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.

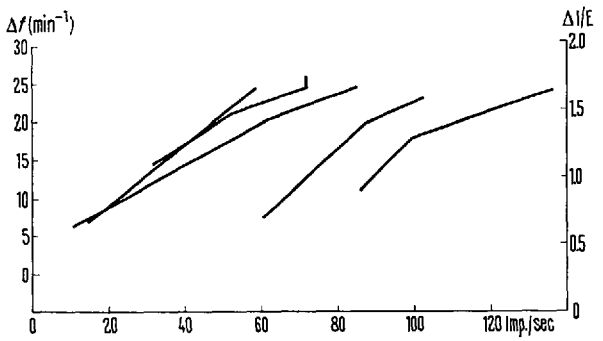

Fig. 3. Calculated influence of the deflation receptors on respiratory frequency (Δf) and inspiration-expiration duration quotient (Δ I/E) correlated with lung deflation receptor discharge (imp./sec) during thoracic compression. Individual results from 5 vagal filaments. 5 guinea-pigs anaesthetized with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

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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

reduced atmospheric pressure and low oxygen tension (hypoxic decompression). The experiments to be described indicate that insulin also can heighten the sensitivity of mice to this physical stress as determined by a significant reduction in survival time.

Female mice of the CFW strain weighing 18 g were subjected to hypoxic decompression by placing them in a glass desiccator and removing air by a vacuum pump. When the desired chamber pressure, based upon preliminary experiments, was reached, as determined by a vacuum gauge, the air outlet valve to the pump was closed. Tests were run at either 252 or 277 mm Hg. In an initial experiment 4 mice were injected i.p. with 0.5 units of regular insulin (Lilly). This dose, although non-lethal to mice, was found capable of depressing their blood glucose levels to about 25 mg/100 ml. 10 min later these mice were placed in the chamber as were a similar number of controls. The chamber was evacuated in about 30 sec to a pressure of 252 mm Hg and survival time at this pressure was carefully noted by 3 observers. The Table shows that the mean survival time for control mice was 71 sec and for insulin-pretreated animals 24 sec. Using Student's t-test for the standard error of the difference between 2 means, a t value of 3.74 was obtained ($P < 0.01$). The experiment was repeated with essentially similar results.

In a second experiment, the pressure was increased to 277 mm Hg to allow a longer observation period. 6 insulin-treated and 6 control CFW mice were used in this experiment. From the Table it may be seen that, as before, all insulin-treated mice succumbed to hypoxic stress sooner than control animals. One control was still alive after 30 min. The mean survival time for controls (excluding the 30 min survivor) was 210 sec, and that for insulin-treated mice 58 sec. This difference in survival time is statistically significant ($P < 0.01$).

The effect of insulin on the susceptibility of animals to anoxic stress appears to be a species-specific phenomenon. Anoxic convulsions, reportedly, do not occur in either the rabbit[13], or the dog[14], after injection of insulin and exposure to low oxygen tensions. GELLHORN et al.[13], however, found that insulin-treated rats, subjected to oxygen-nitrogen mixtures containing 7% oxygen experienced earlier anoxic convulsions and had a higher mortality than control animals. The present results obtained in mice support the suggestion that insulin-induced hypersensitivity to anoxia is characteristic of small animals with a high metabolic rate[13].

That carbohydrate metabolism is specifically involved in the observed effect of insulin on hypoxic decompression is supported by the findings of HERSHGOLD and RILEY[15]. These workers have demonstrated a protective effect of carbohydrates on tolerance of mice to altitude hypoxia[15]. Mice fed sucrose prior to exposure to hypoxic decompression survived significantly longer that fasted animals, or those fed a normal diet. These results were interpreted as pointing towards a mechanism whereby carbohydrates facilitate utilization of available oxygen. The possibility was considered that under hypoxic conditions the function of nervous tissue becomes more dependent on available glucose[15]. Thus, hyperglycemic agents should prolong survival and, conversely, the induction of hypoglycemia would be expected to augment susceptibility to hypoxia. Similar to insulin-treated animals, both pertussis-vaccinated and adrenalectomized mice also display increased susceptibility to hypoxic decompression[12]. It should be noted that both of these treatments, like insulin, induce a hypoglycemic response[3, 7]. These findings add additional support for the existence of a reciprocal relationship between the glycemic state of an animal and its susceptibility to a wide variety of stressful stimuli[3, 4, 7, 11].

Effect of insulin on susceptibility of CFW mice to hypoxic decompression

Insulin treatment	Survival time (sec)	
	252 mm Hg	277 mm Hg
0.5 unit injected i.p. 10 min	15	15
before decompression	15	15
	25	50
	40	50
		90
		130
Mean ± S.E.	23.8 ± 5.9	58.3 ± 18.3
No insulin	45	150
	60	165
	90	165
	90	240
		330
		1800[a]
Mean ± S.E.	71.3 ± 4.2	210.0 ± 30.3

[a] Not included in calculation of mean survival time. $P < 0.01$ for difference of means between experimental and control groups.

Résumé. On a constaté que les souris traitées à l'insuline possèdent une sensibilité élevée à la décompression hypoxique. Ce résultat concorde avec l'hypothèse d'une relation inverse entre la quantité de glucose dans le sang et la sensibilité d'un hôte à une grande variété de «stressors».

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