However, studies on the sodium-potassium activated transport adenosinetriphosphatase of rabbit erythrocytes have suggested that this enzyme is not stimulated by sodium salicylate[2,12].

Studies are in progress to investigate further the site(s) of salicylate stimulated erythrocyte inorganic phosphate release, and to determine whether this phenomenon is related to the salicylate induced acceleration of erythrocyte glycolysis.

Zusammenfassung. Natriumsalizylat in Konzentrationen von $2–20 \times 10^{-3} M$ verursacht einen bemerkenswerten Anstieg an anorganischem Phosphat sowohl in Kaninchen- wie auch in Menschenerythrozyten, die in 0,9% Natriumchlorid oder Tyrode-Locke's Lösung mehrfach gewaschen und suspendiert wurden.

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Respiratory Reflexes During Anaphylactic Bronchial Asthma in Guinea-Pigs

Reversible bronchial asthma is produced in guinea-pigs sensitized to egg albumen by inhalation of antigen aerosol. A series of investigations carried out on several hundred animals with the object of throwing further light on the neurophysiological factors that underlie anaphylactic bronchial asthma – and in particular the role played by the vagus, chemoreceptors and central nervous mechanisms – have led to the demonstration that characteristic structural changes occur in the lungs during an attack, and that these in turn give rise to respiratory and circulatory reactions[1–3].

At the onset of rising bronchial resistance, a marked inspiratory reaction, characterized by tachypnoea, occurs; the resultant increase in lung volume is augmented by air trapping. The inspiratory reaction, observed in anaesthetized animals as well as in animals decerebrated at mid-collicular level, is not due to stimulation of the chemoreceptors for it is not abolished by denervation of the carotid and aortic bodies. At later stages, however, hypoxia develops, and the chemoreceptors come into play. Depending on the strength and duration of a severe asthma attack, hypercapnia bringing about direct reinforcement of central respiratory mechanisms may in addition arise, to which extra-vagal proprioceptive reflexes should probably also be added.

The inspiratory reaction represents the dominant respiratory effect, and is mainly responsible for the circulatory changes that follow, namely, a reversible fall in mean arterial blood pressure and an increase in heart rate. The inspiratory reaction is not affected by atropine (Figure, signal a) and, as it is abolished following section of the vagus on both sides (signals b and c), is mediated by afferent fibers running in this nerve. It has been possible by means of reversible cold block, selective electrical stimulation, and recording of the neurogram from vagal filaments, to establish that the fibers specifically concerned with the reflex arise from deflation receptors. The latter become active during the expiratory phase of asthmatic breathing. Further studies have shown that these receptors respond to forced deflation (i.e., increased intrathoracic pressure) during shift of the intrapleural negative pressure to positive values. This increase in intrathoracic pressure in turn leads to increase in bronchial resistance. Compression of the chest wall augments the inspiratory reflex, whereas thoracic distension, during which the expiratory intrapleural pressure reverts to subatmospheric values, diminishes it. These results lend support to the conclusions of Wyss[4,5] that stimulation of the deflation receptors enhances inspiratory efforts, and thereby suppresses pulmonary collapse, or local effects such as atelectasis and pulmonary compression, but hampers the mechanisms subserving the self-regulation of respiration[6,7].

It has been shown by Paintal[8] that the deflation receptors in the cat are situated in the respiratory bronchioles, atria or alveoli. Our histological studies of lungs fixed in vivo during an asthma attack reveal that the anaphylactic narrowing or obstruction, which occurs predominantly in the bronchioles, leads to emphysema and microscopic atelectasis, conditions which imply a disturbance in the intrapulmonary distribution of air ventilating the alveoli, in particular, an increase in functional residual capacity. These findings strongly suggest that the afferent vagal fibers responsible for the inspiratory reaction arise in atelectatic areas dispersed throughout the overinflated lungs, whereas augmented pulmonary stretch receptor activity is correlated with emphysema. A chain of events would thus be set up which appears to develop in the following order: Structural pulmonary changes, i.e., anaphylactic obstruction of bronchioles resulting in emphysema and atelectasis; atelectasis, giving rise to the inspiratory reaction associated with tachypnoea and increase in functional residual capacity. These events – in which the Hering-Breuer reflexes are suppressed by deflation receptor activity – lead to ever-increasing disturbance of the lung mechanics described. The cycles succeed one another as long as reversible anaphylactic airway obstruction persists.

The inspiratory reaction is produced by inhalation of antigen aerosol particles that do not exceed 0.5–10 μ in

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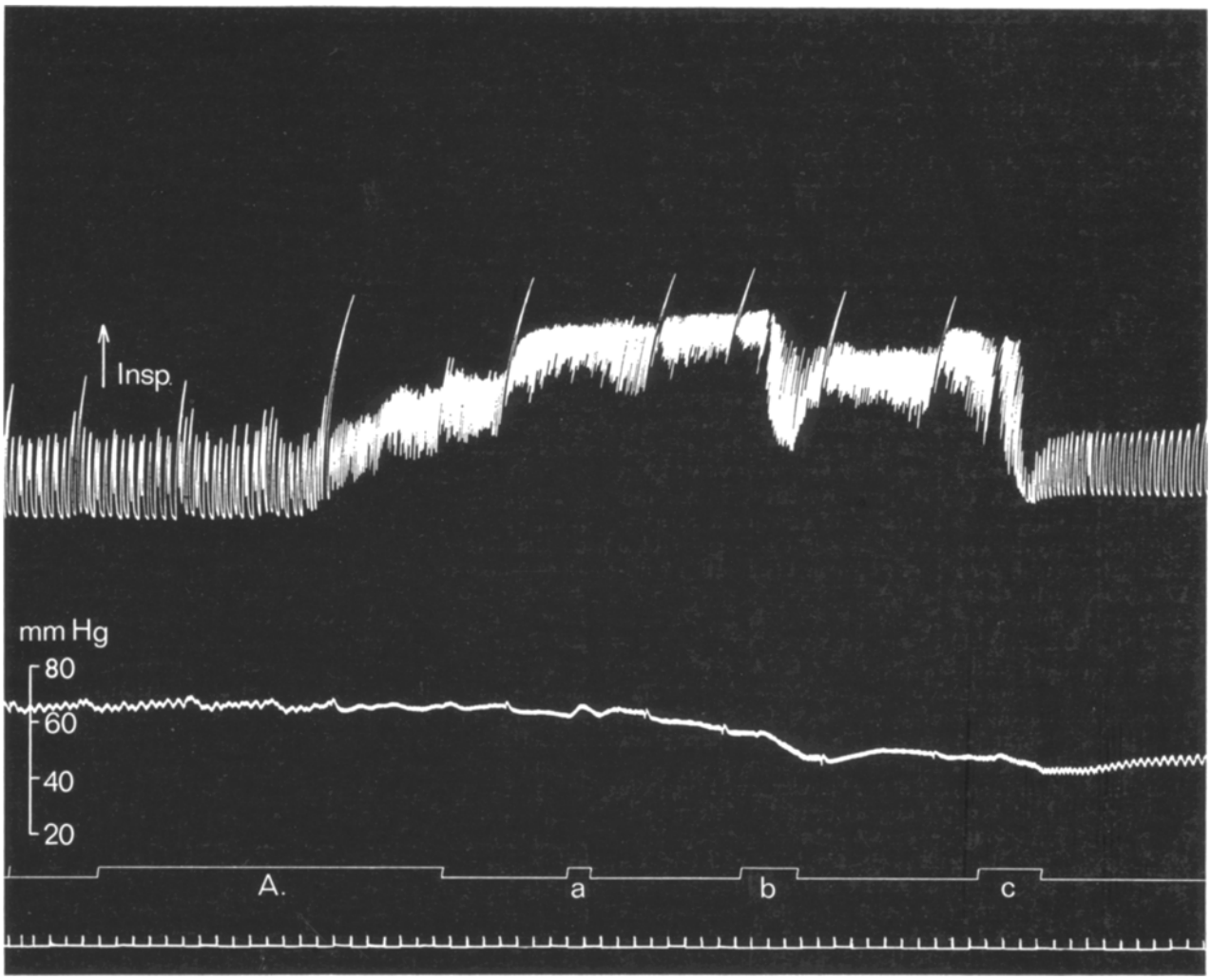

Vagal respiratory reflex during anaphylactic bronchial asthma. A, inhalation of antigen aerosol; a, i.v. administration of atropine sulfate (2 mg/kg body weight); b and c, vagotomy on both sides. Guinea pig anaesthetized with Urethane. Body plethysmography, respiration upwards. Time intervals = 3 sec.

size. Larger particles – even when inhalation is prolonged – produce a respiratory reaction characterized by bradypnoea and active expiration, responses indicating that stenosis has occurred in the upper airways, and closely resembling the effect on breathing produced by occlusion of the trachea. During severe asthma attacks or anaphylactic shock, bradypnoea and active expirations may follow upon the inspiratory reaction.

COLEBATCH, NADEL and OLSEN[9] have described 2 types of airway constriction in the cat, namely 'larger airway' and 'peripheral airway' constriction. Our results suggest that 2 similar types of airway constriction may also occur in the guinea-pig. Bradypnoic breathing would then be the result of larger airway constriction, tachypnoic breathing the result of constriction of the peripheral airways. In conclusion it should be pointed out that the respiratory reflexes mediated by the vagus depend to some extent on the species studied[10,11].

The marked inspiratory reaction during anaphylactic bronchial asthma in the guinea-pig is a 'Fremdreflex der Atmung'[12], a reflex in our animals brought about by the disturbance in the mechanics of breathing produced by structural changes in the lungs. The latter set up a series of events which in turn start off a vicious circle in which the inspiratory reaction represents a defence mechanism of the lungs 'constrained' by overinflation in the thoracic cage.

Zusammenfassung. Im anaphylaktischen Asthma bronchiale des Meerschweinchens führen Störungen der Lungenentfaltung zu einer starken inspiratorischen Reaktion, welche auf die end-exspiratorische Erregung von Kollapsrezeptoren zurückgeführt werden kann.

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