

EDITORIAL

INFLUENCE OF OPIATES UPON EXPERIMENTAL RESULTS

THE use of opiates for preanesthetic or preoperative medication is a time honored procedure. Except in a few medical centers almost every patient scheduled for operation receives a narcotic before he is anesthetized. It is not the intent of this editorial to enter into the controversy as to whether or not opiates should be employed preoperatively. It is its purpose, however, to point out that opiates are powerful drugs with widespread, diverse, and prolonged effects upon most physiologic systems. The recognition of this fact by clinicians is important, but of far greater significance is the failure of investigators to recognize the influence which the administration of opiates to man or animals may have upon their experimental results.

In general, there is little qualitative difference between the action of the opiate alkaloids and the synthetic opiate-like agents such as meperidine (Demerol®) or alphaprodine (Nisentil®). Consequently, no attempt will be made to differentiate between opiates and opiate-like drugs in this discussion.

Respiration. Opiates profoundly affect the respiration by reducing respiratory rate and minute volume and increasing alveolar $p\text{CO}_2$. The response of the respiratory center to carbon dioxide is depressed, leaving the reactivity of other centers (for example, inhibitory vagal centers) relatively intact. Because of the decreased sensitivity to carbon dioxide, the influence of the respiratory center over respiratory activity is diminished. The chemoreceptor drive of respiration, however, is enhanced. Under such circumstances sudden removal of the chemoreceptor drive by increasing the arterial oxygen tension may result in respiratory depression. Without opiates, oxygen apnea or depression is more difficult to produce. In addition, data are available to indicate that opiates may influence respiratory rhythm and relationships of the phases of the respiratory cycle.

Circulation. In normal individuals opiates do not usually affect blood pressure while the patient remains supine. They do depress compensatory vasomotor mechanisms, and circulatory stress (for example, tilting or turning) may lead to vascular collapse. Under certain conditions without stress, as in the elderly, debilitated or acutely ill patient, hypotension may be observed following the administration of opiates either intravenously, intramuscularly, or subcutaneously.

Central Nervous System. Morphine has been alleged to depress to a mild degree both facilitating and inhibiting mechanisms. An increase in the threshold to pain, a reduction in the reactivity to pain, a diminution of anxiety induced by the anticipation of pain, and a tendency to sleep have been noted. As with many other pharmacologic

agents, a biphasic response is not uncommon. For instance, euphoria may be followed by dysphoria. In the occasional patient sedation fails to appear and excitement is experienced instead. Specific hypothalamic effects ascribed to the opiates have included an antidiuretic effect, a sensitization of the anterior hypothalamus to heat, and a hyperglycemic effect upon regulation of blood sugar. Finally, there is evidence that opiates stimulate the trigger zone initiating emesis.

Gastrointestinal. Morphine increases intestinal tone and decreases the propulsive and nonpropulsive movements. A complete absence of propulsive movements may occur. These actions may persist for many hours.

Smooth Muscle. Opiates cause contraction of smooth muscle. An increase of pressure within the biliary tract may occur because of smooth muscle spasm, bronchiolar constriction may develop, and retention of urine may occur because of the effect upon the sphincteric mechanism.

Miscellaneous. Data are available to indicate that morphine inhibits the action of cholinesterase in animals. The importance of this in relation to the use of local anesthetic esters and to employment of succinylcholine in man is unknown. Opiates also have the ability to cause the release of histamine and to produce the typical histaminic effects of erythema, urticaria, sneezing, and pruritus. Asthmatic attacks may be precipitated. Opiates are frequently presumed to have exerted their maximum effect within one to one and one-half hours following subcutaneous administration and to have expended their action within three to four hours. Neither assumption need be true. The maximum respiratory effect may not appear for three to four hours, and the duration of action may approach twenty-four hours. Pain does not necessarily counteract the respiratory depressant effects of opiates.

It is evident that careful attention must be paid to the advisability of administering opiates to patients or subjects upon whom an investigation pertaining to anesthetics or anesthetic techniques is to be made. It should not be assumed that preanesthetic medication has little influence upon the results of such a study, since in many instances the opiate may have a more pronounced effect than the anesthetic studied. In research the administration of opiates or other medication should be ordered only after the investigator has satisfied himself that the drugs will not influence the results of his investigation. When preanesthetic drugs are employed, authors should report specifically the doses employed and the methods of their administration. The influence that these drugs might have upon the results of the experiments and the conclusions drawn should likewise be discussed. An investigator should not presume that preliminary medicaments have had no bearing on his findings. He should take their actions into consideration when he analyzes his data.