkward dichotomy. Many of the causes of system perturbation in the hospital are directly related to the demands for and implementations of new medical research results and technology. This of course, we must aid and abet to the best of our ability, so that patient care is continuously improved. While we struggle to keep the patient-care system under control, on the one hand, we must at the same time encourage the new procedures and techniques which of necessity bring about greater perturbations. It is only by welding together the best possible performance and information system that we can provide the opportunity for improving patient care. Thank you.

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Cryocautery and Aqueous Humor Dynamics*

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During the past decade the application of low temperatures to selected tissues has become an important and fascinating tool in various surgical fields. Numerous systems have been designed to facilitate cryo-applications to various organs. The first instruments devised to produce localized freezing of ocular tissues were crude, and consisted primarily of metallic cylinders filled with various low-temperature mixtures. One such device was used as early as 1933 by Bietti (1933; 1934) and Deutschmann (1933; 1935) in the treatment of retinal detachments. While Bietti used a mixture of solid carbon dioxide and acetone in a metal probe, Deutschmann applied carbon dioxide snow directly to the sclera, both modes of application resulting in the production of an adhesive chorioretinitis.

Bietti (1950) was the first to apply freezing techniques to the ciliary body as antiglaucomatous treatment. He reported tonometric results in both experimental animals and humans following the application of solid carbon dioxide to the sclera over the ciliary body. No further reports have appeared in the literature until recently when Polack and de Roetth (1964) reported their studies on the effect of freezing of the ciliary body. These authors used a conically-tipped copper vessel filled with dry ice and alcohol which they applied repeatedly over the ciliary body area of rabbit eyes. Tonographic results of these experiments showed a lowering of intraocular pressure averaging 4 mm Hg with a concomitant reduction of outflow facility and aqueous flow.

This study was undertaken primarily for the purpose of obtaining data for statistical evaluation of the effects of ciliary body freezing on aqueous humor dynamics. Such data is not presently available in the ophthalmic literature. Another objective has been to measure temperatures in various ocular structures during cryo-application and to study histologically eyes subjected to cyclocryocautery.

Methods

The first technique employed was to freeze the entire ciliary body with a cryo-applicator ring built in our laboratory. This consisted of brass tubing, the ring diameter corresponding to the rab-

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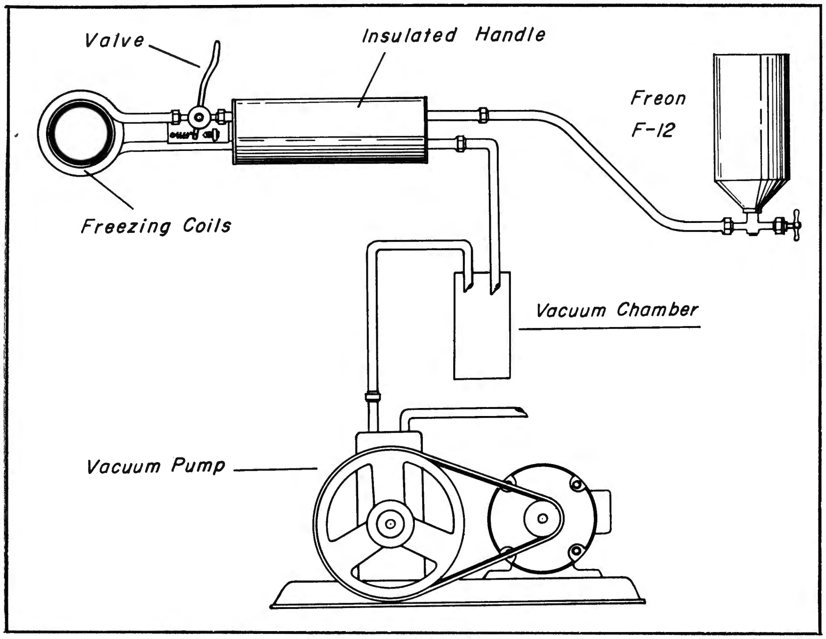

Fig. 1—Schematic diagram of freezing apparatus using ring-type applicator.

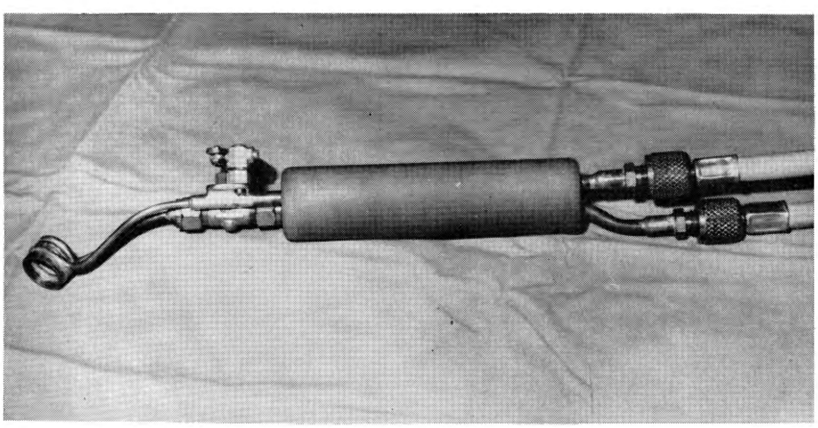

Fig. 2—Handle with Freon regulating valve: ring-type freezing applicator.

bit ciliary body area (18 mm for most mature chinchilla rabbits). The brass tubing was attached to a closed system which was fed continuously with Freon gas. The ring was attached to an insulated handle which also contained a gas regulating valve. The used gas was discharged into a vacuum pump (figs. 1 and 2). The circulating Freon gas cooled the brass ring to a temperature of −23°C. When this ring was applied to the ciliary body area, freezing was almost instantaneous and extended grossly about 1.5 mm on either side of the applicator. Since in the rabbit eye the ciliary body is located close to the limbus (Sheppard, 1961), freezing of the peripheral cornea and the chamber angle was unavoidable by this technique. After using this technique on a number of rabbit eyes, certain disadvantages became obvious. Immediately following cyclocryocautery by this technique a substantial rise in intraocular pressure occurred in all eyes. The intraocular pressure rose an average of about 15 mm Hg, and tonography immediately following thawing showed a greatly reduced facility of outflow. This rise in intraocular pressure was thought to be due to obstruction of aqueous outflow channels by freezing, similar to that reported by Gazala et al. (1965) following circumferential experimental limbal diathermy. After 24 hours the intraocular pressure in these animals returned to preoperative values, followed by a lowering of intraocular pressure and reduction of aqueous flow in some eyes. Histological examination of rabbit globes following this mode of cryoapplication also showed a number of undesirable side effects, primarily disruption of the chamber angle structure which would in all probability nullify any effect of reduced aqueous production by the ciliary body. It could also be shown that many of the small vessels surrounding the limbus were permanently occluded by a process of endarteritis obliterans, whereas larger channels remained patent. Similar findings were recently reported by Dan and Priestley (1965) on newly formed conjunctival and corneal vessels. Consequently it was felt that this procedure would be too traumatic for human application. In all subsequent studies interrupted cryo-applicataions have been employed.

At this time I became aware of the commercial availability of the Kelman Cryostylet (Frigitronics, Inc., Bridgeport, Connecticut). All further experiments were carried out with this instrument (fig. 3). The instrument utilizes the Peltier effect to produce low temperatures (Kelman, 1964). A number of modules (electric current passing through two dissimilar metals) are connected in series. The heat produced at the terminals of the modules is cooled by a coolant, and the cold produced at the junction is used for freezing (fig. 4). The handle of this instrument carrying the freezing tip also has a micro switch accessible to the surgeon's index finger, which activates a heating coil, thus allowing for termination of the freezing process within 3 to 5 sec (figs. 5 and 6). While this instrument was primarily designed for use in cataract surgery, it can easily be used for ciliary body freezing when somewhat lower temperatures are used.

Freezing was carried out with the Cryostylet by applying the tip of the instrument firmly over the conjunctiva for 1 min 1 mm from the limbus. Two applications were made in each quadrant. The frozen surface was slightly larger than the tip of the instrument, measuring about 4 to 5 mm in diameter. With the reservoir temperature of the coolant (saturated salt solution and ice) at $-2°$ to $-4°C$, the temperature of the tip was $-40°C$. Since the ciliary processes of the rabbit eye extend to the posterior surface of the iris, complete freezing of all processes was not obtained. All rabbits used were mature chinchilla, weighing from 2.5 to 3.5 kg. All

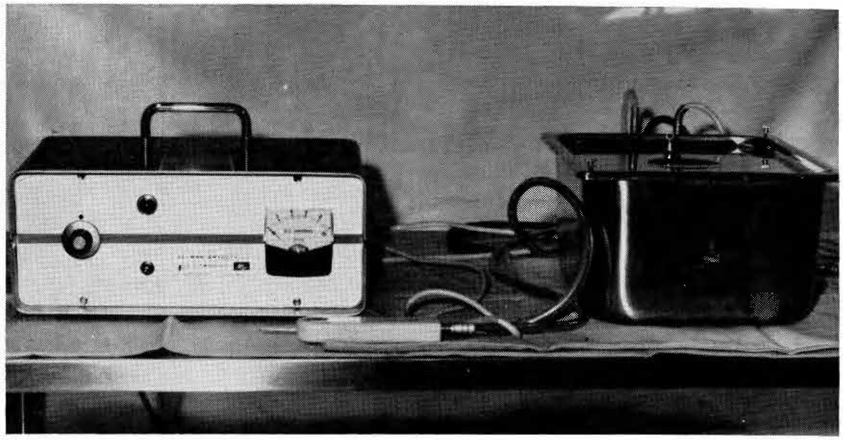

Fig. 3—Kelman Cryostylet consisting of power supply, cooling reservoir, and freezing applicator tip with handle.

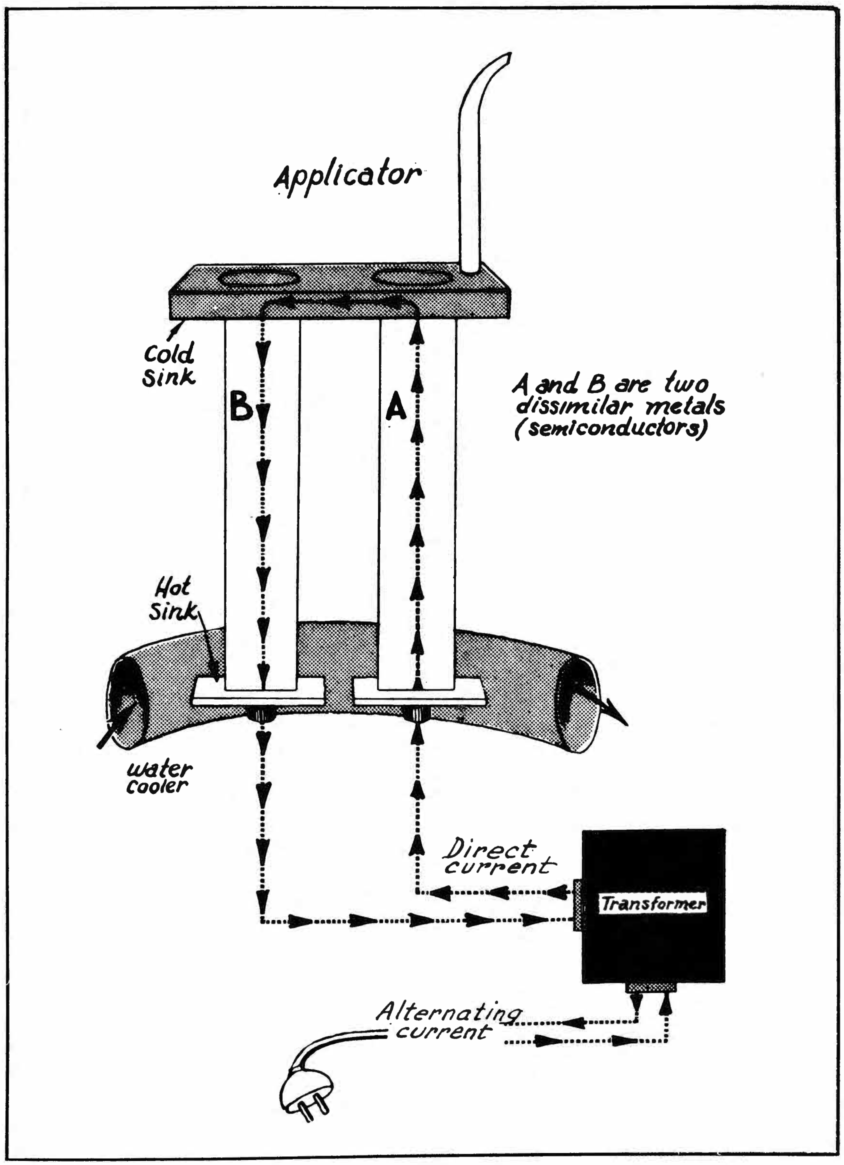

Fig. 4—Schematic diagram of thermoelectric module, the principle of the Cryostylet (courtesy Frigitronics, Inc., Bridgeport, Conn.).

eyes had tonograms before cryoapplication and at varying periods afterwards. A total of 60 eyes were treated. Twenty eyes were enucleated for histological studies at various intervals; 40 eyes were observed clinically and tonographically for a total of 12 weeks. Immediately following withdrawal of the freezing tip from the conjunctiva, hyperemia of the surrounding tissue and occasionally subconjunctival hemorrhages were observed. On a few occasions a small part of the peripheral cornea became slightly hazy, but cleared completely after 24 hours. During cryocautery of the ciliary body miosis ensued, lasting for about 30 min. Slight turbidity of the aqueous was observed on the slit lamp immediately following eight cryosurgical applications, but this also cleared in all instances after 48 hours. After one week the gross and slit lamp appearance of all eyes was normal. Only results of the two-per-quadrant applications will be discussed, since this mode gave the most consistent results in a small pilot study.

Results of Tonographic Study

All mature chinchilla rabbits were anesthetized with intravenous Sodium Pentothal and locally with two drops of 0.4% Dorsacaine. Tonographic tracings were obtained on all rabbits before the study with

TABLE 1
Tonographic values in rabbit eyes before, 2, 4, and 12 weeks after cyclocryocautery

		Before freezing			After 2–4 weeks			After 12 weeks		
		PO	C.	F.	PO	C.	F.	PO	C.	F.
A243	OD	27	.23	3.51	21	.26		26	.24	
	OS	28	.40	8.40	20	.28		28	.38	
A286	OD	24	.23	3.22	21	.30	3.30			
	OS	28	.26	3.68	30	.39	3.80			
A328	OD	17	.17	1.19				9	.15	
	OS	22	.24	2.68				16	.33	1.98
A329	OD	17	.17	1.19	15	.37	1.85			
	OS	17	.19	1.33	16	.33	1.98			
A360	OD	24	.27	3.78	20	.24	2.40	21	.24	2.64
	OS	24	.20	2.80	19	.17	1.53	18	.17	1.37
A361	OD	24	.20	2.80	19	.17	1.53	18	.17	1.36
	OS	24	.27	3.78	20	.24	2.40	21	.24	2.64
A362	OD	22	.20	2.40				21	.30	3.30
	OS	22	.40	4.80				17	.40	2.80
A363	OD	21	.18	1.98	22	.19	3.28			
	OS	19	.17	1.53	21	.24	2.64			
A364	OD	24	.35	4.90	12	.20	.40	19	.23	1.37
	OS	22	.32	3.84	15	.20	1.00	16	.26	1.56
A365	OD	24	.27	3.78				21	.24	2.64
	OS	27	.30	5.10				21	.10	1.98
A366	OD	21	.24	2.64	19			22	.13	1.56
	OS	19	.23	2.07	17			21	.24	2.64
A367	OD	19	.29	2.61	6			6		
	OS	17	.22	1.54	7			7		
A371	OD	19	.23	2.07	12	.15	.30	14	.25	1.00
	OS	21	.24	2.64	16	.21	1.26	16	.26	1.56
A372	OD	24	.38	5.47	19	.23	2.07	17	.32	2.24
	OS	22	.40	4.96	17	.32	2.24	15	.28	1.40
A373	OD	22	.27	3.34	19			15	.28	1.40
	OS	24	.35	5.04	20			19	.38	3.42
A374	OD	29	.41	7.79				19	.42	3.78
	OS	24	.44	6.33				21	.55	5.05
A375	OD	24	.44	6.33	21	.30	3.30			
	OS	24	.44	6.33	22	.32	3.84			
A376	OD	26.6	.39	6.25	21	.30	3.30			
	OS	26.6	.39	6.25	22	.32	3.84			
A377	OD	26	.39	6.24	19			21	.30	3.30
	OS	26	.33	5.28	19			22	.32	3.84
A378	OD	27	.30	5.10	19	.17	1.53	21	.24	2.64
	OS	29	.33	6.27	19	.23	2.07	22	.25	3.00
A483	OD	33	.18	2.64	20			29		
	OS	36	.24	5.40	17			29		
A484	OD	23	.25	2.25	17	.33	4.55			
	OS	22	.41	4.92	17	.54	3.78			

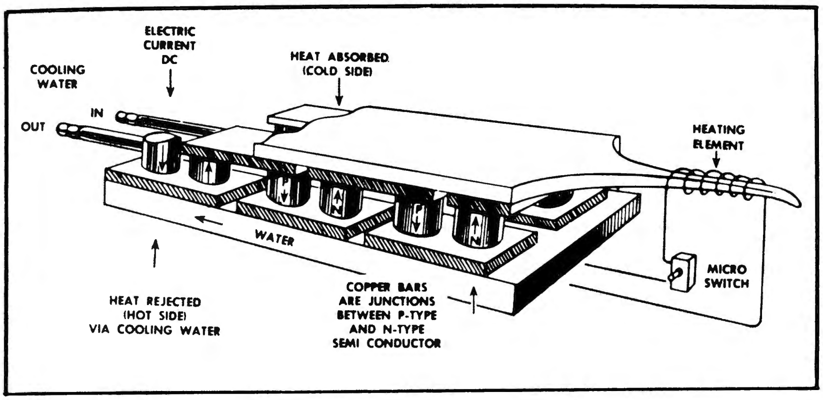

Fig. 5—Schematic diagram of Cryostylet freezing handle showing thermoelectric modules connected in series. A micro switch allows for defrosting of tip by a heating element (courtesy Frigitronics, Inc., Bridgeport, Conn.).

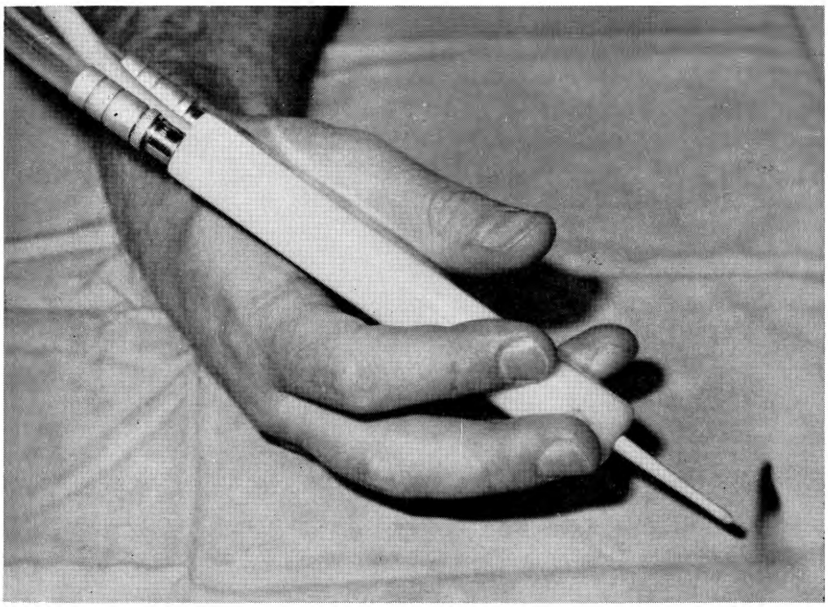

Fig. 6—Freezing handle of cryostylet. The surgeon's middle or index finger can activate a micro switch to defrost tip and disconnect the tip from frozen tissue after application with minimal trauma.

TABLE 2
Summary of tonographic study following cyclocryocautery

Weeks after cyclocryocautery	1	2	4	8	12
Average decrease in PO (mm Hg)	8.52	4.89	4.62	5.77	4.75
Significance p <	.0001	.001	.001	.001	.01
Average decrease in F (μl/min)		1.78			1.36
Significance p <		.001			.001
Average change in C	No definite trend demonstrable				

a Mueller electronic tonometer and recorder. The values for PO (opening intraocular pressure in mm Hg), F (rate of aqueous flow) and C (facility of outflow) were calculated using the tonographic tables by Schimek (1964). I was fully cognizant that the calculation of aqueous production from tonographic recordings is inaccurate and that constants used for the human eye cannot be used for the rabbit. Since my primary interest, however, was a relative change rather than absolute values, I felt that an adequate means of evaluating aqueous dynamic changes could be found by this method. This also makes it easier to compare results with those of other investigators who applied the same formula for their experimental tonographic findings (Polack and de Roetth, 1964; Bietti, 1950). Tonographic tracings on all treated animals were repeated at one- to two-week intervals following the procedure.

Intraocular Pressure

Immediately following the completion of the cryocautery there was usually a slight rise of intraocular pressure (5 to 8 mm Hg), but in some instances there was a slight drop. In no instance did the rise reach the proportions previously described using the ring-type applicator. Since this did not occur in the human, it is probable that in the rabbit the closeness of the application to the limbus is responsible for the pressure rise.

After one week the intraocular pressure in 42 eyes fell an average of 8.52 mm Hg. Only two of the 42 eyes showed a slight rise in intraocular pressure. The drop of the PO ranged from 2 to 19 mm Hg. When the findings were subjected to a statistical analysis using the "t" test for paired observations, the $t^*\left(t^* = \frac{\bar{x}\sqrt{n}}{\hat{\sigma}}\right)$ was found to be 10.456, giving a significant P value of less than .0001.

The PO values at the end of the second week were subjected to a similar analysis. The average drop in PO after two weeks was 4.89 mm Hg. Four out of 38 eyes showed a slight rise in pressure, while the decrease in PO ranged from 2 to 12 mm Hg. t^* was calculated to be 6.21 for a P value of $< .0001$. This is also statistically significant.

Further analysis after four weeks showed an average decrease of intraocular tension of 4.62 mm Hg. Four of 34 eyes showed a slight rise in pressure, and in two eyes it was impossible to get a technically acceptable tracing. The drop in intraocular tension ranged from 1 to 10 mm Hg. Values for t^* were 4.204 and $P < .001$.

After eight weeks the situation was essentially the same with an average PO drop of 5.7 mm (from 1 to 10 mm Hg) and a t^* of 7.816, giving a significant P value of $< .001$. Before the animals were killed (at the end of 12 weeks), tonographic tracings were repeated, and the average drop of intraocular pressure at that time was 4.75 mm Hg. Six of 34 eyes showed increases from 1 to 4 mm Hg, while the decrease in the PO ranged from 3 to 13 mm Hg. Statistical evaluation still showed a significant level of $< .01$ for the P value.

Rate of Aqueous Flow

Calculated values for F before cyclocryocautery were compared to F values 12 weeks after treatment. Values for forty eyes thus obtained were paired. In 10 eyes the F values either remained the same or increased slightly. In 30 eyes the F value decreased. The average F value before treatment was 4.22 μl/min and after treatment, 2.85 μl/min. When subjected to a statistical analysis, a t^* value of 5.112 was obtained, giving a highly significant P of $< .001$.

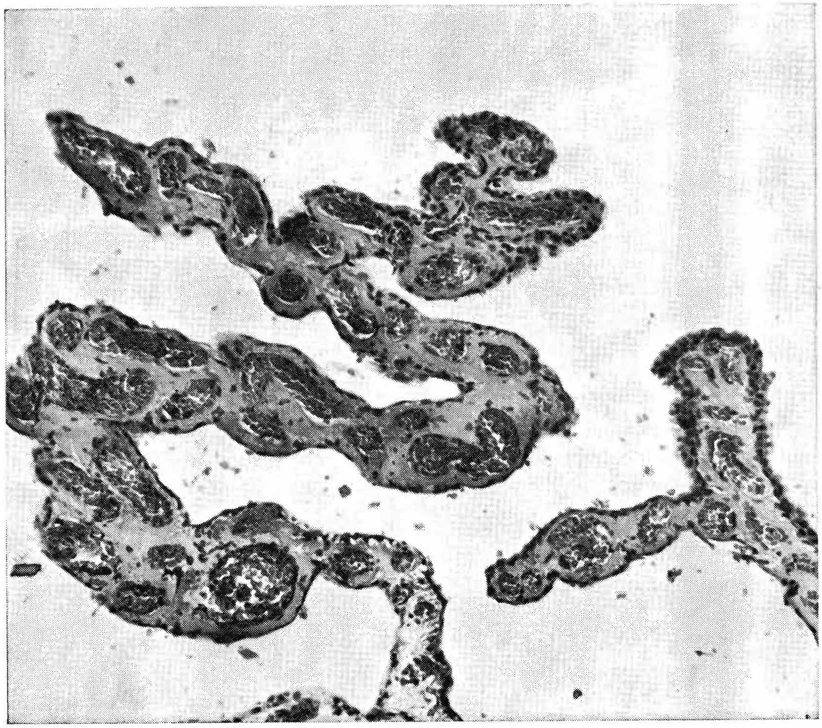

Fig. 7—Ciliary processes 12 hours after freezing showing hyperemia, hemorrhages, and endothelial changes of small vessels.

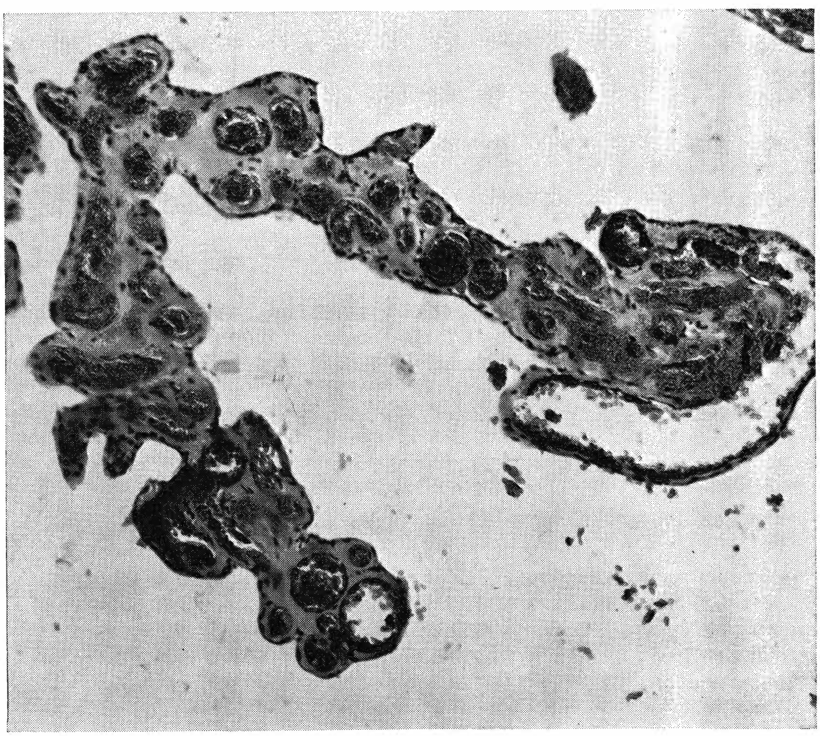

Fig 8—Intraepithelial cyst 12 hours after freezing: hyperemia and hemorrhages into stroma.

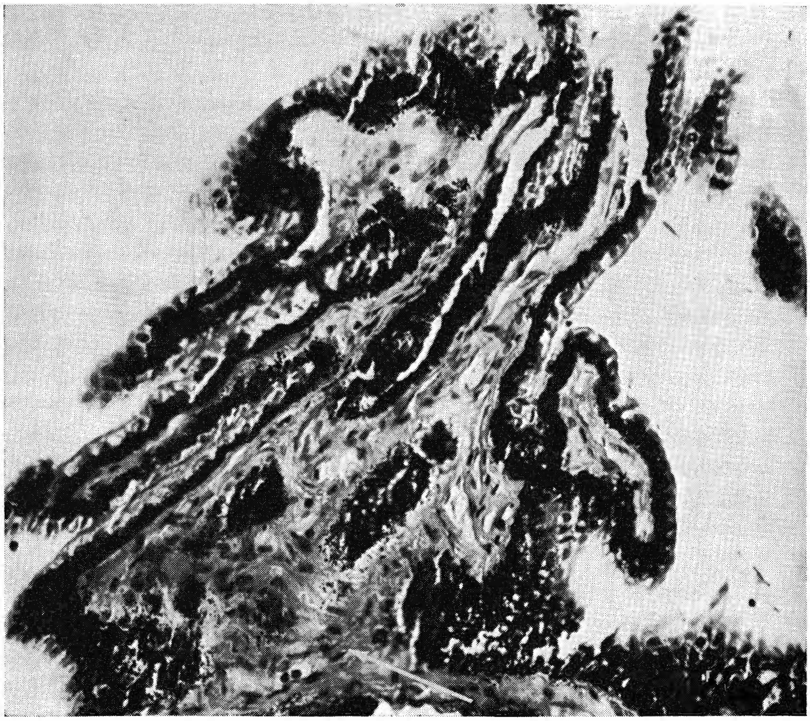

Fig. 9—Hyalinization of ciliary processes three weeks after freezing.

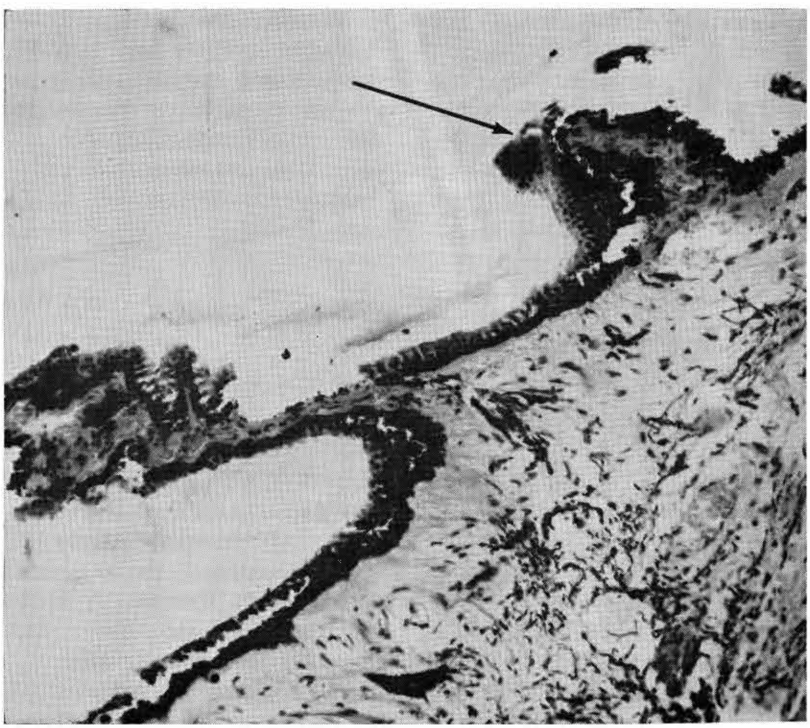

Fig. 10—Hyalinization of ciliary processes, partial atrophy, and areas of hyperplasia of pigment epithelium four weeks after freezing.

Facility of Outflow

Calculated values for C were paired like the values for F before and 12 weeks after cryocautery. No definite trend in C values could be established. C values were greater in 21 eyes at the end of observation, and less or equal in 19 eyes at the end of the observation period. C values calculated at various times of the 12-week observation period likewise showed no definitely established trend. Tonograms for individual eyes both before, in the middle, and at the end of the 12-week period will illustrate the findings discussed above (table 1). Table 2 summarizes the results of the tonographic study.

Histology

Sections of globes enucleated six to 12 hours after freezing showed swelling of the ciliary processes due to hyperemia, edema, and hemorrhages into the stroma (fig. 7). There was an apparent alteration of the endothelium of some small and medium-sized ciliary vessels. In most ciliary processes the non-pigmented epithelium was absent, except in those globes where ciliary processes continued on to the posterior surface of the iris. Such processes appeared fairly normal. Edema caused the formation of cystic spaces between the epithelial layers in some processes (fig. 8). A variable amount of pigmented epithelium was also destroyed, although in most sections some pigmented cells remained, covering the congested ciliary process. The hyperemia also involved the iris root, causing some thickening. Some edematous changes were also present in the chamber angle of most globes, but no fibrin or blood was observed in the anterior chamber.

After 48 hours most edematous changes in the ciliary processes, as well as in the chamber angle, had

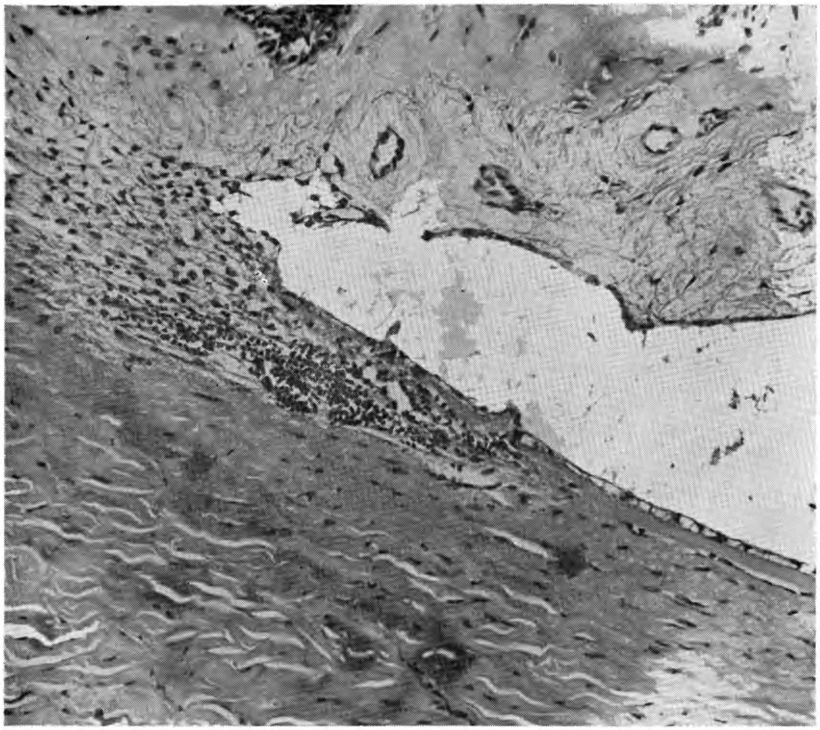

Fig. 11—Chamber angle of rabbit four weeks after freezing appears normal.

subsided. Hyperemia and hemorrhages persisted and there were seen free pigment granules in the posterior chamber surrounding the processes and an occasional fine vitreous strand, suggesting some alteration of its structure as a result of the freezing process.

In globes observed one to two weeks after freezing, the pigmented epithelium had regenerated. The only histological changes of significance were the deposition of hyaline-like substance around some blood vessels, a decrease in smaller vessels, and a general increase in the amount of connective tissue within the individual processes. These changes persisted over the observation period. After 12 weeks, in some globes there was an apparent decrease in the number of processes, and a number of ciliary processes appeared atrophic and fibrinous, but still were covered with ciliary epithelium (figs. 9 and 10). No permanent changes following this method of ciliary-body freezing were observed in either cornea, sclera, or chamber angle (fig. 11). A similar observation was made by others (Polack and de Roetth, 1964).

The histologic changes observed were in good accord with those found by Polack and de Roetth (1964) who reported edema and hemorrhages followed by hyalinization and hyperplasia of pigment epithelium and an increase in connective tissue. They also observed more severe anterior chamber reactions and alterations in the vitreous which were largely absent in our study. The fact that these authors used a freezing tip with a temperature of $-79°C$, probably accounts for the greater severity of changes, although the decrease in PO reported was less than that observed in our study. The same authors showed also that regeneration of the ciliary epithelium takes place most actively from 24 to 48 hours after freezing. They used radioautographs of the ciliary body labeled with tritiated thymidine to show the active regeneration of the ciliary epithelium at this stage of the reparative process.

Measurement of Intraocular Temperatures During Cryo-application

Some measurement of freezing temperatures at the various tissues of the globe was felt desirable to select the temperatures best suited for the desired result and, at the same time, to leave unaffected other structures of the eye, notably the chamber angle, lens, and vitreous. For these measurements HT Ultra-Miniature Thermocouple probes of copper constantan with stainless steel sheathing material for a total diameter of .008 inch are well suited. These probes feature fast, accurate temperature response, with minimal disturbance of the environment. The read-out device for these experiments consisted of a Keithley Milli-microvolt meter and a Photovolt Varicord recorder.

When the Kelman Cryostylet was operated in the manner recommended by the manufacturer for cryogenic cataract extractions, the temperature of the applicator tip was measured at $-12°C$. All measurements were taken on anesthetized rabbits with the eye in its normal position so as to not alter the physiological conditions of blood flow. The surface temperature of the sclera in the palpebral fissure area with the fissure held open was $+32.9°C$. The miniature thermo-couple probes were placed in various parts of the globe (fig. 12), and temperature measurements taken before, during, and after removal of the cold probe until tissues returned to normal temperatures. As expected, the temperature drop was fastest and most pronounced in the superficial scleral lamellae, dropping to $-9.2°$ C in this experiment. In the deep sclera the temperature was $-6.6°$ C. With the tip temperature at $-12°C$, no other freezing temperatures could be measured anywhere else in the globe. The temperature

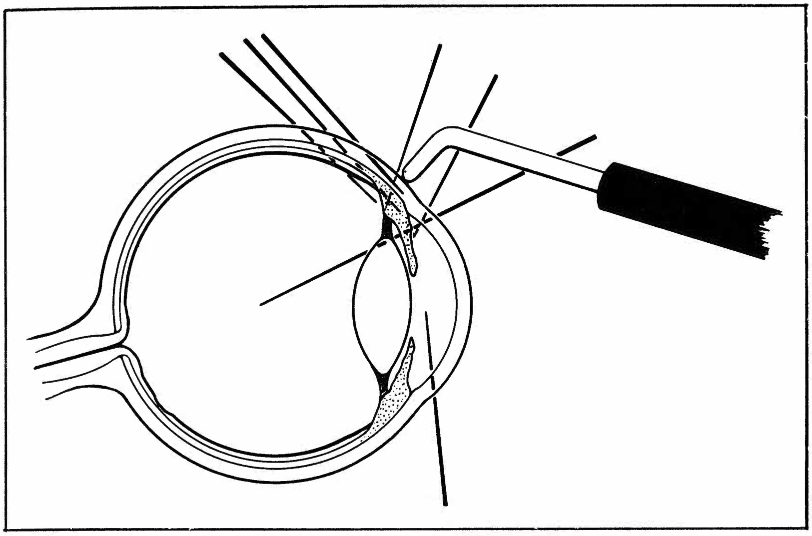

Fig. 12—Position of micro-thermocouples for intraocular temperature measurement during cyclocryocautery.

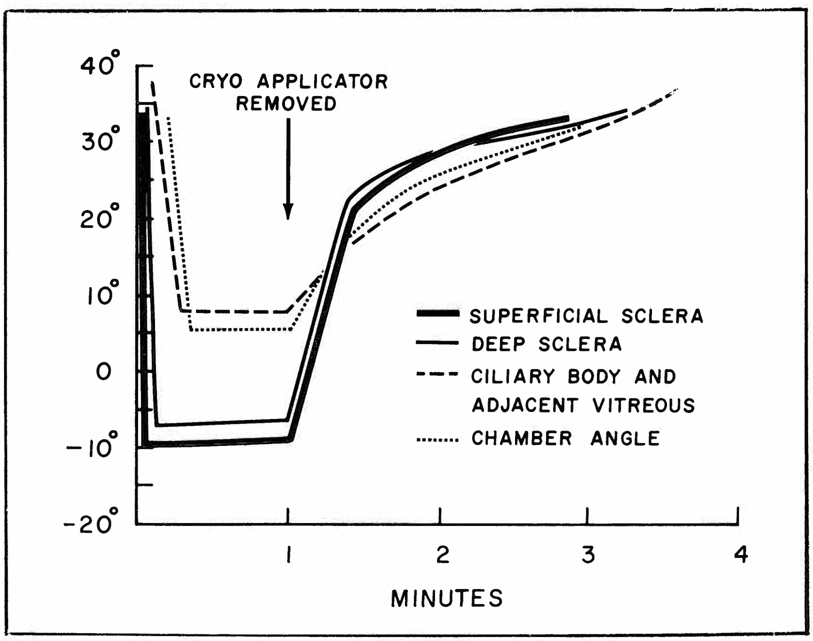

Fig. 13—Intraocular temperatures at various levels with applicator tip at temperature of −12°C.

in the ciliary body dropped more slowly to +7.9°C, and the same reading was taken in the peripheral vitreous adjacent to the ciliary body where a temperature of 38° was measured just before cryo-applications. The temperature recorded in the chamber angle was +5.3°, whereas midway between the iris and pupillary margin a temperature of +13.2° was recorded in the anterior chamber during cryo-applications. It was obvious that the temperature of the applicator tip was insufficient to bring about freezing of the ciliary body. Following removal of the probe all temperatures returned to pre-application levels within 2½ min, the sharpest rise occurring during the first 15 to 20 sec, after which a more gradual rise to normal temperatures took place. Figure 13 illustrates the temperature response of miniature thermo-couple probes at four different positions to cryo-applications over the ciliary body area with a tip temperature of −12°C.

The experiment was repeated with the temperature of the applicator tip at −40°C, a temperature found sufficient in previous animal experiments for the desired result, yet causing a minimum of undesirable side effects. During this experiment the temperature in the superficial and deep sclera dropped to −37° and −32°C, respectively, while in the ciliary body and adjacent vitreous, temperatures of −25° to −19°C were recorded. An even slight movement of the thermo-couple tip in this area during the experiment caused a change in temperature of several degrees. This was thought to be due to the varied character of the ciliary body structure containing connective and muscle tissues and a rich vascular network. In the anterior chamber angle sub-zero temperatures were recorded; however, midway between the pupillary margin and chamber angle the temperature did not fall below +5°C. Following removal of the freezing tip, all tem-

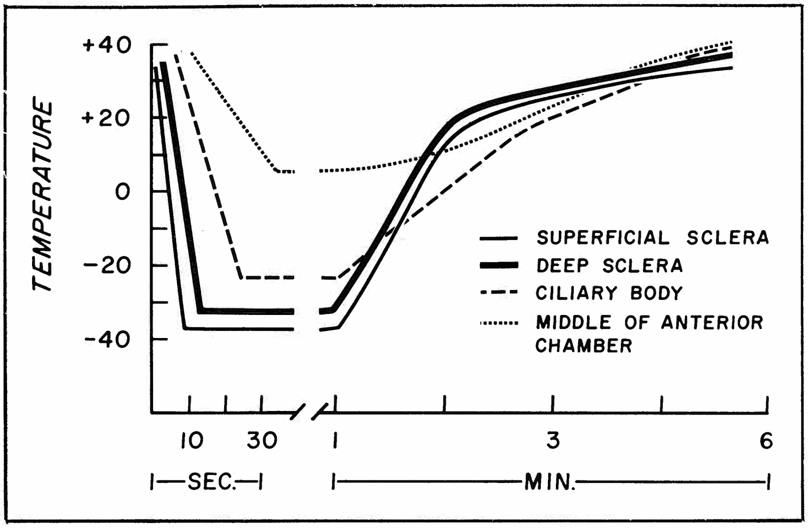

Fig. 14—Intraocular temperatures at various levels with applicator tip temperature of —40°C.

peratures rose rapidly during the first 30 sec. In this experiment it took 6 min for the temperatures to reach starting levels. Figure 14 illustrates the temperature-time relationship during cryo-application with an applicator temperature of —40°C.

Influence of Angio-cryocautery of Long Posterior Ciliary Arteries on Intraocular Pressure

As early as 1890, Wagenmann, in a treatise on the influence of retinal and choroidal circulation upon the nutrition of the eye, studied and described the effect of severing the long posterior ciliary arteries in rabbits. Since a reliable tonometer was not available at this time, his findings went largely unnoticed. In 1944, Guerry reported his findings on angiodiathermy of these vessels in a detailed study. He concluded that electrocoagulation of one long posterior ciliary artery reduced the intraocular pressure in both rabbits and humans for about two weeks and was relatively harmless. Coagulation of both long posterior ciliary arteries in the rabbits resulted in phthisis bulbi in 50% of the animals.

We have conducted a limited number of preliminary experiments to study the effect of cryocautery of one or both long posterior ciliary arteries on the tonographic tracings of rabbit eyes. A conjunctival incision was made about 5 mm from the limbus from the horizontal meridian, followed by incision of Tenon's capsule and identification of the artery after retraction of the rectus muscle with a strabismus hook. Cryo-coagulation for periods of 3 to 5 min was then carried out just anterior to the entrance of the vessel into the sclera, using a tip temperature of —40°C. Immediately following the withdrawal of the tip the surrounding sclera was white, and numerous hemorrhages appeared. In six eyes one artery was so treated. This was followed by a mean drop in intraocular pressure of 6.2 mm Hg. The flow values and C values showed inconsistent changes. Six days following treatment the mean decrease in the PO was 2.4 mm; after 12 days the pressure in all but one eye had returned to preoperative levels or slightly above. The one eye with decrease in pressure showed only a 2 mm Hg change which was thought to be insignificant. Similar results were obtained when both arteries were treated with the cryocautery. Intraocular pressure fell on the average of 5.8 mm Hg in six eyes. Flow rates increased slightly and C values were increased also. After six days the intraocular pressure change was still an average of 5.5 mm Hg lower, but at the end of two weeks the intraocular pressure of all eyes had returned to pretreatment levels. During this period slit lamp examinations revealed none of the corneal and anterior chamber reactions reported by Guerry (1944) for diathermy coagulation of these vessels. After two weeks the conjunctival and Tenon incisions were reopened, and the arteries inspected. There was no visible change in the vessel wall, and when it was severed, all vessels bled freely. It was felt that interruption of blood in large vessels by cryocautery was not practical or feasible. However, one important lesson can be learned from these experiments. The inadvertent electro-coagulation of one or both of these vessels during retinal detachment surgery is a dreaded complication, especially in cases where retinal breaks are located in the horizontal meridian.

In such cases the use of cryocautery to produce adhesive chorioretinitis as advocated by Deutschmann (1933; 1935) and presently advocated by Lincoff et al. (1964) and Kelman and Cooper (1963) will avoid this complication.

Clinical Cases

Since the animal experiments have shown cyclocryocautery to be a safe procedure and one that is effective in reducing intraocular pressure in a significant number of animals, we felt justified in using the procedure on a number of selected human cases. The following routine was followed in human cryo-coagulations. All eyes were prepared and draped, using the standard technique followed at

MCV. Ophthaine and 2% Xylocaine were used for surface anesthesia, akinesia, and retrobulbar injection. The applications were made with the Kelman reservoir temperature at −1° to −3°C, the tip temperature at approximately −40°, through the conjunctiva 3 to 5 mm posterior to the limbus, using a total of eight to 12 applications and avoiding the meridians of the recti muscles. Immediately following the procedure the only effects noted were conjunctival congestion and subconjunctival hemorrhages at the application sites.

The most recent patients were treated in the same fashion except that the Freon operated Cryosurgical unit manufactured by Frigitronics was used. Tip temperatures of −40° to −45°C were used with this instrument also.

A total of eight patients with various forms of glaucoma (secondary glaucoma due to central retinal occlusion, advanced chronic open angle glaucoma, secondary glaucoma following trauma and hyphema) were tested by the method described above. In six patients the pressure was normalized and remained normotensive in the observation period of from 3 to 10 months. In two cases the intraocular pressure rose again to pre-treatment levels after two and four weeks, respectively. Retreatment was successful in one case; in the second case of traumatic glaucoma the second procedure succeeded in lowering the pressure from pretreatment levels of about 45 mm Hg to 32 mm Hg, but could not be lowered any further.

Discussion

This study has shown that freezing of the ciliary body can reduce the intraocular pressure of experimental animals. Tonographic evidence suggests the mechanism by which this is brought about to be a reduction of aqueous production. Histologic evidence of this study and previous reports by other authors on this subject suggest a slight, but permanent, alteration in the ciliary processes as the cause of the reduced aqueous flow. It is not clear at present whether the epithelial or stromal changes in the processes are primarily responsible for the decrease in their function. Further experiments to elucidate this point are planned for the near future. Our study on intraocular temperature measurement indicated that a tip temperature of −40°C is sufficient to bring about the desired result. Experiments by other investigators with much lower temperatures have shown no enhanced effect and that their use might conceivably lead to extensive destruction of neighboring structures, especially the vitreous.

A pilot study on a limited number of animals suggests that a permanent reduction of intraocular pressure by freezing one or both long posterior ciliary arteries cannot be achieved. Histologic evidence points to the fact that only small vessels and capillaries can be permanently occluded by freezing through a process of endarteritis obliterans. While freezing of the long posterior ciliary arteries could not be recommended as a glaucoma procedure except in such cases where only a temporary reduction of pressure is desirable or as a preliminary procedure before intraocular surgery as suggested by Guerry (1944), it would seem that its use would be indicated in retinal detachment surgery, where retinal breaks are located in the horizontal meridian to obviate permanent accidental closure of these vessels by electro-diathermy.

The primary indication of cyclocryocautery in the human is in cases of hemorrhagic glaucoma where other intraocular surgery is extremely hazardous. The procedure, however, is completely free of complications and side effects and could be tried in such cases as congenital glaucoma or chronic simple glaucoma where previous filtering procedures have failed, or where extremely constricted visual fields make such operations undesirable. Cryocautery has the advantage of not altering the anatomy of the ocular structures appreciably and, therefore, not making any further procedures more difficult. Its advantage over cyclodiathermy or cycloelectrolysis seems to lie in the fact that it is extremely unlikely to result in a phthisis bulbi. Deliberate attempts to over-treat some rabbit globes have not resulted in permanent damage other than a somewhat longer lasting anterior chamber reaction than was encountered in the routine treatment cases.

Reports from other cryo-surgeons (de Roetth, 1965, unpublished data) indicate a similar experience of absence of complications. Recently, however, Harrison (1965, unpublished data) made the statement that cyclocryocautery "can be overdone," and lists complications such as massive conjunctival chemosis, posterior synechiae, complicated cataract, and iris atrophy following treatment. It is my opinion that the excessively low temperatures of −106°C, used in these experiments for long periods of time, are responsible for the undesirable side effects, and add little to the efficacy of the procedure. Permanent corneal opacities have been reported, but are extremely unlikely to occur, as at temperatures of −80°C, it requires freezing of 60% of the cornea, according to Chi (1965, unpublished data), to result in permanent damage. Similar experiments by Kaufman (Kaufman, Capella and Robbins, 1964) have demonstrated the remarkable ability of the cornea to repair damage from freezing.

While my series of patients is small, it indicates that the procedure was successful in six out of eight cases of glaucoma which would otherwise have had a very poor prognosis. The immediate rise in intraocular pressure which was observed to a marked degree in the rabbit experiments, using a ring

TABLE 3

	Preoperative		Postoperative	
	C.	F.	C.	F.
Case 1	.008	2.64	0.21	1.05
Case 3	0.22	12.32	0.33	5.94
Case 5	0.13	3.64	0.12	0.60

type applicator and to a lesser degree when the Cryostylet was used, was not observed in the human eyes. This phenomenon is probably caused by the fact that applications over the ciliary body of man were carried out 4 to 5 mm behind the limbus, thus largely avoiding even temporary occlusion of aqueous outflow channels and freezing of chamber angle structures. In those three eyes where comparative tonographic studies were possible before and after the procedure, the C values increased materially in two and remained steady in the third. In all three eyes flow rates were materially reduced also. These figures are summarized in table 3.

Summary

1. A method of cyclocryocautery, using the Kelman Cryostylet, is described. On rabbit eyes this brings about a statistically significant lowering of intraocular pressure and reduction of aqueous flow over an observation period of three months. The effects upon the facility of outflow are variable. Side effects are minimal.

2. The intraocular temperature was measured at various points during and after cryocautery. An applicator temperature of about −40° C was found sufficient for the desired result with minimal side effects.

3. Angiocryocautery of one or both long posterior ciliary vessels resulted only in a temporary reduction of intraocular pressure, as permanent obliteration of these vessels was not possible by this method.

4. In a small series of eight patients with primary and secondary glaucomas, the procedure described was effective in six cases. Possible indications in other forms of glaucoma are discussed.

Acknowledgement

I wish to acknowledge the help and guidance of Dr. DuPont Guerry, III, professor of ophthalmology at MCV, in the critical evaluation of this study and of R. C. Williams, R. S. Ruffin, and Dr. S. F. Cleary of the department of biophysics in technical problems and statistics.

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Medical Manpower: The Medical Auxiliary

Discussion based on The Assistant Medical Officer. The Training of the Medical Auxiliary in Developing Countries *by E. F. Rosinski and F. J. Spencer. University of North Carolina Press, 1965.*

Before the activation of Medicare in July 1966, there were dire predictions of overwhelming demands on hospitals and hospital staffs throughout the country. At this writing (July's end), the anticipated upsurge in hospital admissions has not materialized, although there has been a significant increase in the number of elderly patients seeking hospital care. It is not unlikely, however, that ultimately the addition of 20 million "senior citizens" to the hospitalization-covered population is bound to aggravate the present serious shortage of physicians and nurses, even to make it a critical shortage.

Concern in this regard is not new, but the problem has received little attention by either professionals or non-professionals until recently. Rutstein (1960) examined "The Crisis in American Medicine" and suggested that it might be necessary to train various paramedical people to provide services once considered in the province of the family doctor. More recently, Jones (1966) pointed out the growing need for nurse-midwives in view of mounting physician shortages and increased demands on obstetricians.

Edwin F. Rosinski, director of research in medical education, and Fredrick J. Spencer, chairman of the department of preventive medicine, at the Medical College of Virginia, have produced the first definitive study of the so-called medical assistant; *The Assistant Medical Officer* is a thoughtful, provocative study of certain aspects of this question.

The "assistant medical officer" is almost unknown in this country and only little better known in most of the Western countries. Nevertheless, he is the basic medical practitioner in many countries in the world today, and, indeed, the sole practitioner in some.

Drs. Rosinski and Spencer present much factual data based on their personal observations of five medical schools in as many developing countries in Africa and the South Pacific area, where they lived and worked with preceptors and students. This close association is reflected in the detailed description of the background of study, "pre-medical" education and "medical curriculums" in each area visited, and a great deal of space is devoted to the details of recruitment and of the actual training program. Although the education and training of the assistant medical officer is of considerable interest and importance, one wonders if too much detail has been included in presenting so fine an analysis of each course of study in each institution served. This detailed descriptive reporting, probably valuable to a student comparing the several curriculums, or to a faculty bent on establishing a new school, tends to be repetitous and somewhat confusing. A more general presentation of the composite curriculums "pre-medical" and "medical," with a comparative analysis of strengths and weaknesses, would have been more effective. However, the authors certainly succeed in meeting their stated objectives, "to survey, collect and summarize data on the training of these personnel" and "to provide guidelines through which similar training programs can be initiated, accelerated and improved."

In Chapter 7, "The Assistant Medical Officer as Practitioner," the authors succeed most admirably in their effort "to obtain information on the way graduates of these programs functioned in clinical settings." This chapter, the most significant and valuable section of the book, relates most immediately to our own manpower problems in stating what the medical auxiliary actually does in his practice—how, where, and with what supervision. Generally speaking, "the assistant medical officer practices the same type of medicine as a general practitioner in other countries," limited by the physical facilities available to him, and by the rules and statutes of his government. For the most part, the authors are favorably impressed and acknowledge that ". . . within his capabilities [the assistant medical officer] practices good general medicine" and that ". . . it is not improbable that the assistant medical officer,* in time, will become the professional equivalent of the "degree physician" in many of the developing countries, at least in the eyes of the government." Although it is not explicitly stated, the authors seem to suggest that the assistant medical officer would be a

* The assistant medical officer probably derives from the *feldcher* of Russian medicine, who has been described as the *leib-medic*—half-fledged, half-educated medical assistant—originally deputized by the government to take care of the vast hordes of farmers, who comprised most of the population of pre-war Russia (Maystrakh, 1956). In the early 19th Century, schools for *feldchers* were developed, and today in the Soviet Union there are approximately 560 "middle medical schools" with a total enrollment of approximately 220,000 where "middle level" or "pre-medical" personnel are being trained as midwives, *feldchers,* and technicians.

valuable asset to the medical personnel of any area. And while Chapters 2 and 6 focus primarily on how the assistant medical officer is selected for training and how he is actually trained, Chapter 7 describes his achievements in his practice and presents an excellent analysis of public health in each of the developing countries visited. Although the training institutions are called "medical schools," the authors emphasize that they are *not* accredited graduate medical schools, and do not give the M.D. or M.B. degrees, and that their graduates are not certified to practice outside their own country or territory.

The amount of information and material packed in this short volume is the more impressive since the authors spent only a matter of several weeks in the areas they visited. The point is well made that all these schools are located in "emerging countries," where the entire educational system is undergoing development. And in spite of too much background information concerning the system of pre-professional education which seems to be in direct contrast to our own systems of pre-medical education, it is to the authors' credit that they have presented and evaluated the assistant doctor in his own culture and have not attempted to judge him in terms of American standards. The authors admit that their report was the more difficult because "it was apparent" that more data had been collected than their most liberal expectations had predicted, and one of the book's prime weaknesses is this inclusion of far too much detail in areas where more general observations would have sufficed to make their point.

The problem of supplying personnel to fill the health needs of our own country is brought into focus by this book. There is no question that some source of additional medical and para-medical personnel must be found, in our own country, to augment and supplement the physician population. To increase the number of doctors seems hardly a solution in the foreseeable future, in spite of plans to open some 10 to 15 new medical schools within the next decade. What is needed, therefore, and soon, is a reasonable, rational, and coordinated program to train auxiliary medical personnel, at the approximate level of the assistant medical officer of Drs. Rosinski and Spencer's report. This can probably best be accomplished through the already existing facilities of the 87 American medical schools where physical plants and faculties are currently training physicians, nurses, technologists, etc. While I do not here propose any arbitrary "pre-medical" requirements for admission to these "medical auxiliary" schools, high school graduates may be generally well qualified for admission to this level of training.

None would propose that the assistant medical officer be the equal of the degree physician in his practice, but certainly the assistant medical officer is a potential junior partner in medical practice. Jones (1966) suggests that the nurse-midwives be employed to broaden the available supply of obstetrical specialists. Nurse-anesthetists are already rendering a significant service in anesthesiology in this country. There are probably many other areas where the graduate nurse can be educated and trained further to perform many diagnostic and therapeutic procedures with proper supervision. Certainly the field of public health presents a challenging area for this "spread of the doctor supply," and the public health nurse is already performing capably and with distinction in many cities and in many disciplines in this country. In the Home Care Program at the Medical College of Virginia, the public health nurse is an invaluable member of the medical team, and the addition of more public health nurses would enable this program, as well as other similar programs, to enlarge case loads without the addition of significant numbers of physician members to the home care personnel. Unfortunately, a serious nurse shortage parallels the doctor shortage, so that realistically there are simply not enough nurses to be trained as assistant medical officers!

The current problem which Drs. Rosinski and Spencer have sharply delineated, is the provision of adequate medical care for all the people not only in the developing countries, but here in our so-called "well-developed" society. With or without Medicare the health needs of 190 million Americans increase daily with woefully disproportionate growth in the medical manpower needed to meet these needs. Whatever few failings may be attributed to the *Assistant Medical Officer,* Drs. Rosinski and Spencer have contributed the first book in this vital area of medical manpower, and they are to be congratulated.

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Clinicopathological Conference:*
Painful Leg Mass in a 23-Year-Old Male

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SAUL KAY, M.D., *chairman, division of surgical pathology, Medical College of Virginia*

Clinical History

A 23-year-old Negro male truck driver was admitted to the MCV Hospitals on 1-4-66 because of "swelling" of his right leg and "pain" of recent onset. He said he had hit his right leg just below the knee in early 1962, but had had little trouble with the leg until he jumped from a moving truck in July of that year, when he noted pain and the leg became swollen. He spent 24 hours in the dispensary with the leg immobilized. X-rays were said to be negative. The patient stated that approximately a year before this admission the leg was examined, x-rays were taken, and he was told "there was nothing to worry about." The leg had gradually increased in size, but there had been only a slight amount of pain and no increased heat in the affected area. Just before admission he complained of pain and numbness over the dorsum of the right foot.

Past medical history and family history were negative. Review of systems was noncontributory.

Physical examination: Blood pressure 120/60, pulse 76/min, respiration 20 breaths/min, temperature 98.6°. The patient was a well-developed, well-nourished, young man in no acute distress. The pertinent findings were limited to the right leg where a large, firm, immovable mass was noted that extended from just below the knee to about mid-calf on the lateral aspect of the leg. The skin overlying the mass was warm and tense. There was a foot drop on the right, inability to dorsiflex the great toe, weakness of dorsiflexion of the remaining toes, and decreased sensation over the dorsum of the right foot.

Laboratory data: The urine was yellow, clear, and acid with a specific gravity of 1.021. Protein, sugar, and acetone were negative. Microscopic examination of the urine sediment was negative. Hemoglobin 12.6 g/100 ml; white cell count 6,400/mm^3 (60% neutrophils, 34% lymphocytes, 4% monocytes, and 2% eosinophils).

Anteroposterior and lateral x-rays of the right leg showed a large tumor involving the upper shaft of the fibula, and marked linear soft tissue calcification within the tumor which appeared to form septa. A chest film was negative.

The patient underwent surgery on 1-6-66.

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* Prepared and edited from transcripts by R. Page Hudson, M.D., department of pathology, John H. Moon, M.D., department of medicine, and Carole R. Nasr. Address requests for reprints to Dr. Hudson.

Clinical Discussion

Dr. Gerald A. Gildersleeve: The historical and physical findings in this 23-year-old Negro man are limited to the right leg and foot. His complaints date to two episodes of trauma in 1962, with apparently normal radiographs of the area in question in July of that year. Gradual swelling of the area, pain, and now deep peroneal nerve deficit have occurred.

Radiographs of the chest and abdomen are normal. Radiographs of the right leg are abnormal and show (fig. 1) an enormous, expansile, destructive lesion involving the proximal shaft and metaphyseal end of the fibula. The lesion is encased in periosteal new bone which is markedly folded, wrinkled, and absent in some areas, indicating varied degree of tumor aggressiveness in areas of the growth margins. The fairly abrupt distal junction of tumor with intact shaft shows a remarkable absence of sclerosis in the lateral view. Fascial planes are preserved close to the tumor indicating a lack of adjacent soft tissue response. The integrity of the knee joint is preserved. No calcification or ossification is appreciable within the matrix of the tumor, a rather important feature.

Before entering into specific diagnostic considerations, I shall make a few general comments concerning solitary tumor in bone.

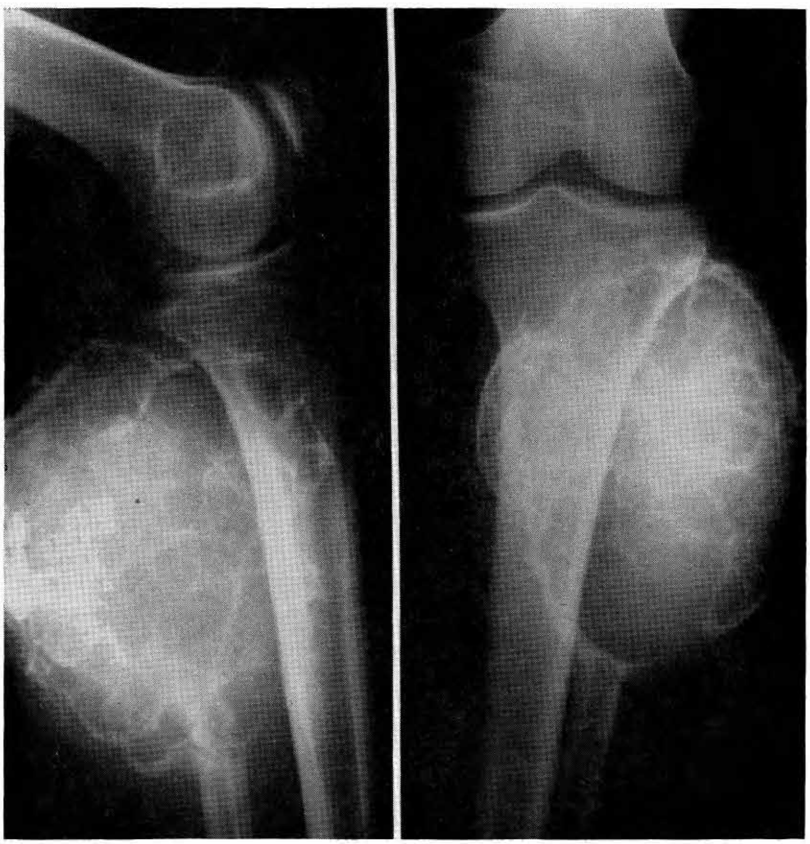

Fig. 1—Lateral and anteroposterior radiographs of the right lower leg revealed an enormous, expansile, destructive lesion involving the proximal shaft and metaphyseal end of the proximal fibula. The lesion is encased in periosteal new bone which is markedly folded, wrinkled and irregular, indicating varied degrees of tumor aggressiveness in areas of the growth margins. No calcification or ossification is seen within the matrix of the tumor.

The radiographic diagnosis of solitary bone tumors is based on a combination of findings which depend on tumor type and which may vary with response of the spongy bone, cortical bone, periosteum, and adjacent soft tissue. Some tumors produce a sufficiently consistent picture to allow accurate specific diagnosis on the basis of x-ray studies alone. Others produce varied appearances. In these the size, shape, and location of the lesion, the presence or absence of tumor matrix calcification and ossification, and the host response will limit the number of possibilities. In general, when these findings are correlated with the historical and physical findings, an accurate diagnosis should be made in at least 80% of the cases.

Metastatic lesions are more common than primary lesions of bone and, therefore, must receive consideration. Approximately 75% of metastatic lesions involve more than one area in the skeleton. They are primarily positioned in the medullary portion of marrow-containing bone (axial skeleton and proximal femur and humerus of adults), and are characterized by relative sparing of overlying cortex, lack of any degree of periosteal response, and absence of adjacent soft tissue mass. They tend to be small, about 1 to 3 cm in diameter. Though metastases from kidney and thyroid are notable exceptions, the extensive cortical destruction, large size, marked periosteal response, solitary character, and distal position of the lesion in question combined with lack of evidence of a distant primary site are all against metastatic lesions. A primary bone tumor is therefore more likely in this case.

Table 1 lists those primary bone lesions which either have no matrix calcification or ossification, or which may have no radiographically appreciable matrix calcification or ossification, and, therefore, resemble the lesion in question.

On the basis of location, size, and shape of the lesion and the age of the patient, adamantinoma, non-ossifying fibromia, chondromyxoid fibroma, chondroblastoma, and enchondroma can be eliminated.

The well-developed, folded periosteal new bone and well-defined junction of tumor and normal shaft eliminate as possibilities such highly aggressive destructive lesions as osteolytic osteosarcoma, Ewing's sarcoma, and reticulum cell sarcoma. The remaining possible primary lesions to be considered are then myeloma, fibrosarcoma, aneurysmal bone cyst, and giant cell tumor of bone.

In the excellent monograph by Dahlin and co-workers (Dahlin, Ghormley, and Pugh, 1956) in which they reviewed 2,276 cases of bone tumors, none of 140 myelomas presenting as solitary lesions occurred in the fibula. Only two occurred in the third decade of life; most were in the fifth to seventh decades.

Fibrosarcoma, a tumor of young to middle-aged adults, with a 2:1 ratio of male to female incidence, frequently involves the end of a long bone. Its usual aggressiveness does not allow the highly developed periosteal response encountered here; however, such an appearance may occur if this tumor grows slowly. It is relatively uncommon, encountered only one-third as often as giant cell tumor.

Aneurysmal bone cyst is only one-half as common as giant cell tumor. Sixty-six percent occur under age 20. The periosteal calcific shell tends to be very thin, and uniformly ballooned over the lesion. This lesion tends to show tumor matrix calcifications or ossification, which our lesion does not do.

The single remaining lesion to be considered is giant cell tumor of bone. Ninety percent of these tumors occur from age 20 on, and most between ages 20 and 35. It is classically an expansile, destructive tumor originating in the metaphyseal end of a long bone after epiphyseal closure, which respects the barrier of joint cartilage, and which elicits no sclerotic response of the adjacent spongy bone. The periosteal response is varied, depending on the rate of growth of the tumor. When various portions of the tumor grow at different rates, the periosteal new bone assumes a folded or wrinkled appearance giving a "soap bubble" appearance. No primary matrix calcification or ossification is seen on radiographs of giant cell tumors. No adjacent soft tissue inflammatory host response is elicited by giant cell tumors.

By correlation of the roentgenographic findings of size, location, shape, matrix appearance, and host response with the history and physical findings, the most likely diagnosis is giant cell tumor of bone.

Ward Diagnosis

Aneurysmal bone cyst
or ? Osteogenic sarcoma
or ? Giant cell tumor

TABLE 1
Matrix Characteristics of Some Primary Bone Tumors

No matrix calcification or ossification:

Ewings
Reticulum cell
Giant cell
Myeloma

May have no matrix calcification or ossification:

Osteolytic osteosarcoma
Enchondroma
Chondroblastoma
Chondromyxoid fibroma
Non-ossifying fibroma
Fibrosarcoma
Aneurysmal bone cyst
Adamantinoma

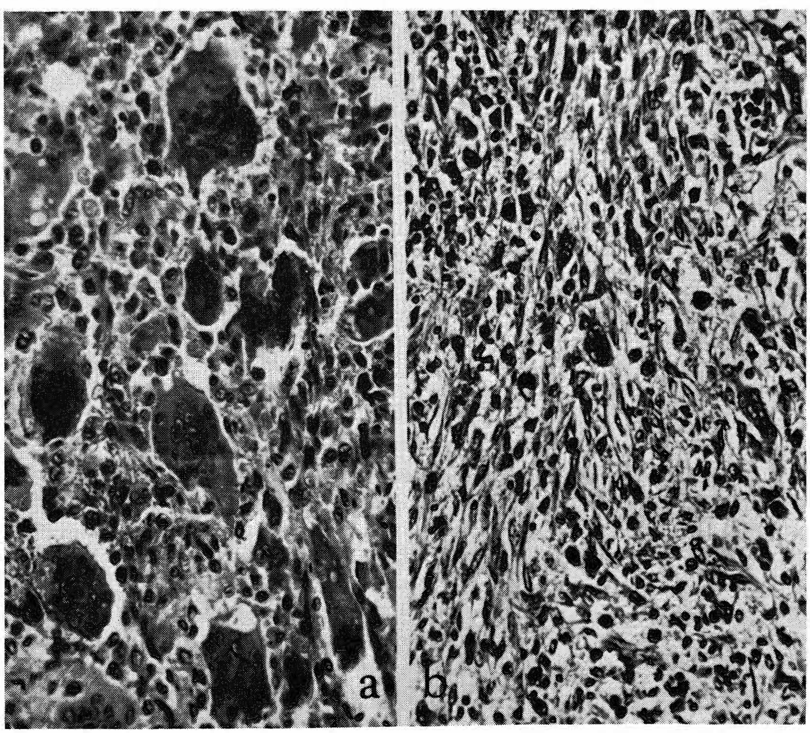

Fig. 2—Most of the tumor was composed of large, multinucleated giant cells against a background of spindly stromal cells (a). Typical giant cells were fewer, and mitoses more frequent in the more aggressive areas (b).

Dr. Gildersleeve's Diagnosis

Giant cell tumor of the fibula

Pathological Discussion

Dr. Saul Kay: The surgical specimen was received in three installments. At first we received a mass of yellowish and maroon tissue, 5 × 2.5 × 2 cm. This was sent for frozen section. Following a diagnosis of giant cell tumor, the proximal fibula was resected; this was received as a bony shell 18 × 12 × 7.5 cm covered by a small amount of muscle tissue. The bone was fractured in several places and was filled with similar soft yellowish and maroon tissue. Following confirmation of the diagnosis of giant cell tumor, the right lower extremity was amputated 17 cm above the knee six days later. The tibia showed an area of tumor invasion, 1.9 cm deep to the tibial plateau in the lateral cendyle. This area measured 2.4 × 1.3 cm, and tumor extended to the periosteal surface posteriorly.

Microscopically, the lesion was a typical giant cell tumor, described as a Grade II lesion by virtue of the presence of many plump spindle cells and occasional mitoses (fig. 2). That it was also clinically aggressive was borne out by its invasion of an adjacent bone not primarily involved and its breakthrough into the soft tissue from the fibula. Amputation was made necessary not by the type of tumor, but by the local invasiveness and destruction by this "benign" tumor.

Giant cell tumors of bone are rare lesions in a general hospital. We have had 11 examples of this tumor in the past 16 years. The most common locations were in the distal femur, proximal tibia, and distal radius. These three locations constitute about 60% to 70% of all giant cell tumors. While the tumors are most often seen in a long bone, they may rarely be found in other bones, and even in the jaw bones. Though all our cases of giant cell tumor have been in males, according to the literature (Dahlin et al., 1956; Hutter et al., 1962) there is a preponderance in the female sex.

Most of us divide the tumor into three grades. About half the cases are Grade I lesions and following conservative treatment the patients have no further difficulty. Grade II lesions constitute about one-third of the cases and are more aggressive. They are apt to recur and may ultimately become frankly malignant and metastasize. Only about 10% of the cases are frankly sarcomatous from the beginning and diagnosed as Grade III tumors. They must be dealt with by radical measures since metastasis to the lung is a real threat.

The grading of tumors is readily accomplished microscopically in most instances. Grade I lesions show closely packed giant cells containing many nuclei (up to 50!) and few stromal cells. In Grade II tumors the giant cells are less frequent and with fewer nuclei. The stromal cells are abundant, plump, with occasional mitosis. Grade III tumors are obviously sarcomatous with only scattered giant cells. The tumor cells are spindly, anaplastic and with frequent mitotic activity.

Dr. Fairfield Goodale (chairman, department of pathology, MCV): What do you consider is the relationship of this process to the so-called giant cell reparative granulomas seen fairly commonly in the jaw?

Dr. Kay: Some authors (Waldron and Shafer, 1966) consider this lesion similar to the giant cell tumor of long bones. In fact, the only difference from the clinical standpoint is that the jaw lesions occur in a younger age group. This difference may be accounted for by the fact that jaw conditions are apt to be clinically evident at an earlier stage than the long bone lesions which are generally hidden from view. The latter, therefore, are diagnosed relatively late in their course.

Pathological Diagnosis

Giant cell tumor (Grade II) of right fibula, with extension to tibia.

Addendum: Ten months after the operation, there is no evidence of recurrence of the tumor. The patient is making good progress in accommodating to his prosthetic leg.

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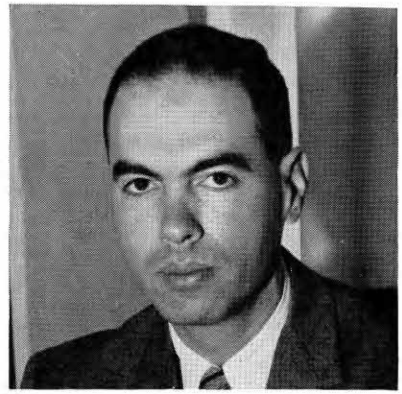
Contributors



Edward N. Brandt, Jr. (*Applications of Computers to Medicine* and *The Future Effect of the Computer and the Research Scientist on Medical Practice*) was the Stoneburner Lecturer at MCV in 1966. He received a Master's degree in mathematics from Oklahoma State University and B.S., M.D., and Ph.D. degrees from the University of Oklahoma, where he has taught in the departments of internal medicine, preventive medicine (biomathematics) and civil engineering since 1961. Dr. Brandt is director of the Computer Operations and Biostatistical Unit at the university's Medical Center and consultant for the Oklahoma Medical Research Foundation and the Upjohn Company.

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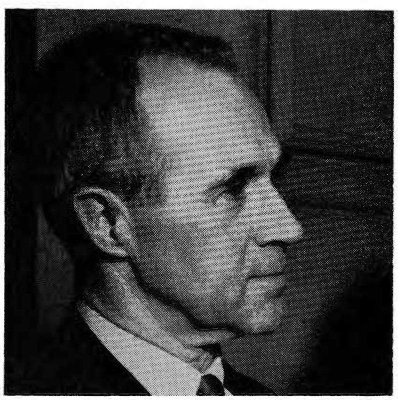

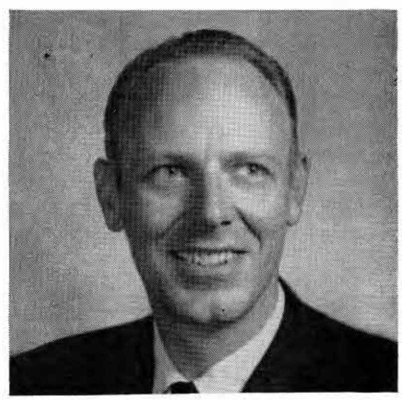

Harold I. Nemuth (*Medical Manpower: The Medical Auxiliary*), a native of Norfolk, Virginia, received his B.A. degree from Columbia University and his medical degree from MCV. He took his hosptial training in New York and Richmond, after which he served in the U. S. Navy. From 1959 through 1962, Dr. Nemuth was acting chairman of the department of preventive medicine at MCV, where he is now associate professor.

Herbert Wiesinger (*Cryocautery and Aqueous Humor Dynamics*) is a graduate of the University of Vienna Medical School, class of 1950. He took his postgraduate training at the University Eye Clinic in Vienna and the Institute of Ophthalmology, Columbia University, New York City. He has been teaching in the department of ophthalmology at MCV since 1954, having been associate professor of ophthalmology since 1958.

Volume Two
SUBJECT INDEX

Volume Two
AUTHOR INDEX

Page references to articles are in boldface, and references to photograph and biographical sketch are in roman.

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VOLUME TWO • 1966-1967

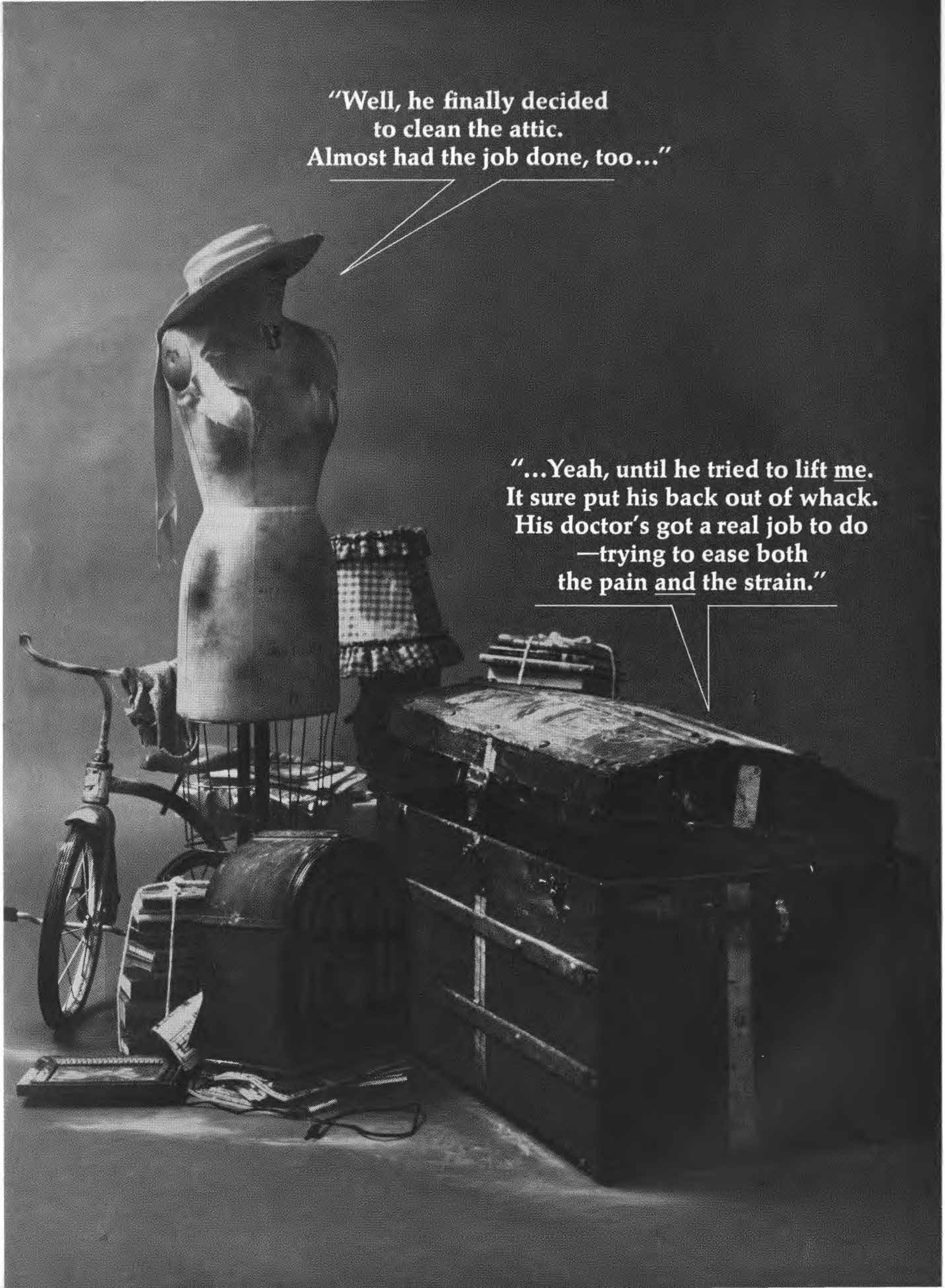
Volume Two
TABLE OF CONTENTS

SPRING 1966 • NUMBER ONE

Symposium on Diabetes Mellitus: The 37th Annual McGuire Lecture Series

SUMMER 1966 • NUMBER TWO

Papers Honoring Dr. Ernst Fischer on the Occasion of His Retirement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