Approach to a Quantitative Differentiation Between the Respiratory Effects Evoked from the Lung Stretch and the Lung Deflation Receptors During Thoracic Compression[1]

In spontaneously breathing animals placed in a body-plethysmograph, moderate and brief increase of the intraplethysmographic pressure in order to produce thoracic compression leads to increase in both respiratory frequency and inspiration-expiration duration quotient. It has been shown in guinea-pigs that these respiratory effects are abolished by bilateral vagotomy and occur in the absence of extravagal-proprioceptive or chemoreceptive influences[2,3]. It is evident, therefore, that they are vagal in origin. They are, on the one hand, due to diminution of pulmonary stretch receptor discharge (and consequently diminution of inspiratory inhibition) during decrease of lung volume to expiratory level ('Lungen-Entdehnungsreflex', corresponding to a weak inspiratory reaction)[4,5]. On the other hand, they are brought about partly by sustained reduction of stretch receptor discharge, but mainly by excitation of lung deflation receptors when decrease of lung volume below normal expiratory level occurs (lung deflation reflex, corresponding to a marked inspiratory reaction)[4-6]. The 2 reflexes have been differentiated by progressive cooling of the vagus nerves in which run the afferent fibers from the lungs[7].

The purpose of the present study was to carry out quantitative differentiation of the 2 reflexes just described. Calculations were based on results obtained in previous investigations[2,3], in which the respiratory effects were evaluated by correlating respiratory frequency and inspiration-expiration duration quotient with the intraplethysmographic pressure applied, as well as with the action potentials recorded from afferent vagal filaments. The records obtained from 15 guinea-pigs were utilized, and in addition the following observations made on over 100 animals: 1. Respiratory frequency and inspiration-expiration duration quotient do not increase appreciably when the plethysmographic pressure ranges from -5 to $+1$ cm H_2O. Plethysmographic pressure, however, ranging from $+1$ to $+11$ cm H_2O results in a marked increase of both parameters. 2. Changes in respiratory frequency and inspiration-expiration duration quotient which are due to pressure variations in the lower range (p_l), i.e., -5 to $+1$ cm H_2O, occur as a result of diminished stretch receptor activity, whereas the changes due to pressure increase in the higher range (p_h), i.e., $+5$ to $+11$ cm H_2O, are a result of deflation receptor activation as well as sustained reduction of the stretch receptor discharge. At pressures between $+1$ and $+5$ cm H_2O, although stretch receptor activity always occurred, it is uncertain whether the deflation receptors came into play; the effects obtained in this middle pressure range were hence not utilized in the calculations presented in this paper. The relationships between respiratory frequency (f) and plethysmographic pressure (p), and inspiration-expiration duration quotient (I/E) and pressure (p) are approximately linear in the pressure ranges p_l and p_h.

All these observations can be expressed by the following relationships: f and I/E as function of the lower pressure range:

$$f_l(p_l) \text{ and } \mathrm{I/E}_l(p_l),$$

and f and I/E as function of the higher pressure range:

$$f_h(p_h) \text{ and } \mathrm{I/E}_h(p_h).$$

These 4 functions can be approximated by 4 regression lines with their respective confidential limits. The influence of the stretch receptors of f and I/E was separated from that of the deflation receptors by assuming: a) that the effects on f and I/E due to diminished stretch receptor activity are linear throughout all pressure ranges; b) that the effects on f and I/E due to deflation receptor discharge and diminished stretch receptor activity are additive in the higher range (p_h).

The sole influence of the deflation receptors (D) in the p_h-range was determined as follows:

$$f_D = f_h(p_h) - f_l(p_l) \text{ and } \mathrm{I/E_D} = \mathrm{I/E}_h(p_h) - \mathrm{I/E}_l(p_l).$$

The confidential limits of the minuend were added to those of the subtrahend.

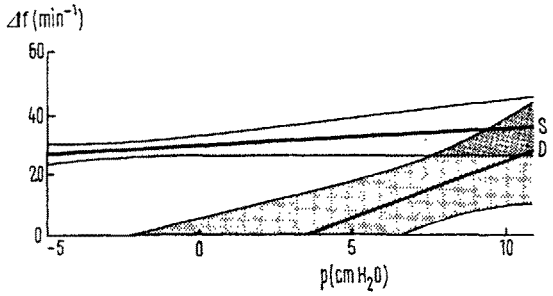

Fig. 1. Influence of the lung stretch (S) and the lung deflation receptors (D) on respiratory frequency (Δf) in response to increase of the intraplethysmographic pressure (p) from -5 to $+11$ cm H_2O. 15 guinea-pigs anaesthetized with urethane.

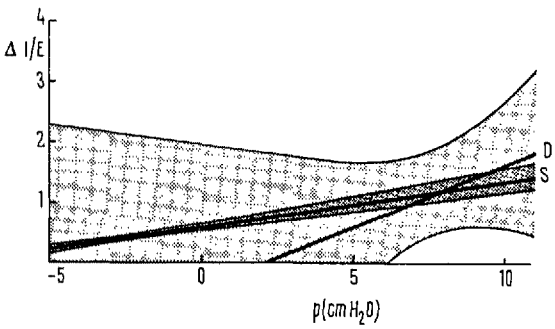

Fig. 2. Influence of the lung stretch receptors (S) and the lung deflation receptors (D) on inspiration-expiration duration quotient (Δ I/E) in response to increase of the plethysmographic pressure (p) from -5 to $+11$ cm H_2O. 15 guinea-pigs anaesthetized with urethane.

[1] Presented at the 2nd Meeting of the Swiss Physiological Society, Zürich, 8 November 1969.

[2] P. Ferrer and E. A. Koller, Helv. physiol. Acta *26*, 365 (1968).
[3] P. Ferrer and E. A. Koller, Revta esp. Fisiol. *26*, 273 (1970).
[4] O. A. M. Wyss, Ergebn. Physiol. *54*, 1 (1964).
[5] O. A. M. Wyss and E. A. Koller, Beitr. Klin. Tuberk. *138*, 243 (1968).
[6] J. D. Widdicombe, in *Handbook of Physiology*, Section 3 (Eds. W. O. Fenn and H. Hahn; American Physiological Society, Washington 1964), vol. 1, p. 585.
[7] E. A. Koller and P. Ferrer, Respir. Physiol. *10*, 172 (1970).

The results obtained are shown graphically in Figures 1 and 2. In Figure 1 it is apparent that the influence of the stretch receptors (S) on respiratory frequency (Δf) in relation to intraplethysmographic pressure (p) may be regarded as slight ($P > 0.05$). In contrast, that of the deflation receptors (D) on respiratory frequency may be regarded as significant ($P < 0.05$) as soon as plethysmographic pressures of 3.5 cm H_2O and above are applied. Attention at this point may be drawn to the fact that this extrapolated threshold value for the activation of deflation receptors is not inconsistent with the values necessary to elicit lung deflation discharge.

In Figure 2 it is evident that the reverse holds true with regard to the influence of both types of receptors on I/E in relation to intraplethysmographic pressure (p). The influence of the stretch receptors (S) is represented by a marked decrease of I/E ($p < 0.01$), while that of the deflation receptors (D) shows great variance and may hence be regarded as problematic ($P > 0.05$).

The respiratory effects evoked from the lung stretch and from the lung deflation receptors during brief thoracic compression have therefore been separated from each other quantitatively, and it has been possible to determine theoretically the sole influence of the lung deflation receptors of f and I/E. To test the validity of the results obtained, the calculated influence of the lung deflation receptors of f and I/E was correlated with the results obtained in previous investigation by means of action current recording from the vagal deflation fibers in response to changes of extrathoracic pressure. By substitution, plethysmographic pressure may be represented by the electrical activity of the deflation receptors at the corresponding pressure, which gives the following relationships: Changes of the respiratory frequency (Δf) and of the inspiration-expiration duration quotient (Δ I/E) as function of the deflation receptor activity (imp./sec). The results obtained from 5 vagal filaments are depicted in Figure 3. As the filaments varied in size and did not carry the same number of active fibers arising from the deflation receptors, average approximation was impossible. It will be seen that the 5 tracings are nevertheless directed toward the origin of the coordinate system, from which it may be deduced that the isolated respiratory effects in the calculated tracings disappear at zero electrical activity.

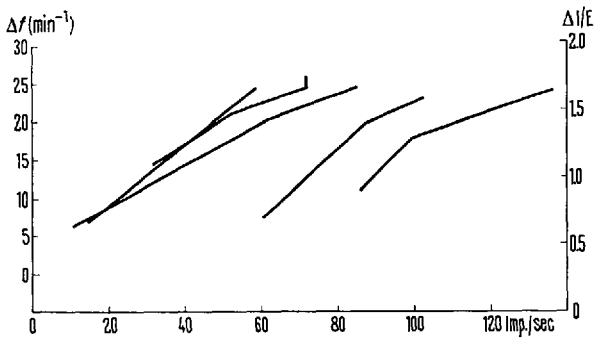

Fig. 3. Calculated influence of the deflation receptors on respiratory frequency (Δf) and inspiration-expiration duration quotient (Δ I/E) correlated with lung deflation receptor discharge (imp./sec) during thoracic compression. Individual results from 5 vagal filaments. 5 guinea-pigs anaesthetized with urethane.

In brief, it may be concluded that the assumptions on which the calculations are based are sufficiently accurate for practical purposes, and that the influence of the lung deflation receptors on f and I/E have been demonstrated quantitatively. Stated in another way, it has been possible to separate the marked inspiratory lung deflation reflex ('Lungen-Kollaps-Reflex') from the weak inspiratory influence of the reduced activity of the lung stretch receptors ('Lungen-Entdehnungs-Reflex') during thoracic compression. The present study, in addition, underlines the significant increase of respiratory frequency due to activation of the lung deflation receptors (respiratory frequency effect of the lung deflation receptors) and the significant decrease of inspiration-expiration duration quotient due to the activity of the lung stretch receptors (respiratory phase effect of the lung stretch receptors). In view of the fact that the influence of the deflation receptors on I/E varies considerably, it is suggested that the I/E variations observed are secondary to increase of f. This assumption is supported by the fact that the significant phase effect of the lung stretch receptors in the guinea-pig is practically independent of variations of respiratory frequency.

Zusammenfassung. Die beiden Annahmen, dass sich bei Thoraxkompression die Verminderung der Impulssequenz der Lungendehnungsrezeptoren analog zum Lungenentdehnungsreflex auswirke, und dass sich dessen inspiratorische Atmungseffekte zu jenen des Lungenkollapsreflexes addieren, erscheinen gerechtfertigt. Diese Annahmen ermöglichen eine quantitative Differenzierung zwischen dem respiratorischen Einfluss der Lungendehnungs- und Lungenkollapsrezeptoren bei Thoraxkompression. Damit können die auf die Erregung der Lungenkollapsrezeptoren zu beziehenden Atmungsveränderungen (Δf, Δ I/E) erstmals isoliert und quantitativ dargestellt werden.

E. A. KOLLER, D. G. RÜEGG and P. FERRER

Department of Physiology, University of Zürich, Rämistrasse 69, CH-8001 Zürich (Switzerland),
18 September 1970.

Decreased Survival Time of Insulin-Treated Mice Subjected to Hypoxic Decompression

Bordetella pertussis is unique among bacteria in its capacity to increase the susceptibility of mice and rats to a wide variety of stresses and stressor agents[1,2]. Possibly related to the organism's sensitizing capacity[3,4] is its ability to induce hypoglycemia and augment endogenous blood insulin levels in rodents[5,6]. Insulin has been shown to share with *B. pertussis* the capacity to sensitize mice to diverse stresses. In addition to their hypoglycemic effect, both *B. pertussis* and insulin are capable of increasing the susceptibility of mice to the vasoactive amines, histamine and serotonin[5]. Both agents augment sensitivity to immediate[7] and delayed-type[8,9] hypersensitivity states, as well to experimental immune hemolytic anemia[10]. Recently we reported that insulin, like *B. pertussis*, can increase the susceptibility of mice to the anaphylactoid agent, peptone[4], as well as to bacterial endotoxin[11]. KIND[12] has shown that pertussis-inoculated mice have diminished tolerance to the physical stress of