RESEARCH AND ITS RELATIONSHIP TO CLINICAL ANESTHESIOLOGY •

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During the past decade medical research has attracted more workers, cost more money, aroused more interest and led to the publication of more articles than at any other time in its history. It is not my purpose to determine the value of this expansion but rather to analyze it from the standpoint of its effect on anesthesiology as a specialty.

Such an analysis may logically begin by emphasizing certain changes which have occurred in the field of research.

The first change is essentially a shift from the study of animals to the use of man as the experimental subject. It is axiomatic that a laboratory worker must warn against the hazards of transferring directly to man measurements obtained on animals. Species difference has been an obstacle which has had to be faced by every investigator studying the guinea pig, mouse, cat or dog. The first step in correcting this objection to animal experimentation was the use of monkeys as the experimental animal with the hope that these measurements would more closely represent those found in man. A second and more satisfactory solution to the problem was to use man himself as the experimental subject.

This shift in emphasis towards clinical investigation has been made possible in part because of the development of new instruments and new techniques for recording experimental data. The advances of the past decade have not been made because there are men with greater intelligence or greater imagination, but because these men have better "tools" with which to work. Some of these new methods which enable one to analyze normality or abnormality in the human being will be described. The discussion will be limited to investigations of the circulatory and respiratory systems, since these are of great interest to the anesthesiologist.

For the investigator of the human circulation there are methods available which measure cardiac output, direct arterial and venous


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pressures and pressure pulse waves, and blood flow in a variety of tissues and organs. Although less reliable, there are also methods for the estimation of blood volume.

Cardiac output can be determined in man by the direct Fick principle. There are two objections to this approach. First, the method demands samples of blood from the right heart and at the present time the only method of obtaining such samples is the introduction of a catheter into the cardiac chamber. In the second place, a single determination requires the collection of expired air for not less than one and a half to two minutes. The resultant cardiac output is an average for that period of time and hence rapid changes in output cannot be determined. A second method of estimating cardiac output is the ballistocardiograph (1). This apparatus essentially measures the amount of blood ejected at each cardiac contraction and permits, therefore, an analysis of instantaneous changes in the stroke volume of the heart. The ballistocardiograph may be made in the form of a table and as such may be used in the operating room if study of the cardiovascular system is contemplated during anesthesia and operation. The table can also be tilted so that cardiac output can be recorded with the head up or down. The instrument is most accurate in the normal subject and has the limitation that unless its findings in a specific condition have been correlated with more direct measurements of cardiac output in the same condition one cannot predict its accuracy. In shock, for example, the ballistocardiograph may be unreliable.

Quantitative measurements of blood flow in man are now possible, using one of four technics: the clearance of radioactive sodium, the speed of up-take from the blood stream of an inert gas such as krypton or nitrous oxide, the introduction of catheters into the venous outflow of an organ or, finally, the application of a plethysmograph. These methods have supplied the investigator with quantitative data on such fundamentals as the blood flow through the brain, the coronary circulation, the kidney, liver, skin and muscles. Studies of these circulatory beds have been made in normal and diseased subjects.

The most recent method for studying the circulation is the method described by Peterson and co-workers for measuring continuously direct arterial pressure and pressure pulse contours in man (2). This method provides a beat-to-beat analysis of the circulation from the standpoint of stroke volume and total peripheral resistance. It has several advantages over methods previously in use. It eliminates photographic recording, it avoids the maintenance of a rigid needle in an artery and it permits relative mobility of the subject.

Using the technics just described, a clinical investigator can obtain information of great value to the anesthesiologist. For example, he can study the circulatory changes associated with spinal anesthesia. He can analyze circulatory abnormalities related to posture, to the
surgical manipulation of viscera, the application of positive pressures in the respiratory tract and the use of various drugs. Results of such studies will inevitably make the practice of anesthesiology safer, more rational and more accurate.

It is encouraging to report that at the present time there are many excellent men actively engaged in defining normal lung function and quantitatively measuring the degree of abnormality associated with disease.

Reasonably accurate estimations of the saturation of hemoglobin in the arterial blood can be made continuously with the oximeter. Wood, of the Mayo Foundation, has made a significant contribution to anesthesiology in perfecting this apparatus (3). There will soon be available more precise methods for measuring arterial oxygen tension in the blood directly. Davies and Brink have described an electrode which can record oxygen tension when placed directly into tissues (4). Scholander and co-workers have perfected micro methods for the analysis of carbon dioxide and oxygen (5, 6, 7). The small amounts of blood required for these technics suggest a re-evaluation of the gaseous disturbances in asphyxia neonatorum, since they obviate the risk to the newborn associated with the withdrawal of comparatively large volumes of blood.

The evenness of gas mixing in the alveoli has been measured. Although the rate and depth of breathing and the lung volume may be normal, ventilation is not efficient until there is even distribution of air to the alveoli through which blood is circulating. The nitrogen analyzer of Lilly and Hervey permits an estimation of the uniformity of alveolar ventilation in a fraction of a minute (8, 9). The diffusion of gases across the alveolar-capillary membrane can now be studied more accurately. Pulmonary blood flow can be measured. Finally, not only can one study the lung as a whole but, with the technic of bronchospirometry, one can estimate the contribution which each lung is making to the total. This may be of assistance to the anesthetist and the thoracic surgeon attempting to decide whether a particular patient has sufficient pulmonary reserve to withstand pneumonectomy or lobectomy.

Having obtained data directly from human beings the investigator has been drawn closer to the clinician and has begun to share the latter's problems. In the Hospital of the University of Pennsylvania, for example, there is a staff appointment termed "clinical physiologist." Individuals so designated make ward rounds, study patients, record their findings on the hospital records as part of the patient's work-up and act as consultants to the physicians in charge. In addition, the descriptive type of conference, called the clinicopathological conference, has been augmented by a more dynamic discussion group termed the "Clinicophysiological Conference." In this latter meeting, biochemists, physiologists, pharmacologists, bacteriologists and others
directly associated with the preclinical sciences join with clinicians in a common discussion of a patient’s problems as they are presented in the hospital wards. Both groups benefit by this association. The fundamental research worker is made immediately aware of the gaps in knowledge which exist in clinical medicine. The clinician no longer has to wait for years before he can apply in his practice the newer knowledge arising from the work of his basic science colleagues.

Anesthesiology is in a particularly strong position from the standpoint of bridging the gap between fundamental research and clinical practice. It has been a source of pride that our own department of anesthesiology was asked to found the Clinicophysio logic Conference and to effect a union of practitioner and research worker. Such a request was naturally the outcome of the direction which has been taken by the specialty of anesthesiology, which combines a dependence upon the sciences of physiology, pharmacology, chemistry and physics with clinical skill and acumen. Do not underestimate your own ability to make such contributions. It is a challenging and stimulating experience and one which will go far towards establishing the specialty high in the ranks of the medical sciences.

Certain other trends in research are also apparent. It is becoming evident that an individual working in the fundamental sciences must have a broader training than is offered by the average premedical and medical school curricula. Depending upon his field of research he should have knowledge of electronics, physics, mathematics or chemistry, to mention but a few. This realization of the breadth of knowledge required for the execution or supervision of research work has led to the appointment of individuals so trained as integral members of departments of anesthesiology. It is our aim to establish the position of Professor of Research Anesthesiology, and to have in this position a man with a broad background in the fundamental sciences. It is no longer possible for one person to be in charge of clinical anesthesia, the teaching of students, interns and residents, to be the administrator of a department and finally, to assume direction of a research program. The hours in the day are not sufficient nor are the abilities of a single person great enough to encompass satisfactorily all of these fields of responsibilities.

It has also become evident in recent years that physicians making reports of their clinical experiences have begun to recognize the need for more accurate records, more careful follow-up and a statistical approach to their data. The medical literature of fifteen years ago contains many examples of clinical reports attempting to prove that the result of one type of therapy was superior to another, the conclusion usually being based on the percentage difference between two series of cases. Statistical analysis of the data proved that such a conclusion was justified in certain instances, but too frequently an examination of the reported material failed to reveal a statistical sig-
nificance to support the clinicians' thesis. A great deal of progress has been made in correcting this fault during the last few years.

I should like to make certain predictions as to the direction which research in anesthesiology is likely to take during the next ten years. At the University of Pennsylvania and at the Mayo Clinic a start has been made for recording continuously and simultaneously a variety of observations on the circulation and respiration during anesthesia and operation. Direct recording of blood pressure has replaced the much less accurate sphygmomanometer. The clinical diagnosis of suboxegenation has been replaced by direct readings obtained from a photoelectric oximeter. Determinations of cardiac output are being made with the ballistocardiograph as an operating table. Skin resistance and skin and muscle temperature readings give indications of the level of sympathetic block associated with spinal anesthesia. Respiratory minute volume is being recorded, as is the velocity of inpired and expired air. The degree of pressure exerted in the respiratory passages is being measured with less distortion than formerly.

These and other measurements involve expensive, complicated equipment. They demand the presence of a number of trained scientists and technicians. They require the interest and cooperation of the surgeon and often of the patient. The results, however, are worth the time, effort and expense involved. Facts soon replace impressions and the over-all result of the simultaneous use of a variety of procedures is a far better integration of these facts than is possible from employing the same methods singly in a succession of human subjects. I believe that this group approach to the patient will be the approach of the future. With each investigator bringing to a project his own particular skills and knowledge the combined effort cannot help but be more productive.

What remains to be learned in anesthesiology? A great deal. We have few facts either related to clinical practice or to more fundamental questions. For example, there is little significant information on such a common-place problem as the incidence of nausea and vomiting following administration of a particular anesthetic agent. Such data may not be easy to obtain because of the large number of factors entering into the production of nausea and vomiting but we must have the information and I feel confident that it can be gathered. Far at the other end of the scale is the problem of narcosis itself. What is the mechanism of the narcotic process? This is as fundamental as life itself, and has so far resisted analysis. The ultimate solution of this problem probably lies in the far distant future, but the pure scientist in the field of neurophysiology, cellular metabolism and physiologic chemistry is making important contributions to our understanding.

What should be done about the relationship between our specialty and the fundamental sciences? I would like to suggest several steps
1. Meetings of anesthesiologists should be addressed by scientists interested in and able to interpret significant developments in their own special fields. Such men should be encouraged to prepare articles on such material for publication in the clinical journals.

2. We, as clinicians, must continue to view our daily work critically. There are many problems in the practice of anesthesia which demand attention. For example, what is the basis for emergence excitement; why is there more oozing during one type of anesthesia than another; how can one anticipate circulatory inadequacy before it assumes serious proportions; what are the hazards of “controlled respiration”; why is the diaphragm more resistant to depression than are the lower intercostal muscles? These and countless other questions are raised by the clinical anesthetist. He must not be content merely to muse about their meaning, but must actively attempt to interest his preclinical associates in their solution.

3. Talented young men and women in the specialty of anesthesiology must be encouraged and supported if their inclinations are toward investigation. Provision must be made for these individuals to become associated with established research units so that proper habits may be formed at the start. Once trained, these young scientists will require budgets, laboratories and time free from clinical responsibilities.

Anesthesiology is beginning to mature. We have reached the time for taking stock of past accomplishments, present practices and future aims. Research must never take precedence over patient care or teaching, but research is essential for a rounded program. The extent and nature of its role and some of the problems involved have been considered. They must receive attention if the specialty is to advance most effectively and most productively.

REFERENCES