

## CLINICAL RESEARCH IN ANESTHESIOLOGY \*

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Received for publication July 16, 1949

UNTIL comparatively recent years, advances in the field of anesthesiology did not keep pace with those in most other specialties. This may be explained in part by the fact that there were only a few anesthetic agents and the equipment to administer them was most inadequate. But more important than this was the lack of interest by the medical profession in general as to the importance of a well-chosen and skillfully administered anesthetic to the welfare of the surgical patient. It would seem that the main idea was to render the patient oblivious to pain and provide enough relaxation to satisfy the surgeon. Little thought was given to the physiologic disturbance occasioned by the anesthetic agent.

Broadly speaking, all anesthetic agents are protoplasmic poisons. The poison in effect is enhanced when an anesthetic agent is given in excess, when it is incorrectly administered, when an agent is given which accentuates the effects of pathologic processes already existing, and when the vital functions of respiration, oxygenation and circulation are not adequately managed. Conversely, these untoward effects in the anesthetized patient may be largely eliminated by choosing the most suitable anesthetic agent and method for a particular patient and administering it correctly and skillfully with due regard to its effects on normal physiologic activity and physiopathologic process.

Through research in anesthesia and its related sciences during the past three decades, an approach to anesthetic problems, heretofore undreamed of, has been made. This progress seems to gain momentum as time goes on, and many new and interesting fields of investigation are being opened.

The impetus for this investigative progress in anesthesiology has not arisen within the specialty only. We, as anesthesiologists, have been most fortunate that specialists in all fields of the basic sciences have taken an interest in anesthetic research. The contributions made in the field of anesthesiology have been legion, and we owe much to the physiologists, pharmacologists, biochemists and biophysicists as well

\* Read as part of a symposium on "Research in Anesthesiology" at a Joint meeting of the American Society of Anesthesiologists and the Philadelphia Society of Anesthesiologists, October 9, 1949, Philadelphia, Pennsylvania.

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as to those men in various phases of engineering who have helped us so much with our many technical problems. Particularly during more recent years, the use of complicated electric equipment has increased. By means of equipment of this type, it has been possible to obtain controlled information, the accuracy of which could not be approached with older types of apparatus. As a result, this trend toward more accurate investigative work in anesthesiology has not only played an important role in the advancement of the specialty but the results have been reflected in many other fields of medicine and surgery. It is now well recognized that problems in surgery and problems in anesthesia are essentially inseparable, and if a patient is to receive the maximal benefit from the operation and the anesthesia, each must be carefully integrated and correlated.

Perhaps the greatest benefit of this renaissance in anesthetic research has accrued to the anesthesiologist himself, and is reflected in the caliber of the specialist in anesthesia who is now being turned out from various centers for training in anesthesiology. In the physiology and pharmacology laboratories of our medical schools, the student is now exposed to laboratory research bearing on many phases of anesthesia and related subjects. During his internship, he may have an opportunity to witness problems in clinical research by the anesthesia staff of the hospital. Later, when he chooses a training center in anesthesiology, he should have the opportunity to participate in both experimental and clinical research, and he also may have the opportunity to conduct a research problem of his own. This type of modern training in anesthesiology has raised the anesthesiologist from the role of a skilled technician and has made him a scientist in his own right. As such, he does not have to guess about his patient's condition when untoward reactions occur. With a thorough background in physiology, pharmacology and the other basic sciences, he is able to distinguish between the normal and the abnormal; he can give reasons for his opinions and can institute rational treatment promptly.

When the fully trained anesthesiologist goes out into practice he may have an opportunity to continue experimental investigative work along with his practice, but what of the man who goes out into the private practice of anesthesiology as many men are doing today? Should he feel that he is through with the scientific side of anesthesia and settle down to the technical rounds of administering his daily anesthetics? What if anything can this man contribute to his specialty?

Most of us working in the field of anesthesia have had, at one time or another, a yen to produce something, but we often feel hampered or frustrated by limitations of certain types of anesthetic practice.

The part-time anesthetist often feels that any type of research is beyond his sphere. The full-time anesthetist in private practice may feel he is either too busy or lacks the facilities to conduct investigative work. Even the man in hospital practice, clinics or teaching institu-

tions may be content to leave research to his laboratory confreres who have the time, educational background and physical setup for doing such work.

The point I wish to emphasize is that every anesthesiologist can or should be a research worker to a greater or lesser degree. In the first place there are two main types of research—experimental and clinical—and all anesthesiologists can carry out a certain amount of investigative work along one of these lines. In the field of clinical research, we all have a common ground regardless of the type and nature of our anesthetic practices.

All types of research must of necessity have certain common denominators since they must be interrelated at many points. On the other hand, the field of clinical research is a different world from that of the experimental laboratory and, while the fundamental aims are the same, the approach varies. In the experimental laboratory, a proposed problem may be planned well in advance and down to the last detail, unhampered by the many variables that can occur when one is dealing with human beings. In the operating room or the hospital ward, the convenience of the patient must come first, as well as the convenience of the surgeon or clinician on whose service the patient is. One must also enlist the patient's cooperation and frequently must wait for the patients who are suitable for the proposed study.

We often are inclined to think that because we do not have the facilities for controlled experimental research in our institution we are in no position to conduct research of any kind. We tend to overlook the possibilities on the clinical side that are staring us in the face and waiting to be explored. A well-illustrated example of what I mean may be a story told by Dr. Alan Gregg (1) of the Rockefeller Foundation in his book, "The Furtherance of Medical Research." It goes as follows: "I think of a day on the boat returning from China when one of our fellow passengers lost his wrist watch. Of course, he looked for it, as he said 'Everywhere,' but later the number one boy set his relatives to work on a 'Re-search' whose essence was method and thoroughness. Not only did this procedure return the wrist watch but it discovered a necklace, two gold rings and a stickpin."

Much scientific information may be obtained from the clinical patient by persistent and meticulous observation combined with accurate recording of the clinical observations. This can be accomplished without doing anything detrimental to the patient in any way.

I should like to digress for a moment to consider briefly the prerequisites of the research worker, since it has frequently been stated that the type of man is often more important than the research problem. In the first place, the main prerequisite of the successful research worker, whether he be devoted to the experimental or to the clinical side, is curiosity. This curiosity refuses to accept verbal explanations and unverified conclusions.

Code (2) has stated that there is something childlike in this persistent curiosity. Somewhere along the path of our formal education, most of us lose this all-important quality, probably during the course of the acquisition of great quantities of information that we accept as fact. This fundamental curiosity may be reborn at any age, even if it has been lost, provided the proper stimulus is applied and provided the delay has not been so prolonged that hardening of the arteries has placed anatomic restrictions on cerebral function! In addition to curiosity, the research worker must have the intellectual capacity and judgment to make possible the asking of significant questions. He must also have a thorough insight into what the answers to those questions should elicit, and he must be able to judge whether the answer, when obtained, will be of trivial or of fundamental consequence.

Another attribute that a clinical research worker must have is the desire to overcome the inertia that so frequently besets many of us. Most of us are inherently lazy and feel that, having successfully conducted the clinical anesthetic chores of a long surgical list, we have fulfilled our duties and deserve a well-earned rest. We all recognize the fact that a busy clinical anesthesiologist, with his variety of duties, often does not have the time or energy to make detailed clinical investigations. Nevertheless, we can find time for a certain amount of such work, and it is our duty to see that those working under us are provided with sufficient stimuli toward clinical investigation.

Honesty is another essential attribute. Code said that "When a man can appraise his own investigations in their true light and seeing them as they really are, can call them worthless, if they are worthless, then and then only may he be correctly placed among the great research workers."

The ideal physical setup for investigative work in anesthesiology is not common. How fortunate is the clinical anesthesiologist who, having had some experimental background, finds himself with the time, opportunity and physical setup which permits him to investigate his ideas in the laboratory and then personally to prove or disprove his findings in the operating room!

In the operating room, clinical research in anesthesia must necessarily be confined to patients who are destined to undergo anesthesia for surgical procedures. This often eliminates that group of investigations in which professional subjects are used. However, medical volunteers for investigative work are often available in various medical centers and hospitals.

For this reason clinical research in anesthesia must be conducted or, at the very least, supervised by clinical anesthesiologists, men who are primarily concerned with the clinical side of anesthesia and who are doing the work as a service to surgery. Now, as one considers these limitations as defining the field of clinical research, it must follow that the scope of clinical research is limited to conform with this field. If

the type of problem that we wish to study involves measures which would injure the patient or cause him unnecessary discomfort, then this investigation is not suitable for purely clinical research.

As an example, if we wished to study the effects of various anesthetic agents on the histopathologic structure of the liver, such a problem would hardly fall within the realm of clinical research because we should have to make sections of every patient's liver, a procedure which, obviously, would not be justified. Many of the pathologic aspects of anesthesia are immediately rendered impossible to approach through clinical research for this reason.

Certain aspects of physiology are difficult to investigate on a purely clinical basis because of the fact that adequate controls are impossible without subjecting the patient to added risks. However, a hopeful sign is the fact that many of these restrictions in clinical research are being relieved with the advent of new methods which allow the obtaining of controlled information without risk to the patient.

As an example, I might cite the work of Faulconer (3) at the Mayo Clinic, where he is currently engaged in the simultaneous recording of the respiratory rate and amplitude taken from the mask pressure, instantaneous recording of heart rate, electrocardiograms, electroencephalograms, electromyograms, the percentage of anesthetic gases and vapors, and the percentage of oxygen saturation of the arterial blood in surgical cases. All this information may be obtained without risk or injury of any kind to the patient.

We no longer need to do arterial punctures to determine the oxygen saturation of arterial blood because we are able to get the same information from a photo-electric cell and an earpiece which does not harm the patient in any way. We shortly hope to be able to determine the patient's blood pressure continuously by a photo-electric method which does not harm the patient.

I cite these things only as an example of how the adaptation of some of the newer physical methods for measurement to our needs in research greatly increases the scope of the information that we can obtain in the operating room from the intact human being.

While I am not attempting to minimize in any way the importance of information gained in the animal laboratory, where controls may be set up almost at will, it remains a fact that the *modus operandi* of the human being is usually not found in members of another species. We must and eventually will carry the information derived from animal study over into the operating room and finally confirm or disprove our conclusions by means of clinical research. Until this change in obtaining research information has been made, the complete story has not been told.

Probably it is wise to consider that research should be divided into two general groups, one of which is not applicable in the operating room and the other of which is applicable. Investigations into the

fundamentals of pathology, physiology and pharmacology must necessarily be done in the animal laboratory. These fundamental facts require strict control impossible to achieve in the operating room by the clinical research worker.

For example, suppose some new gas is discovered which has great potentialities as an anesthetic agent. It would be extremely unwise to administer it to our first patient in the operating room tomorrow morning to see how it works. We should be justified in beginning our clinical research with this agent only after an exhaustive study of all its effects in the animal laboratory, with the help of the physicist, the chemist, the pharmacologist and the many technicians to be found in such a laboratory. Once these data have been gathered, it would be equally wrong to publish a paper on the application of this agent in producing anesthesia in human beings until exhaustive clinical research had been done to show that the agent is advantageous in treating the human patient.

Another approach that may be made to the scope and field of clinical research is through the fact that statistical studies and accurate statistical records will go far toward supplanting the lack of control inherent in clinical research. I think the clinical research worker should have a good working knowledge of statistical methods. If we make a practice to keep detailed and accurate preoperative, operative and postoperative records, and to utilize the material available to us on these records, all of us should be in a position to contribute something to the field of clinical research from time to time.

As an example, let us suppose that we are investigating the effect of nutrition on a certain anesthetic agent as applied to rats. Our control in the laboratory, by being able to get a group of rats of exactly the same weight, size, sex and hereditary background, eliminates the necessity for having a great number of such animals before we arrive at a conclusion. In the operating room we have no such control. We have to take our patients as they come. They will be of various ages, sex, and hereditary backgrounds, and of various nutritional states; therefore, we must get greater numbers of patients and make accurate statistical studies before we can arrive at conclusions with the same certainty that the worker with rats may have arrived at his conclusions.

Many of us have a wealth of statistical material waiting to be explored, and some of us have failed to take proper advantage of the material available. If the data gathered at the operating table and at the hospital bed have been carefully observed, recorded and catalogued, then one can sit down at leisure and unfold much interesting and useful information.

An advance in clinical research in anesthesiology need not necessarily be revolutionary or startling in order to constitute a valuable contribution. The unfolding of one small, seemingly insignificant fact,

or the evolution of a piece of equipment or even a negative finding may be the keystone about which some really valuable contribution can be made.

Interest in clinical research in anesthesiology in any institution has more far-reaching effects than the mere evolution of scientific data and the experience derived by the investigator. For one thing, it is bound to stimulate the interest of surgeons and other specialists in the importance of a well-organized anesthesia department. It will help to demonstrate to them how research in anesthesia may be applied to some of their own problems. Furthermore, the interest thus engendered is one other means of advancing the importance of anesthesiology as a specialty to the high plane where it rightfully belongs. So in conclusion, the point I have been trying to make is that each time an anesthesiologist goes to the hospital to administer an anesthetic agent he is approaching a potential problem with possibilities for clinical research. The same applies to data accumulated on preoperative and postoperative rounds. With this approach in mind he will find innumerable little points worthy of recording that were not apparent before.

The pursuit of such an attitude will cost the anesthesiologist something in time and energy but at the same time it will improve his status as an anesthesiologist, and although he may administer only a few anesthetics a year it may well lead to some useful contribution to the specialty.

#### REFERENCES

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