EFFECT OF NARCOSIS AND AMINAZINE ON RESPIRATION UNDER EXCESSIVE INTRAPULMONARY PRESSURE

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The afferent impulsation of various modalities, as is well known, exerts a substantial effect upon the regulation of respiration [10, etc.]. The inhibition of the activity of the respiratory apparatus during deepening of narcosis may be explained not only by a reduction of the reactivity of the neurons of the central nervous system, but also by a substantial contraction of the influx of afferent pulses to the respiratory center as a result of blockage of the reticular formation of the brain stem by narcotics [12, 13, 14, 17]. When excessive intrapulmonary pressure is created, the influx of afferent pulses into the central divisions of the nervous system, both from the receptors of lung distention and from most of the other receptor fields, is undoubtedly intensified [11]. Consequently, the changes in the respiration under the action of excessive pressure in a narcotized animal should differ from those in a nonnarcotized animal. Only individual facts indicating a weakening of the adaptive mechanisms for respiration under excessive intrapulmonary pressure have been described in the literature [1, etc.].

Since a direct relationship of the reticular formation of the brain stem to the reception, reprocessing, and transmission of the flux of afferent impulses entering the central nervous system has been demonstrated, it is believed that under the action of aminazine, which blocks the reticular formation and influences respiration under normal conditions [2, 5-8], changes should occur in the neuroreflex regulation of the respiratory apparatus under conditions of excessive pressure. We have encountered no such investigations in the literature.

The purpose of this work was to determine the influence of narcosis and aminazine on the nature of respiration in a state of excessive intrapulmonary pressure and to determine more precisely the significance of afferentation in the change in the work of the respiratory apparatus under conditions of excessive pressure in the lungs.

EXPERIMENTAL PROCEDURE

Acute experiments were conducted on cats under ether and nembutal narcosis (30-40 mg/kg intraperitoneally). In an investigation of the effect of narcosis, a waking state and ether (or nembutal) narcosis was alternated in each animal. In another series of experiments, 10-15 min after cessation of the delivery of ether vapors, the animals received injections of aminazine into the muscles of the femur (5 mg/kg). The excessive intrapulmonary pressure of medicinal oxygen, equal to 30 mm Hg, was created with a series-produced aviation oxygen instrument, connected to the lungs of the animal through a tracheotomy tube. In response to a 2 min increase in the intrapulmonary pressure, the animals exhibited a delay in respiration (apnoea), then the respiratory motions were resumed—the so-called slipping away occurred, immediately followed by stoppage of respiration. Sometime after the excessive intrapulmonary pressure was disconnected, normal respiration was restored. Such influences were repeated many times. In the intervals between them, the animals breathed atmospheric air. It was shown earlier [1] that the effects of respiration under excessive intrapulmonary pressure of oxygen do not differ from the effects of respiration under excessive air pressure.

The effect of narcosis and aminazine on the work of the respiratory apparatus under conditions of excessive intrapulmonary pressure was judged according to the electrical activity of the intercartilaginous portion of the internal

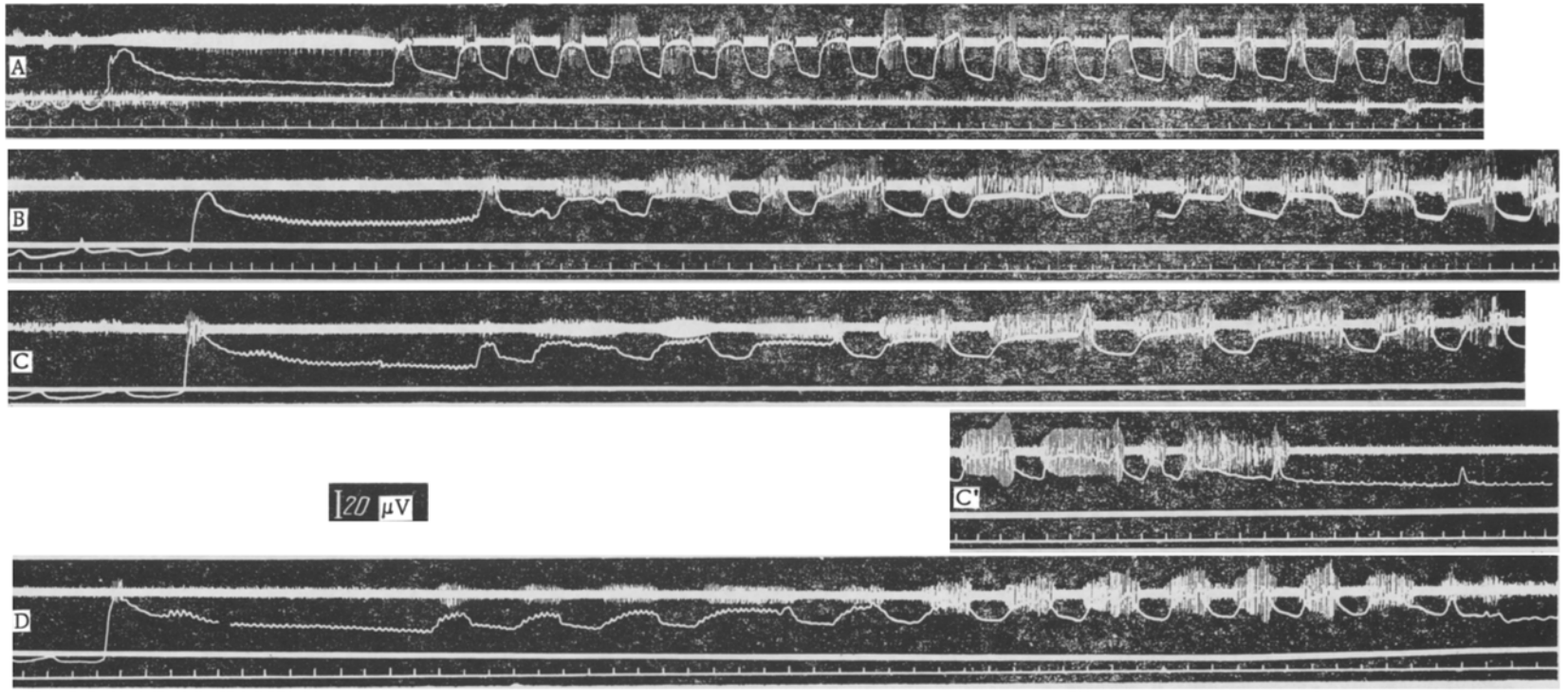

Fig. 1. Effect of narcosis on the change in respiration and electrical activity of mice in a state of excessive intrapulmonary pressure. A) Nonnarcotized animals; B) 10 min after injection of nembutal; C) after 20 min; D) after 30 min; C') continuation of recording of C. The meanings of the curves (from top to bottom): EMG of internal intercostal muscles; respiratory motions of the lower part of the thoracic cavity; EMG of the rectus abdominis muscle; time marking 1 sec.

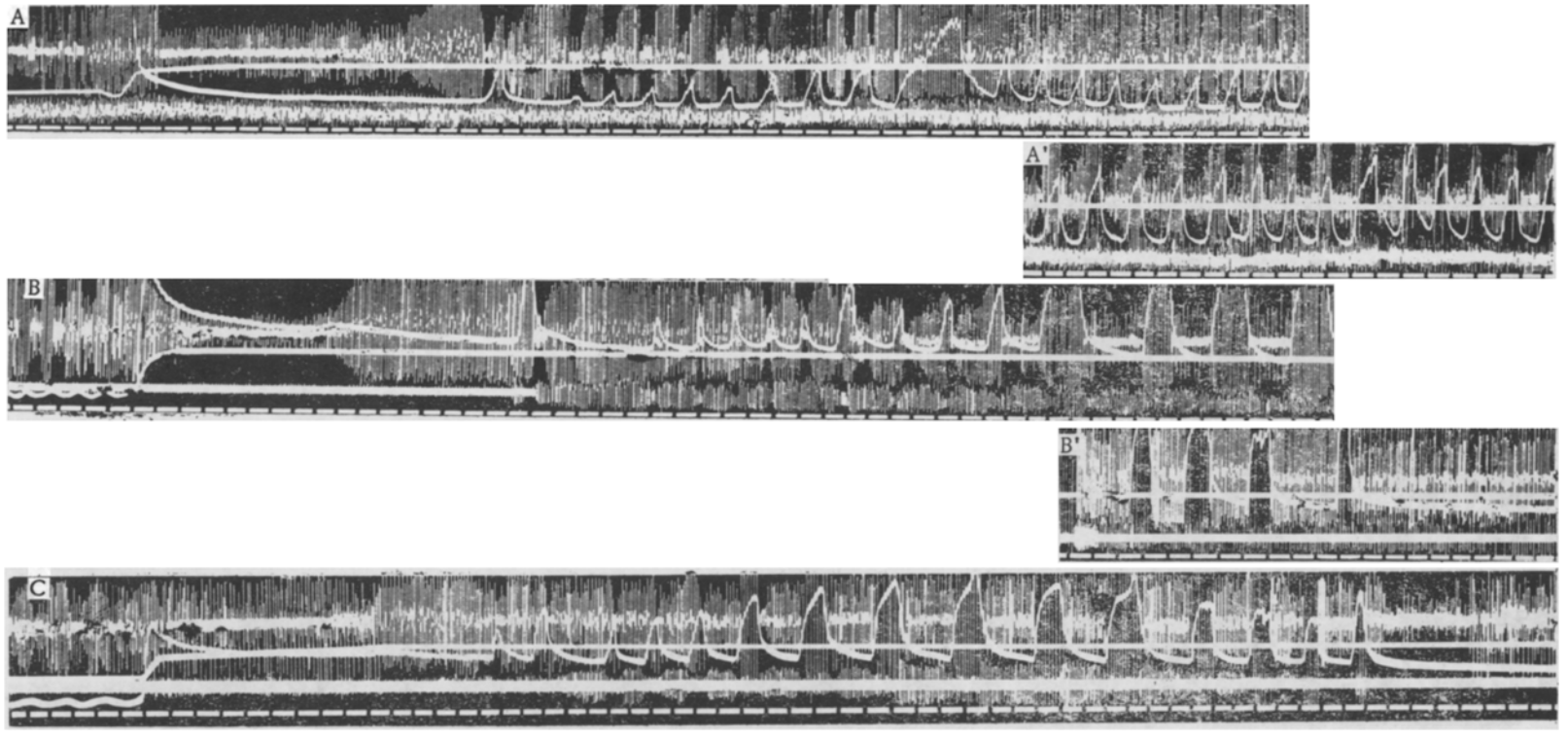

Fig. 2. Effect of aminazine on the nature of respiration and the electrical activity of the muscles during excessive intrapulmonary pressure. A) Before injection of aminazine; B) 10 min after injection; C) after 45 min; A' and B') continuations of corresponding recordings. Meaning of curves (from top to bottom): EMG of internal intercostal muscle; respiratory motions (inhalation—top); marking of connection of excess intrapulmonary pressure: EMG of rectus abdominis muscle.

intercostal muscles in the 3rd-4th intercostal space and of the rectus abdominis muscle, the duration of the respiratory lag, moment of onset of stoppage of respiration, and duration of the period of slipping away before and after the injection of these substances.

Steel needle electrodes were used to draw off the electrical activity of the muscles. The influence of narcosis was investigated on 15 cats, that of aminazine on 14.

EXPERIMENTAL RESULTS

We had noted earlier [3] that the duration of the lag in respiration under the action of excessive intrapulmonary pressure in animals under superficial narcosis was shorter than in animals in a state of more profound narcosis. It was also shown that when narcosis is deepened, the duration of the respiratory lag increases [9].

In this investigation, in which a state of narcosis and a waking state were alternated in each animal, the respiratory lag under excessive intrapulmonary pressure lasted an average of 22±5 sec during ether narcosis. After the delivery of ether had stopped, and the animal had awakened, the lag was reduced on the average to 12±3 sec; i.e., was decreased by 45% ($P = 0.001$). A subsequent injection of nembutal again led to an increase in the duration of the lag period, to 21±5 sec on the average.

In addition to increasing the period of lag in respiration, narcosis induced a substantially earlier onset of stoppage of respiration. During ether narcosis, 64±13 sec elapsed before the onset of stoppage of respiration; in the same animals, the stoppage of respiration without narcosis occurred 50% later, ($P < 0.001$), while after the injection of nembutal, the time until the onset of stoppage of respiration was reduced to an average of 56±12 sec.

Thus, in the narcotized animals, the duration of the period of slipping away was reduced both as a result of lengthening of the respiratory lag and as a result of the earlier onset of the stoppage of respiration.

It might be felt that the contraction of the period of slipping away, i.e., the reduction of the tolerability of respiration under excessive intrapulmonary pressure during the action of narcotics shows the importance of neuroreflex mechanisms in regulating the work of the respiratory apparatus under these conditions.

The sequence of changes in the respiration under excess pressure, i.e., the replacement of the lag by slipping away, followed by stoppage of respiration, just like the nature of the participation of the muscles in the respiratory motions, was found to be the same in animals in a state of narcosis and in animals not subjected to its action. However, in nonnarcotized cats, the respiration during the period of slipping away was distinguished by great constancy of the duration of inhalation, the frequency and depth of the respiratory motions (Fig. 1, A, B). In the narcotized animals, during respiration under excessive intrapulmonary pressure, the duration of inhalation was substantially increased, while the duration of exhalation changed little. Continuous (nonphase) activity during the period of the respiratory lag was sharply weakened, and a more substantial reduction of the frequency of the respiratory motions and decrease in the amplitude of the electrical activity of the muscles were noted (especially the rectus abdominis muscle in respiration under excessive intrapulmonary pressure) (see Fig. 1, B-D).

After the injection of aminazine, the respiration of the animals under normal pressure became less frequent and somewhat deeper. Correspondingly to the increase in the duration of inhalation, the activity in the internal intercostal muscle also became more protracted (Fig. 2, A, B, C). In the rectus abdominis muscle, the activity was substantially reduced in a number of experiments (see Fig. 2, B, C).

The injection of aminazine did not produce any significant changes in the duration of the respiratory lag.

The time until the onset of stoppage of respiration after the injection of aminazine was reduced from 117±7 to 68±11 sec, i.e., by 42% on the average ($P < 0.001$), so that the duration of the period of slipping away was appreciably contracted.

The nature of the respiratory motions did not change significantly during respiration under excessive pressure. After the injection of aminazine, when excessive intrapulmonary pressure was created, the respiratory motions became less frequent than under the conditions of excessive intrapulmonary pressure before the injection of aminazine; moreover, exhalation became longer than inhalation (see Fig. 2).

The activity of the muscles after the injection of aminazine under conditions of respiration under excessive intrapulmonary pressure did not differ significantly from the activity of the muscles before the injection of this preparation.

Narcotics of various kinds substantially change the reactions of the animal to external influences. The predominant effect of narcosis on the central nervous system, i.e., the inhibition of the activity of the higher divisions of the nervous system, reduces the functional potentialities of the animal. In addition to the generally accepted ideas of the mechanism of the action of narcosis, as a pharmacological deafferentation of the cerebral cortex, the hypothesis has been advanced that the narcotic state develops as a result of the disconnection of the nonspecific toning impulsation of the ascending reticular formation of the brain stem [15, 16, 17]. Probably narcotics, acting on the reticular formation of the brain stem, weaken the influx of afferent impulses and thus reduce the inhibiting effect on the nervous system of the activating reticular formation. The more substantial inhibiting effect of nembutal in comparison with ether is indicative in connection with this.

Such an effect of narcosis as a whole does not change the rearrangement of the regulation of respiration, which occurs under the influence of excessive intrapulmonary pressure, since it does not disturb the intimate mechanisms of the function of the neurons of the respiratory center, but weakens the possibility of conservation by the neurons of the intracentral coordination relationships in the nervous system, newly developed during excessive intrapulmonary pressure. It has been shown [4] that the discharging activity of the inspiratory neurons gradually decreases toward the end of the period of slipping away, and the frequency of pulses in the discharge decreases. Thus, as narcosis becomes deeper, the supplementary reserve potentialities of the neurons of the bulbar respiratory center in maintaining new intracentral interrelationships are reduced.

The basic processes or reorganization of respiration under excessive pressure in the lungs (respiratory lag, period of slipping away, and stoppage of respiration) also undergo certain changes under the influence of aminazine. Probably the mechanism of adaptation of the respiratory center to excessive intrapulmonary pressure is closely related to the functioning of the reticular formation. In view of this, the antagonistic influences of aminazine and adrenalin on respiration under excessive pressure are of definite interest: adrenalin in large doses causes a lengthening of the respiratory lag and inhibition of the activity of the muscles, but does not affect the frequency of respiration under excessive intrapulmonary pressure and the duration of the period of slipping away [3]; aminazine, on the other hand, does not significantly affect the duration of the respiratory lag and the electrical activity of the muscles, but caused a slow down of respiration and a substantial reduction of the period of slipping away. Moreover, the injection of one of these substances against a background of the action of the other exerts an opposite influence.

The antagonism of the influence of aminazine and adrenalin indicates the participation of reticular neurons in the reorganization of the work of the respiratory apparatus during the creation of excessive intrapulmonary pressure [4]. Moreover, the different effects of aminazine and adrenalin once again emphasize the different physiological nature of the appearance of the respiratory lag and the onset of stoppage of respiration; i.e., these substances exert different effects upon individual units of the complex chain of intracentral relationships during the action of excessive intrapulmonary pressure, although they do not disturb the sequences of unit development.

Hence, investigations of the influence of narcotics and aminazine on respiration under excessive intrapulmonary pressure show the definite significance of the state of the central nervous system in the peculiarities of the reticular formation, in the toleration of difficult conditions of respiration, i.e., in the maintenance of new intracentral relationships of the neurons of the respiratory center, developed under the action of changed afferentation.

SUMMARY

Creation of excessive intrapulmonary pressure (EIP) in cats at first caused delay in respiration followed by resumption of respiratory movements (i.e., escape) and by arrest of respiration after a certain time. In narcotized animals the duration of the escape period decreased both as a result of prolongation of respiratory delay and also as a result of a faster onset of cessation of respiration.

In animals under deep anesthesia the duration of inspiration under excessive intrapulmonary pressure increased considerably while the duration of expiration changed but slightly.

In respiration under excessive pressure following aminazine injection, substantial changes in respiratory delay are absent, while the period before the onset of respiratory arrest decreases $1^1/_2$ times as a result of which the duration of the escape period becomes less. Respiratory movements becomes less frequent than before aminazine injection, expiration growing to a greater length than inspiration.

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