the end that we will attract to our profession men interested in practicing the applied pharmacology of anesthesia.

There are other aspects which merit our attention. Not long ago in an address at the seventy-second annual meeting of the Association of American Medical Colleges, Dr. George E. Miller, the Director of Research in Medical Education at the University of Illinois College of Medicine, pleaded that medical educators should take a new look at their preconceived notions of time to be spent in preparation for a specialty. Attention should be directed at learning rather than teaching. The American Board of Anesthesiology has done some intensive soul searching in trying to equate their certification procedures with the evidence that the candidate has learned. We need to evolve methods by which we can measure the more complex cognitive levels to determine what the physician retains permanently.

What should be the role of the Board Certificate in hospital appointments and promotions? Queries by hospitals and complaints by Society members directed to our Executive Office indicate that, on occasions, certification has been used, or misused, in connection with staff appointments. There should be definition by the Boards to place their certification in clear perspective. Possibly we should evaluate knowledge acquired by means other than solely by academic bookkeeping.

We need to re-examine our American College in this connection. Inasmuch as there is an American Board of Anesthesiology, the sphere of the American College should be different and should not require a repetitive certifying procedure. To my knowledge no other specialty has dual certification.

We should intensify the use of the advice of the Council on Medical Education and Hospitals of the American Medical Association and the Residency Review Committee. We should encourage closer connections between organizations such as the American Board of Anesthesiology, the Association of University Anesthetists, the Academy of Anesthesiology, the International Research Society and the World Federation of Societies of Anaesthesiologists. We have the opportunity to lead the way for other specialties to adopt the same methods of close coordination in their groups which may in the future extend to a closer coordination between all specialties.

This is the time for our Society to establish a study to explore the future course of our specialty. To this end, I will propose that the Society underwrite a three year study; that a full-time director and field staff be appointed. This study would gather and correlate all available information in the areas of practice, teaching and research. It would make appropriate recommendations for necessary changes. Let us set our sights high, so that we may develop better teachers, spur broader investigation, and attract the best qualified physicians into our specialty. The coalescence of these functions will surely improve the quality of care and ensure the safety of the patients entrusted to us.

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The Design of Experiments Evaluating Analgesics

MANY physicians participate in clinical studies evaluating analgesic drugs. Frequently the published reports of these investigations are contradictory. The most important cause of confusion is failure of the investigators and of the readers to appreciate the importance of differences in experimental design. In any study of analgesics, methodology is of paramount importance.

Subjects for Analgesic Tests. The use of pathological pain seems superior to experimental pain for testing purposes. In humans pain threshold determinations are altered by distraction (lack of attention), fatigue, and other factors. The subjects which are suitable may be categorized on the basis of the expected duration of pain as follows: (1) patients with chronic painful diseases and (2) patients with acute painful conditions.

The Cross-Over Method. The cross-over

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method may be of value in investigations involving patients with chronic or static pain. In these studies each medication is administered to every patient. Thus, each patient serves as his own control. The differences between or among medications, therefore, may be determined within each of the patients.

When the subjects available for study are expected to have pain of short duration, the cross-over method may not be feasible. Then, different groups of patients are required in order to determine differences among medications. Dissimilarity among the patients assigned to the groups may influence the outcome of these experiments. This bias may be avoided by assigning similar patients to each group. Such pairing of patients may not be necessary if large numbers are included. Whether pairing is accomplished by chance or by design, some estimate of the differences among the groups must be made before conclusions can be reached. This may be accomplished by administering the same medication to two or more groups, by using graduated doses and obtaining a dose response, and/or by the use of control medications.

Inactive and Active Control Medications. The administration of blank (dummy or placebo) medications may produce significant clinical effects in many patients. It is possible to include a dummy in many studies in order to establish a base line from which to measure the effectiveness of the therapeutic agents. This is essential if the activity of medications is to be judged meaningful, unless dose-ratio assays are being made. An effective medication in acceptable doses should also be included. This is an attempt to test the sensitivity of the experiment and must be done if the inactivity of other medications is to be interpreted.

Randomization of Medications. A random or unplanned order of administration assures a random distribution of certain biases, but does not assure an equal distribution. Therefore, in cross-over studies it is preferable for the drugs to be given according to a plan. In such a program, consideration must be given to the effects of preceding drugs upon those that follow and to any orderly changes which may occur in the patients during the course of the study. Tables presenting such plans (Latin squares) are available in many textbooks on statistics.

The Double-Blind Technique. The double-blind method is essential to the evaluation of pain relieving drugs. This design assures that neither the observer nor the subjects know which medicine or dose is given on a particular occasion. It is used to distribute biases randomly among the medications. It does not assure that they are distributed equally. It certainly does not substitute for careful consideration of other factors in the design of the experiment.

Methods for Obtaining Data. Two general methods have been used to obtain subjective data. The first is the use of direct questions. This method may be preferred since the data are obtained quickly and routinely. The main objection to the use of check lists is that the questions suggest to the patients that certain answers are desired. Therefore, this method may bias an experiment by favoring responses which are more common for one drug than for another.

The second method is the use of informal questions with studious avoidance of leading questions. When this method is used, pertinent information may not be volunteered by the patients, especially if they consider it irrelevant or not of interest to the observer. Thus, valuable data may be missed and/or bias may be present.

Time Factors in Obtaining Data. The interrogation of the subjects may be accomplished (1) before and at repeated intervals during drug action (*e.g.*, after one, two, and four hours); (2) at a fixed interval after the drug is administered (*e.g.*, after two hours), or (3) at the end of a period of therapy (*e.g.*, after one day or one week). The first supplies time-effect data not obtained by the other means. Maximum and total analgesic effectiveness may, therefore, be determined. However, this method demands the attention of a full-time observer and cannot be carried out as a minor responsibility to be completed along with other tasks.

The estimates obtained at a fixed interval after medication may favor one medication more than another if differences in onset and/or duration of effects exist. Therefore, careful

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attention must be given to these factors in choosing the interval to be used.

Estimates of effectiveness obtained at the end of a period of therapy depend upon the recollections of the patient. They, therefore, are subject to the inaccuracies associated with memory failure.

Quantitation of Subjective Phenomena. (1) EMPIRICAL SCALES: No rational scale is available for the measurement of a "subjective" phenomenon such as pain. Therefore, empirical scales related to pain intensity and/or to pain relief must be used to estimate analgesia. When a pain intensity scale is used, the estimates of analgesia are obtained by calculating decreases or changes in intensity; pain relief scales provide direct estimates of analgesia.

(2) ARBITRARILY ASSIGNED SCORES: Since the scales used in determining analgesia are empirical, one point cannot be established as a fixed proportion of another, *i.e.*, slight pain is not necessarily one-half of moderate pain nor one-third of severe pain. Therefore, any scale which is useful may be applied in order to evaluate the data.

Pain is a familiar symptom. Of all subjective phenomena, it is most frequently brought to the attention of the physician. Therefore, it was chosen as a model for the presentation of several factors to be considered in the design of experiments. These factors are equally important in studies concerned with the generation of or the relief of other "subjective" phenomena (such as nausea, drowsiness, and itching) and apply to many "objective" clinical phenomena (such as blood pressure, pulse rate, and physical strength), which change with time and/or psychological stimuli. The investigator should attempt, by means of experimental design, to control and/or distribute the differences in the responsiveness of the subjects equally between or among the medications under test. This may be accomplished by the use of the cross-over method and randomization of medications. The usefulness of this method is limited by the clinical condition under study.

The method to be used in obtaining data must be selected by the investigator. To a considerable degree this decision should be based on the experience and aptitude of the observer, the time factors in obtaining information, the scales and scores to be applied to these data, and the control medications to be included in the study. The most important single factor, however, is the purpose of the study. Four questions which the investigator must ask himself are: (1) What do I want to learn? (2) Whom can I depend on as an observer? (3) Whom can I depend on as subjects? (4) How can I answer question one within the limitations of questions two and three? The reader should ask question four as follows: Did the authors answer question one within the limitations of questions two and three?

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Analeptics: Outmoded Therapy of Barbiturate Poisoning

THE administration of an antidote, if one is known, is a fundamental toxicological approach to any poisoning. It would seem rational indeed to employ a stimulant drug in order to counteract the effects of a depressant one. Unfortunately, there is no safe antidote for barbiturate poisoning. Nor is there yet available a true barbiturate antagonist analogous in its action to the role of nalorphine or levallorphan in the narcotic category. The so-called analeptic drugs, despite their shortcomings, once represented a well-considered approach to these desiderata. In the years preceding the development and widespread application of the principles of resuscitation and the postanesthetic recovery room, the use of analeptics enabled the salvage of many patients who would otherwise have contributed to the high death rate from barbiturate poisoning. For more than a decade, however, it has been evident that the mortality figures can be drastically reduced (below 2 per cent) with good

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