Preface

Some important constraints of anesthesia must be taken into consideration when the pharmacological properties of modern anesthetics are discussed. The most important of these could be that the target effect be achieved preferably within seconds, at most within a few minutes. Similarly, offset of drug action should be achieved within minutes rather hours. The target effects, such as unconsciousness, are potentially life-threatening, as are the side effects of modern anesthetics, such as respiratory and cardiovascular depression. Finally, the patient's purposeful responses are not available to guide drug dosage, because, either the patient is unconscious, or more problematically, the patient is aware but unable to communicate pain because of neuromuscular blockade.

These constraints were already recognised 35 years ago, when in 1972 Volume XXX entitled "Modern Inhalation Anesthetics" appeared in this Handbook Series. The present volume is meant as a follow up and extension of that volume. At the beginning of the 1970's anesthesia was commonly delivered by inhalation, with only very few exceptions. The clinical understanding of that time considered anesthesia as a unique state achieved by any of the inhalation anesthetics, independent of their specific molecular structure. "The very mechanism of anesthetic action at the biophase" was discussed within the theoretical framework of the "unitary theory of narcosis". This theoretical understanding was based on the Meyer-Overton correlation and the apparent additivity of MAC when several inhalational anesthetics were given simultaneously, MAC being the measure of anesthetic potency and anesthetic depth developed in the mid-1960's. Since the 1980's this understanding has changed completely. Today "general anesthesia" is commonly considered a collection of neurophysiologically very different states, achieved by a multitude of very different drugs (delivered not only by inhalation) acting on a plethora of subcellular structures. Unconsciousness and absence of pain are always included in this collection of different states.

Three main factors contributed to this changed understanding:

1) the increasing use of intravenous anesthesia, facilitated by the development of new intravenous anesthetics, not only for the induction but also for the maintenance of anesthesia
2) the discovery of non-additive types of anesthetic interactions,

3) the development of molecular techniques (biological, pharmacological and physiological) to study the interaction of anesthetic drug molecules with receptive cell structures.

For these reasons, when the outline of this Handbook was discussed at a brainstorming meeting in Erlangen in February 2005, it became clear that it should be entitled "Modern Anesthetics" and contain in addition to a section on "Inhalation Anesthetics" one on "Intravenous Anesthetics", preceded by another on "Molecular Mechanisms of Anesthetic Action". Emphasis was put on the term "molecular" to draw attention to the discovery in the past decades of a great many findings on the interaction of anesthetic compounds with subcellular entities. On the other hand, this emphasis was to underline the lack of our understanding concerning the summation of all the different interactions from the molecular level through the progressive stages of integration within the CNS, which needs to be studied in the future. While these considerations may be considered mainstream of current research in experimental anesthetic pharmacology, it was strongly felt that the particularities of anesthetic drug therapy discussed above require not only specific drugs, but also very particular modes of their delivery and administration. It is not only the properties of the compounds but the combination of compounds plus drug delivery system which turns the compounds into a clinically effective and safe drug. It was therefore thought necessary to integrate a fourth section on "Pharmacokinetics-Pharmacodynamics based Administration of Anesthetics". This final section illustrates a strategy, still at an experimental stage, in which the integration of drug, medical technology and computational medicine leads to optimized anesthetic therapeutic systems.

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