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BENJAMIN G. COVINO
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LOCAL ANESTHETICS
MECHANISMS OF ACTION
AND CLINICAL USE

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THE SCIENTIFIC BASIS OF
CLINICAL ANESTHESIA
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LOCAL ANESTHETICS

Mechanisms of Action
and Clinical Use

Chemical Aspects of Local Anesthetic Agents

CHEMICAL ASPECTS

Local anesthetic drugs are defined as a class of compounds which are used to produce reversible loss of sensation in a specific area of the body. They are used in a variety of clinical situations, including dental procedures, minor surgical operations, and obstetric analgesia. The chemical structure of these agents is characterized by a central aromatic ring substituted with an amine group and an ester group. The amine group is responsible for the drug's ability to cross the lipid bilayer of cell membranes, while the ester group is responsible for its hydrolysis and subsequent elimination from the body. The chemical structure of a typical local anesthetic is shown below:

CC(=O)Oc1ccc(cc1)N(C)C

The chemical structure of a typical local anesthetic is shown above. It consists of a central aromatic ring substituted with an amine group and an ester group. The amine group is responsible for the drug's ability to cross the lipid bilayer of cell membranes, while the ester group is responsible for its hydrolysis and subsequent elimination from the body.

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Dedicated to
Lorraine, Paul and Brian

THE SCIENTIFIC BASIS OF CLINICAL ANESTHESIA

Series Editors

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ANESTHESIA AND THE KIDNEY

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LOCAL ANESTHETICS

Mechanisms of Action and Clinical Use

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Introduction

As this series begins it is time to ask ourselves several questions. Is the practice of anesthesia exclusively art rather than science? Has the specialty achieved a level of sophistication where at least a part of the anesthesia experience has a rational explanation? Have we reached that stage when new concepts and understanding are evolving from within the specialty at a rate adequate to assure growth and permanence? We have good reason to believe we are approaching the latter evolutionary phase and are bending to retrieve the gauntlet cast in 1950 by William T. Salter, M.D., Professor of Pharmacology at Yale. In "The Leaven of the Profession" (*Anesthesiology* 11:374-376, 1950) he wrote:

"At this juncture, however, those who have the future of Anesthesiology close at heart will realize that no professional specialty can maintain itself on the basis of service alone. In the case of Surgery, for example, Harvey Cushing—one of the most skilled technicians of his day—once intimated that it might be well if amputation of the fingers were a requirement for an appointment to the Chair of Surgery in every progressive university." This remark annoyed quite a few of the contemporary super-technicians whom Cushing counted among his colleagues! Nevertheless, his remark contained a very important germ of truth; namely, that professions do not live by service alone, but rather by the words of wisdom which issue out of the mouths of those few demigods who in every generation lead and inspire the multitude of their professional associates.

"In this day and age there is a tendency for the routine anesthetist to 'pass the buck' to the professor of physiology or the professor of pharmacology, in the vain hope that the answers can be learned from mice or monkeys. The respective professors named are usually only too eager to cooperate and interested in fostering the development of applied studies on man. They realize all too well, however, that such studies must be made by an applied pharmacologist, appointed by the Department of Anesthesiology. Such a man should be familiar with the everyday problems of the practicing Anesthesiologist. He should have basic training in the fundamental departments mentioned. He would do well perhaps to commence his

work with experiments on animals performed under the aegis of the pre-clinical departments. Ultimately, however, the problem must be taken into the clinic and the definitive answers resolved there.

“To this end, there must be trained a group of so-called ‘academic Anesthesiologists.’ These individuals must have the special training and sufficient leisure to advance the basic concepts of applied science. In their earlier years they must be supported by adequate fellowships. In their mature years they must receive adequate recognition in the form of staff appointments and university affiliation. They must not be run ragged with routine assignments, but must be protected from the irate surgeon who demands service now in the name of all humanity and the Trustees. At the present time the fellowships and funds available for this purpose are pitifully meager. . . . The conscientious and overworked anesthetist, while rendering invaluable service to the community, fails to appreciate that his ultimate professional status cannot be guaranteed by service alone. Without vision and research, the professions die.”

It is the intention of the editors to provide the specialty with a monograph series targeted to the clinical areas. In the Salter tradition, the authors are clinicians, distinguished additionally by their contributions to the scientific base of our specialty. Superb clinicians who simultaneously function as dedicated investigators are a rare hybrid able to filter effectively the relevant signals from laboratory noise and transduce the data into comprehensible and applicable information. The editors are especially proud to have secured the services of a distinguished faculty for this purpose.

We accept the tenet that the informed practitioner who roots his clinical decisions in a nidus of relevant science is bound to render superior patient care. It is to that end that we dedicate the Scientific Basis of Clinical Anesthesia.

Richard J. Kitz, M.D.
Myron B. Laver, M.D.

Boston, 1976

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