or NOS activity, or both, were measured after NOS inhibitor administration. cGMP concentration and NOS activity were not (and could not be) measured during tail pinch, but were measured in the cerebellum of unstimulated animals that had received the same dose of NOS inhibitors as those that had tail pinch. Therefore, although cerebellar cGMP concentration and NOS activity should reflect those in the spinal cord (proposed nociceptive pathway in tail pinch, see discussion of Ichinose et al.), no data are available regarding NOS activity or cGMP concentrations during MAC measurements (tail pinch).

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Intermittent CPAP during General Anesthesia

To the Editor.—The interesting article by Bratzke et al. uses an unusual measure of ventilatory efficiency: partial pressure of arterial carbon dioxide (P_aCO_2) per minute ventilation. This measure is adequate only during very restricted circumstances. As the authors point out, when comparing two modes of ventilation in rapid succession, an increase in the ratio equates with more efficient ventilation. However, the comparison assumes that carbon dioxide output (V_{CO}_2) and P_aCO_2 are “clamped.” If cellular carbon dioxide production were to increase, say by 10%, unchanged ventilation would cause P_aCO_2 to increase by 10%. The ratio would then also increase by 10%, but this would not signify greater efficiency. In order not to be misleading, the index can only apply to changes in minute ventilation at constant P_aCO_2.

For all-around applicability, an index of ventilatory efficiency must always compare expired and blood gas partial pressure of carbon dioxide (P_cO_2), the basis of the dead space concept. The nearest index to the one the authors have used here, i.e., one that increases with increasing efficiency, would be (1 – V_D / V_T), which is obtained from mixed expired P_cO_2 divided by P_aCO_2. It is the same thing as alveolar ventilation divided by total ventilation.

A second point about the article is that the assumption that anatomic dead space was constant may not be correct. Increases in end-inspiratory pause of a fraction of a second can reduce anatomic dead space significantly (L. Nordström, personal communication, November, 1998), and, therefore, the long continuous positive airway pressure (CPAP) periods used by Bratzke et al. may markedly reduce this dead space, contributing considerably to the increase in alveolar ventilation noted.

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alveolar ventilation, which was precluded by study design. We produced equivalent levels of alveolar ventilation during CMV and intermittent CPAP, as evidenced by similar \( P_a - \text{CO}_2 \) values, but with significantly less total ventilation during the latter. Using the calculation \( P(a-e) / P_a - \text{CO}_2 \), as an indication of the fraction of unperfused, but ventilated alveoli\(^2\) we found a mean alveolar deadspace of 4\% during intermittent CPAP and 17\% during CMV.

It is well known that an inspiratory pause applied during CMV may result in a smaller calculated physiologic deadspace.\(^7\) It is less apparent that \( \text{conducting airways} \), which define the \( \text{anatomic} \) deadspace, are reduced in volume by an end-inspiratory pause. It also is not clear that CPAP will have a pulmonary effect similar to that observed with conventional positive pressure ventilation with an inspiratory plateau. Our data clearly support a significant decrease in \( \text{alveolar} \) deadspace during intermittent CPAP. To test Fitch’s hypothesis that a decrease in \( \text{anatomic} \) deadspace might account for the observed increase in efficiency of ventilation during intermittent CPAP, we calculated the difference in mean anatomic and alveolar deadspace (\( V_{alv} \)\)) volumes during CMV and intermittent CPAP, using data in the manuscript\(^1\) and standard equations.\(^5\) We assumed a normal anatomical deadspace of 194 ml during CMV. During intermittent CPAP alveolar \( V_{alv} \) was 15 ml, anatomic \( V_a \) 149 ml and total physiologic \( V_p \) 153 ml. During CMV alveolar \( V_{alv} \) was 74 ml, anatomic \( V_a \) 194 ml, as assumed, and total physiologic \( V_p \) 268 ml. We observed that intermittent CPAP caused a modest decrease in calculated alveolar \( V_{alv} \), compared with CMV, of 28\%. More important however, was the fivefold increase in alveolar deadspace generated by controlled ventilation. Overall physiologic \( V_p \) was 74\% higher during CMV than during intermittent CPAP. Emphasizing our conclusion that intermittent CPAP provides more efficient ventilation.

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Receptor-specific Reversible Sedation: Dangers of Vascular Effects

To the Editor—The editorial by Dr. Talke\(^1\) enlists about the future role in man of \( \alpha_2 \)-agonist-mediated sedation with easy reversibility after atipamezole administration. He rightly emphasizes the future role of “a new subtype-specific \( \alpha_2 \) agonist with sedative but not vasoconstrictor effects” (italics added).\(^1\) Scheinert et al.\(^2\) briefly allude to the use of \( \alpha_2 \)-adrenoreceptor agonists and antagonists in veterinary practice. We would point out that \( \alpha_2 \)-adrenoreceptor agonists, such as xylazine, have been widely used in veterinary and anesthetic practice for 29 yr. and detomidine,\(^3\) medetomidine, and atipamezole have been used for 10 yr. Some years ago we\(^4\) showed severe cardiovascular changes and bradycardia in horses and, during a similar time period, it has been known that in sheep there is a sudden profound decrease in arterial oxygen pressure (\( P_a(O_2) \)) after xylazine administration. Until recently, the explanation for this has been obscure. However, we\(^4\) and others\(^5\) have shown extensive pulmonary edema after xylazine sedation in sheep. In our animals, \( P_a(O_2) \), breathing air decreased from 97.9 ± 6.7 mmHg ± SEM to 58.1 ± 5.2 mmHg ± SEM immediately after xylazine administration. All our animals had extensive pulmonary edema and microvascular congestion with erythrocytes extravasated into the alveolar space.

We interpreted this as a consequence of pulmonary venospasm, there being no evidence of acute inflammation in the lung, no sign of platelet emboli, and no evidence of free radical release. There are wide species differences in the effect of xylazine on pulmonary function, but it is worth bearing in mind the potency of the vascular effects of some of these \( \alpha_2 \)-agonist sedatives in humans and animals. The different receptor subtypes in the cardiovascular and central nervous systems must obviously be carefully investigated before we can enshrine about the inclusion of new \( \alpha_2 \)-receptor agents in human clinical practice.

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