

AFFERENT VAGAL IMPULSES IN ANAPHYLACTIC BRONCHIAL ASTHMA

E. A. KOLLER

Department of Physiology, University of Zurich, Switzerland

Abstract. The role played by both lung stretch and lung deflation components of the pulmonary vagus has been studied, in order to throw further light on the changes in lung mechanics which underlie the lung deflation receptor activity and hence the activation of respiration during an asthma attack. The discharge pattern of the lung stretch receptors varies from unit to unit, but also in one and the same unit during an asthma attack. The heterogeneous pattern of the stretch receptor units seen during the latter indicates uneven ventilation: the increased stretch receptor activity during both phases of respiration points to overinflation of the lung units concerned during inspiration, and to insufficient relaxation during expiration; the decreased stretch receptor activity in inspiration, combined with deflation receptor discharges in expiration, would indicate that the lung units concerned are poorly inflated during inspiration and subjected to forced deflation during expiration. The reflex mechanisms underlying the activation of respiration during an asthma attack are discussed.

INTRODUCTION

Problems connected with the striking increase of respiratory activity which occurs during a bronchial asthma attack have been studied in this laboratory for several years. In 1967 I was able to demonstrate in guinea-pigs that this increased respiratory activity is mainly due to stimulation of vagal excito-inspiratory fibres arising in the so-called "pulmonary deflation receptors" (Koller 1967, 1968, 1969). The importance of the deflation receptors in the respiratory and circulatory effects of anaphylactic bronchial asthma has also been demonstrated in the rabbit by Karczewski and Widdicombe (1969), who stated that "anaphylaxis stimulates lung deflation and irritant receptors which mediate much

of the reflex responses". It is, however, rather surprising that the lung deflation reflex should be brought about by the well-known increase of lung volume which occurs during a bronchial asthma attack. We therefore decided to study the role played by both lung stretch and lung deflation components of the pulmonary vagus more closely, in the hope of throwing further light on the changes in lung mechanics which underlie deflation receptor activity during an acute attack.

Reversible bronchial asthma was produced in spontaneously breathing guinea-pigs sensitized to egg albumen by adding the antigen aerosol to the air inspired. The animals were anaesthetized with urethane or decerebrated at mid-collicular level. Afferent vagal activity was recorded from single or quasi-single fibres (preparations exhibiting unit activity, but containing at the most 2-4 units) in the otherwise intact vagus. In order to differentiate between lung stretch and lung deflation receptor activity, the thorax of the guinea-pig was compressed or distended by applying increased or decreased plethysmographic pressure. It is well-known that lowered intraplethysmographic pressure, i.e., thoracic distension, enhances lung stretch receptor activity and that raised pressure, i.e., thoracic compression, induces the reverse effect (Hammouda and Wilson 1932, Adrian 1933). At pressure thresholds of roughly 5 cm H₂O and over, the so-called lung deflation receptors also come into play (Ferrer and Koller 1968).

PULMONARY STRETCH RECEPTOR ACTIVITY

If the activity of the lung stretch receptors during normal breathing and during an asthma attack is compared (Fig. 1AB), it will be seen that the stretch receptor discharges during normal breathing are characterized by regular sequences in inspiration (Fig. 1A). A striking change occurs, however, during the asthma attack: The discharges may increase, decrease, or — as in Fig. 1B — continue to fire during expiration, which means that distension persists in the lung unit, instead of giving way to normal relaxation (see inset Fig. 1).

In order to compare the discharge pattern in a single stretch receptor unit during an attack with activity immediately preceding the attack, we averaged the stretch receptor impulses per 10th of a second, which allowed us to determine the stretch receptor activity quantitatively 1 min, 2 min and 5 min after attack onset. Among the results obtained, we shall briefly attempt to describe two examples:

In the first, activation of the stretch receptor diminished at onset of the attack — indicating that the inspiratory distension of the lung unit was impeded. One minute later, the discharges increased, but the

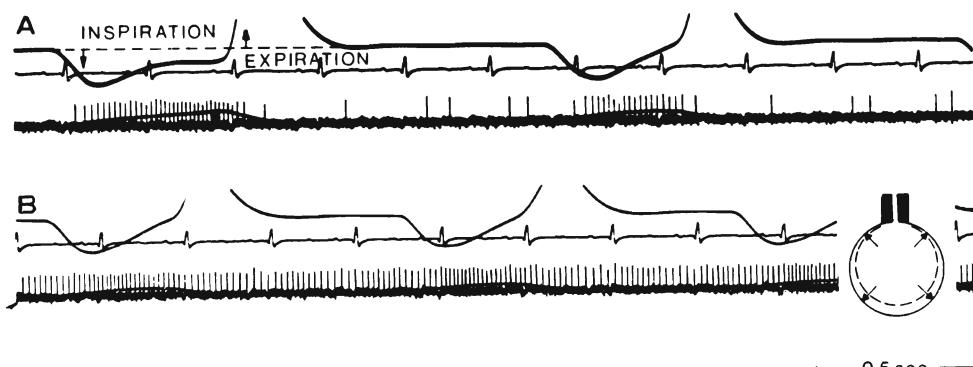


Fig. 1. Pulmonary stretch receptor activity during uninfluenced spontaneous breathing (A) and asthma attack (B). The persistence of the lung stretch receptor activity during expiration in asthma attack (B) indicates impeded expiratory airflow and hence insufficient relaxation of the lung unit (see inset). From top to bottom: Tracheal cannula side-pressure, ECG, afferent vagal neurogram.

pattern seen in normal respiration was no longer visible. The respiratory phases were more or less indistinguishable, because the pulmonary stretch receptor continued to discharge during expiration. Five minutes after attack onset, practically the same picture obtained, although stretch receptor activity had again increased somewhat and could be qualified as tonic. It was at any rate no longer possible to speak of inspiratory activation and expiratory inactivation of the lung stretch receptor.

The second example showed practically the reverse: At first an increase, then a gradual decrease of stretch receptor activity. Inspiratory activation of the stretch receptor was still present, and hence inspiratory distension of the lung unit; but expiratory relaxation had become difficult, as the persistence of the stretch receptor activity indicated. Five minutes after attack onset, the relaxation of the lung unit concerned ceased altogether. In its place appeared a paradoxical increase of stretch receptor activity in expiration. The lung unit, however, — when the low frequencies of the receptor discharges during both respiratory phases are taken into account — was more or less relaxed, and the air content reduced, although it is impossible to say where the air had passed.

The two examples indicate, that regular inspiratory pattern of stretch receptor discharges during normal breathing gives way to a heterogeneous pattern during bronchial asthma, which varies from unit to unit, but also in one and the same unit.

In order to compare the discharge pattern of all the stretch receptor units studied, we averaged the impulse sequences per respiratory phase before and during the asthma attacks, which enabled us to obtain the

frequency and the distribution of mean stretch receptor activity during inspiration, expiration and during both respiratory phases. If the normal distribution of mean activity during inspiration was compared with the attack distribution, it was seen that average stretch receptor discharge increased or decreased during the attack. Consequently, the range of mean inspiratory stretch receptor activity extended, and continued to extend as the attack developed. During the expiratory phase of normal respiration, 60 out of the 88 stretch receptor units studied remained practically inactive. During asthma, however, only about one-half of these units remained inactive 1 min after attack onset; one-quarter, after 2 min; and one-fifth after 5 min; which means that almost all the lung stretch receptors continued to discharge during the expiratory phase of acute asthma. It was hence impossible for the lung units concerned to relax normally. By comparing both phases of respiration during normal breathing and during an attack, it was seen that the narrow and uniform range of mean stretch receptor activity during normal respiration had given way to a broader distribution of mean activity, so that we could now speak of uneven ventilation of the lung units during the asthma attack.

To sum up: The mean activity of the lung stretch receptors increases during the attack in most of the units, particularly during expiration; in a few, however, a decrease occurs.

PULMONARY DEFLATION RECEPTOR ACTIVITY

In connexion with this decrease, we shall now add a few comments concerning the activity of the so-called lung deflation receptors. Figure 2 shows normal stretch receptor activity (top row) and altered afferent activity in the vagus filament during an asthma attack (bottom row). In the latter we can see that stretch receptor activity is reduced, which signifies that expansion of the lung unit concerned is also reduced in inspiration. During expiration, however, it is evident that a fresh set of fibres has come into play. We have come to the conclusion that we are dealing here with lung deflation fibres. This conclusion is based on previous observations (Koller 1968, Ferrer and Koller 1968), indicating that similar activity — as here shown in Fig. 2 B — can be enforced in histamine or anaphylactic bronchial asthma by increasing pressure on the thorax, or by inducing a pneumothorax, and abolished by decreasing the pressure on the thoracic cage. This shows that the fibres are obviously excited by lung compression, or collapse, which would justify the German expression used for them "Lungenkollaps-Fasern", or the old English term "lung deflation fibres".

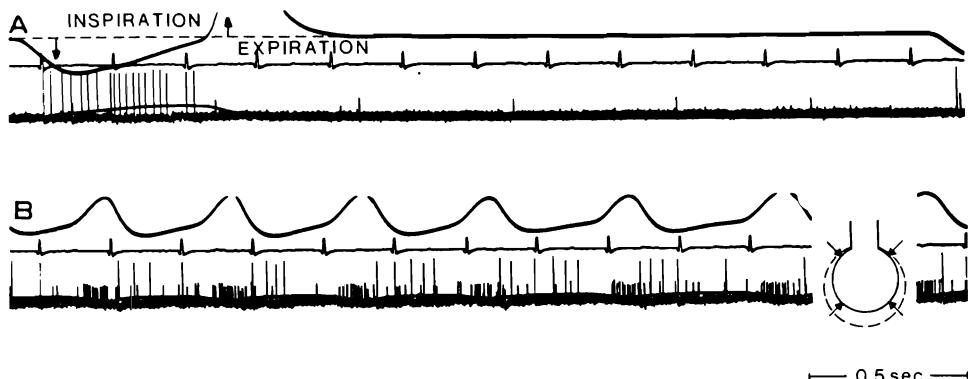


Fig. 2. Afferent impulses in a filament of the lung vagus during uninfluenced spontaneous breathing (A) and asthma attack (B). The reduced stretch receptor activity during inspiration and the excitation of lung deflation receptors during expiration (B) indicate poor inspiratory expansion and expiratory compression of the lung unit (see inset). From top to bottom: tracheal cannula side-pressure, ECG, afferent vagal neurogram.

CONCLUSIONS

The examples just presented have led us to conclude that the neurograms recorded during an asthma attack indicate uneven ventilation. The increased stretch receptor activity during inspiration and expiration,

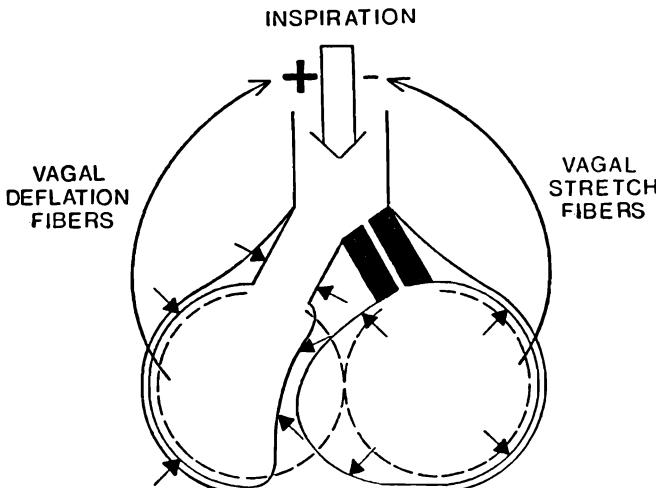


Fig. 3. Reflex mechanisms underlying the activation of respiration during an asthma attack. The two lung units in the thoracic cage indicate uneven ventilation: The overinflated lung unit (right side) elicits the lung inflation reflex, but also compresses the collapsible unit (left side) during expiration, which in turn elicits the predominant lung deflation reflex, i.e., respiratory activation and hence increased uneven ventilation.

seen in some records, points to overinflation of the lung units during inspiration and to insufficient pulmonary relaxation during expiration. The decreased stretch receptor activity in inspiration, combined with deflation receptor discharges in expiration seen in other records, would indicate that the lung units are poorly inflated and cramped during inspiration, subjected to forced deflation during expiration.

The striking increase of respiratory activity during a bronchial asthma attack might hence be explained as follows (Fig. 3): As expiratory air-flow during the asthma attack is impeded in the affected lung areas (Fig. 3, right lung unit), air-trapping and regional overinflation occur. The overinflated alveoli during the expiratory rise in intrathoracic pressure compress the still collapsible alveoli and bronchioli (Fig. 3, left lung unit), which leads to excitation of the lung deflation receptors. The lung deflation reflex in turn reinforces the uneven ventilation and the bronchial obstruction, and overrules the heterogeneous respiratory effects of the stretch receptors (Koller et al. 1971).

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