sively incremented each minute by 150 kg·M/min, and 3) work rate progressively decremented each minute by 150 kg·M/min (following an abrupt increase to a high work rate). The results indicate that \( \dot{V}_{E} \) is better correlated with \( \dot{V}_{\text{CO}_2} \) than with \( \dot{V}_{O_2} \) during both steady and non-steady-state phases of exercise. A steady-state of \( \dot{V}_{O_2} \) was often attained before \( \dot{V}_{\text{CO}_2} \) reached its steady-state. Following reduction of body \( \text{CO}_2 \) stores by ten minutes of voluntary hyperventilation (alveolar \( \text{CO}_2 \) tension \( \sim 25 \text{ mm Hg} \)), the \( \dot{V}_{E} \) response to exercise was markedly reduced during the first minute. This paralleled the low \( \dot{V}_{\text{CO}_2} \) as metabolic \( \text{CO}_2 \) was partially diverted into the depleted \( \text{CO}_2 \) stores. \( \dot{V}_{E} \) increased rapidly after the alveolar \( \text{CO}_2 \) tension approximated its prior control value (Fig 1). These results are consistent with a predominantly humoral mechanism controlling the exercise hyperpnea following the onset of work, which is based on regulation of arterial \( \text{CO}_2 \) tension and which varies as a function of \( \text{CO}_2 \) output.

Reference


Regulation of Ventilation in the Absence of Pulmonary Gas Exchange

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Information concerning ventilatory movements is fed back to the central nervous system respiratory centers via three mechanisms: pleural cavity volume changes transduced by chest wall and diaphragm proprioceptors; lung volume changes sensed by pulmonary stretch receptors; and ventilatory effects on blood-gas levels detected by the chemosensors. A canine preparation was developed in which respiratory gas exchange was independent of ventilation. This constituted an interruption of the chemical feedback path and produced an "open loop" ventilatory control system. The preparation involved the establishment of a closed-chest, cardiopulmonary bypass in which blood gases were maintained at nearly constant levels in normal ranges as determined by continuous, on-line monitoring. The response of the respiratory system to step changes in the effective ventilatory mechanical properties was studied both in the bypass animals and in those with intact respiratory systems. Changes in effective ventilatory elastance and resistance were produced either separately or together by having the animals' lung volume changes displace air from rigid containers and through porous flow resistors. The mechanical property changes spanned the range of \( \pm 100 \text{ percent change in effective ventilatory time constant.} \)

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CHEST, VOL. 61, NO. 2, FEBRUARY 1972 SUPPLEMENT
Factors Controlling $O_2$ Uptake

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Whole body oxygen utilization is influenced by many factors. It has been known for some time that alkalinizing agents have a calorigenic action; however, the mechanisms involved in producing this effect have not been clarified. We considered the stimulation of oxygen uptake by sodium-L-lactate, sodium pyruvate and Na bicarbonate infusions along three possible mechanistic lines: their effect on acid-base balance, $\beta$-adrenergic stimulation and an intrinsic metabolic effect, all of which influenced oxygen uptake.

An 0.3 M solution of each of these agents was infused over a ten minute period in anesthetized dogs. A new steady state with respect to the $H^+$ ion concentration was reached by 30 min and each infusion produced equivalent degrees of alkalemia with respect to the resulting fall in the $H^+$ ion concentration.

The effect of each infusion on the oxygen uptake without and with propranolol induced $\beta$-adrenergic blockade was calculated. The increase in oxygen uptake resulting from the infusion of sodium lactate and sodium pyruvate was markedly attenuated after $\beta$-adrenergic blockade. This was primarily a result of the attenuation of the persistent evaluation of the oxygen uptake following infusion as the immediate rise in oxygen uptake with infusion was similar with and without propranolol. Propranolol was not observed to have a significant effect on the increase in oxygen uptake resulting from sodium bicarbonate infusion. Furthermore, the increase in oxygen uptake resulting from sodium pyruvate infusion was greater than that resulting from sodium lactate infusion which in turn was greater than that resulting from sodium bicarbonate infusion and all were proportional to the amount infused.

As a result of these studies we concluded that there were at least three mechanisms for the calorigenic action of alkalinizing agents. The first is the only one by which sodium bicarbonate acts and that is the small but definite increase in oxygen uptake due to the enhancing effect of alkalosis on cell respiration. The second, because of the attenuation of the calorigenic action of lactate and pyruvate by $\beta$-adrenergic blockade must operate in addition for these agents through stimulation of catecholamine release or $\beta$-adrenergic receptors and their well-known calorigenic action. Finally, after all allowances are made for alkalemic effects and $\beta$-adrenergic stimulation, a discrete increase in oxygen uptake still was measured and this was proportional to the amount of lactate and pyruvate infused. This last mechanism could thus be called, in contrast to the alkalotic effect and beta effect, the intrinsic metabolic effect of stimulating cell respiration possessed by easily metabolizable substrates.

We attributed the increase in oxygen uptake due to a reduction in the hydrogen ion concentration to the stimulation by alkalosis of the activity of a few key enzymes which serve major roles in the regula-

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