CONTROL OF BREATHING

THOMAS F. HORNBEIN

Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington 98195

INTRODUCTION AND GOALS

The primary purpose of this presentation will be to explore the ways in which anesthetics and related drugs - sedatives, tranquilizers, and narcotics - act to produce one of their more notorious side effects, depression of breathing. I will review dose-response relationships, discuss clinical implications, and explore some of the questions of basic ventilatory control revealed by the way in which these drugs modify breathing.

THE NATURE OF DRUG DEPRESSION

Inhalational Anesthetics.

Tidal volume and $P_{CO_2}$. Ventilatory depression may be perceived clinically as a decrease in minute ventilation, manifest as a rise in arterial or alveolar $P_{CO_2}$. The dose-response curve differs for different anesthetics, diethyl ether being the least depressant to resting breathing and enflurane the most, with halothane and isoflurane more closely resembling the latter than the former. In spite of these differences, with all these anesthetics tidal volume decreases with increasing anesthetic concentration. The $P_{CO_2}$ below which spontaneous ventilation ceases to occur in the sedated or anesthetized individual was termed by Fink "the apneic threshold." That value lies 5-9 mm Hg below the resting $P_{CO_2}$ and seems to provide the same information regarding ventilatory depression as does the resting $P_{CO_2}$.

Carbon dioxide response. All inhalation anesthetics, including diethyl ether, produce a dose-proportional decrease in the slope of ventilation-$CO_2$ response curve.

Hypoxic response. The inhalation anesthetics, halothane, isoflurane, and enflurane, all depress the ventilatory response to hypoxia more than the response to carbon dioxide. For example, halothane at 0.1 MAC...
depresses hypoxic ventilatory response to approximately 30% of control, while the CO₂ response is virtually unchanged from the awake value; at 1.1 MAC a ventilatory response to hypoxia is absent, while the CO₂ response is decreased to approximately 35% of the awake value. Nitrous oxide behaves similarly. Droperidol selectively increases the ventilatory response to hypoxia. This greater hypoxic depression of inhalation anesthetics appears to result from an effect of these drugs upon the peripheral chemoreceptors.

Response to loading. The ventilatory response to an externally imposed load, an increase in either resistance or capacitance, was originally presumed to be profoundly depressed by even light levels of anesthesia. More recent evidence suggests that mild to moderate loads are well tolerated without resulting in a rise in arterial $P_{CO_2}$, at least at lower anesthetic concentrations. Little information concerning dose-response relationships is yet available. Increasing anesthetic depth may obtund the ventilatory tolerance to external loads. Response to intrinsic loading (e.g., bronchospasm induced by methacholine in dogs) appears to be unaffected by pentobarbital, which impairs the response to external loading; whether humans behave similarly to inhalation anesthetics is not known. Patients with chronic obstructive pulmonary disease exhibiting increased airways resistance when awake may experience a greater rise in $P_{CO_2}$ during anesthesia than that of normal patients if permitted to breathe spontaneously.

Response to stimulation. Noxious stimulation during surgery will result in an increase in ventilation and a decrease in $P_{CO_2}$ of up to 10 mm Hg from the unstimulated state.

Narcotics, Sedatives, and Hypnotics.

These drugs, except ketamine and marijuana, appear to depress ventilation, resulting in a dose-related increase in alveolar or arterial $P_{CO_2}$. Different classes of drugs appear to affect the pattern of breathing in differing ways: narcotics are associated with a slowing of respiratory frequency but a sustained tidal volume, in contrast to barbiturates and in particular to the inhalation anesthetics, which to varying degrees tend to increase respiratory frequency and decrease tidal volume.