Anaesthesia in pharmacological research

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General anaesthetic drugs are substances which produce a reversible state of unconsciousness and insensibility. In addition to these principal effects, anaesthetic drugs nearly always modify the major functions of the organism. As Claude Bernard remarked more than a century ago, 'An anaesthetic is not merely a special poison for the nervous system. It anaesthetizes all the cells, it invades all the tissues.' Despite these drawbacks, anaesthetic drugs are widely used today for in vivo experiments. However, it must be borne in mind that their use may considerably modify the outcome of a physiological or pharmacological experiment. While a great amount of data has been accumulated with respect to the physiological effect of general anaesthesia, little information is available on pharmacological effects.

The aim of this report is to provide information on the possible interactions between general anaesthetic drugs and other pharmacological agents. This review is limited to drugs currently used only in experimental work.

METHODOLOGY

A specific, defined methodology is necessary to observe the effects of anaesthetic drugs. While the procedure itself is fairly straightforward and amounts to the compilation of two comparative series of data (one with and the other without anaesthetic drug use), it cannot always be followed. All too often, physiological determinants demand surgery with difficult to control situations such as haemorrhage, vasomotor disturbances, stimulation or destruction of sensitive nerve fibres, and, finally, endocrinological changes. Under such conditions, the comparisons between anaesthetic and non-anaesthetic conditions lose their significance. It is difficult to distinguish the physiological effects due to anaesthesia from those effects derived from the surgical procedure itself (or any combination of the two). Thus, irregardless of the intervention required, and whether it be simple (catheterization under
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general anaesthesia) or complicated (laparotomy, thoracotomy), it should be carried out well in advance of the proposed study (several days to 2 weeks). Complete recuperation of the subject must occur before beginning experimentation. Furthermore, it is advisable not to consider results obtained without separation of effects due to anaesthesia and those linked to surgical procedures.

Another difficulty is to maintain a constant level of anaesthesia during the experiment. Cardiac output, blood pressure, and systemic resistances, depend upon the degree of anaesthesia (Figure 45.1 (a)). Moreover, for a given constant level of anaesthesia, the possibility of physiological adaptation has been shown, e.g. during anaesthesia with halothane, a number of

![Figure 45.1](image_url)

Figure 45.1 (a) Influence of anaesthesia level on some cardiovascular parameters in dogs. Light anaesthesia: chloralose 53 mg/kg, urethane 535 mg/kg, and deep anaesthesia: chloralose 98 mg/kg, urethane 980 mg/kg (from ref. 34). (b) Effect of pentobarbital, urethane and chloralose on diameter (µm) of second order vessels in the bat wing (from ref. 33)