Impact of Industrial Hydrogen Sulfide-Containing Natural Gas from the Astrakhan Condensed Gas Deposit on the Activity of Respiratory Neurons

E. B. Velikanov and V. A. Safonov

UDC 613.632,4:546.221.1]-07

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 116, № 7, pp. 32-34, July, 1993. Original article submitted March 4, 1993

Key Words: *hydrogen sulfide; natural gas; brain; respiratory center; respiratory neurons*

The industrial development of the Astrakhan condensed gas deposit with a high content of hydrogen sulfide has led to a considerable deterioration of environmental quality in the Volga-Caspian basin. As a consequence of accidental emissions of a toxic industrial hydrogen sulfide-containing gas from this deposit, cases of poisoning have occurred among people. As demonstrated by clinical and pathophysiological studies, hydrogen sulfide-containing gaseous mixtures are neurotoxic and may be lethal. That hydrogen sulfide exerts toxic effects, notably on the respiratory system, has been known for a long time. The clinical picture of hydrogen sulfide poisoning is dominated by signs and symptoms of damage to reticular and stem structures of the brain, which results in grossly disordered regulation of respiration and cardiovascular activity [4]. In cats under Nembutal anesthesia that inhaled a pure hydrogen sulfide-containing gas from the Orenburg gas field, an increase in the frequency and depth of breathing during the first 10 sec of exposure was followed by severe inhibition and then complete cessation of breathing within the first minute of exposure [2]. These and other findings indicate that acute exposure to hydrogen sulfide causes profound pathological changes in the CNS with a consequent derangement of the regulation of both respiration and circulation [3].

The purpose of the present study was to examine how firing activity of respiratory neurons is affected by exposure to the toxic hydrogen sulfide-containing gas from the Astrakhan condensed gas deposit.

MATERIALS AND METHODS

For the study, 30 male Wistar rats weighing 250-300 g were used. Prior to the tests, they were kept in the vivarium on a 12 h light-12 h darkness schedule and fed a standard diet with food and water given ad libitum. Under chloral hydrate anesthesia (400 mg/kg intraperitoneally), firing activity of the respiratory center neurons was recorded with extracellular glass electrodes (tip diameter 3-5 μ; resistance 5-10 MOhm) using a standard procedure [5, 6]. The outgoing signal was delivered to a VC-9 oscillograph (Nihon Kohden, Japan) through a cathode follower and registered on a Tembr-2M tape recorder (Russia), followed by selective recording on an electroencephalograph. Concurrently, an electromyogram of the diaphragm was recorded by means of bipolar electrodes (hooks made of nichrome wire 0.3 mm in diameter) fixed via the abdominal cavity.

For assessment of the toxic action of hydrogen sulfide on external respiration, pure natural

Department of Medical and Biological Physics, Medical Institute, Astrakhan; Laboratory for Pathophysiology of Respiration, Institute of General Pathology and Pathophysiology, Russian Academy of Medical Sciences, Moscow. (Presented by A. D. Ado, Member of the Russian Academy of Medical Sciences)

0007-4888/93/0007-0798$12.50

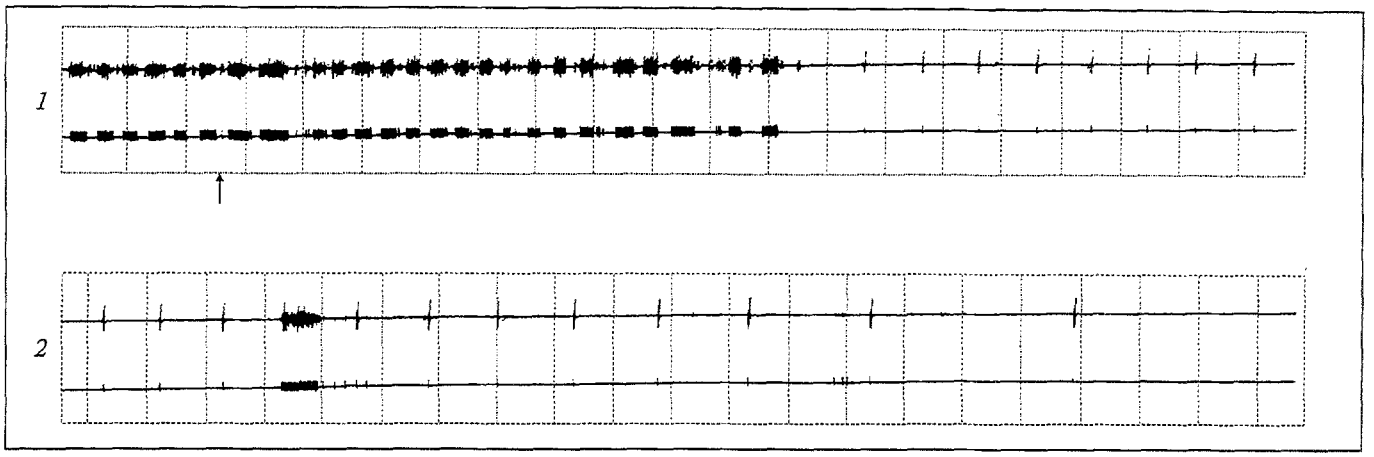

Fig. 1. Activity of the diaphragm and of an inspiratory neuron before and during inhalation of hydrogen sulfide–containing natural gas by a rat. *1* and *2*) continuous recording; the arrow marks the time when inhalation of the gas was started. From the top down: time marks of 1 sec; diaphragmatic EMG; activity of inspiratory neuron.

gas from the Astrakhan deposit was delivered into the rat's trachea.

RESULTS

Rapid changes in the frequency and amplitude of respiratory movements began to be observed as soon as after the first 2 or 3 inhalations of the gas (Figs. 1-4), with marked abnormalities in the duration of the respiratory cycle phases. A sudden and irreversible respiratory arrest occurred after 10 to 15 sec of exposure, accompanied by the disappearance of electrical activity in the diaphragm. The volley-type activity of the respiratory neurons became continuous and remained such for a short time, after which the firing rate progressively decreased to reach zero in several seconds. Firing by the reticular neurons continued for a longer period: it disappeared when no impulses were recorded from any other neurons of the respiratory center.

The subsequent prolonged application of artificial ventilation did not lead to a resumption of natural respiration in any of the rats, even though exposure to the gas was discontinued immediately after the respiratory arrest. Cardiac contractions continued at a decreasing frequency for 3-4 min after the cessation of respiratory movements.

The cessation of respiratory movements and of neuronal activity was of two types. In some rats (Figs. 1; 2, *a*; and 3, *b*) the complete respiratory arrest was preceded by a terminal (agonal) pause of 4 to 12 sec in duration, followed by yet another (the last) inspiration. In other rats (Figs. 2, *b*; 3, *a*; and 4) respiratory movements ceased suddenly without decreasing appreciably either in frequency or in amplitude.

The various types of complete inspiratory neurons that were discharging synchronously from the diaphragmatic EMG terminated their nonvolley activity according to one or other of the indicated types. It should be noted, however, that they were still generating impulses for some time after the last volley (Figs. 1; 2, *a*; and 3). In some cases such firing continued at a diminishing rate for a

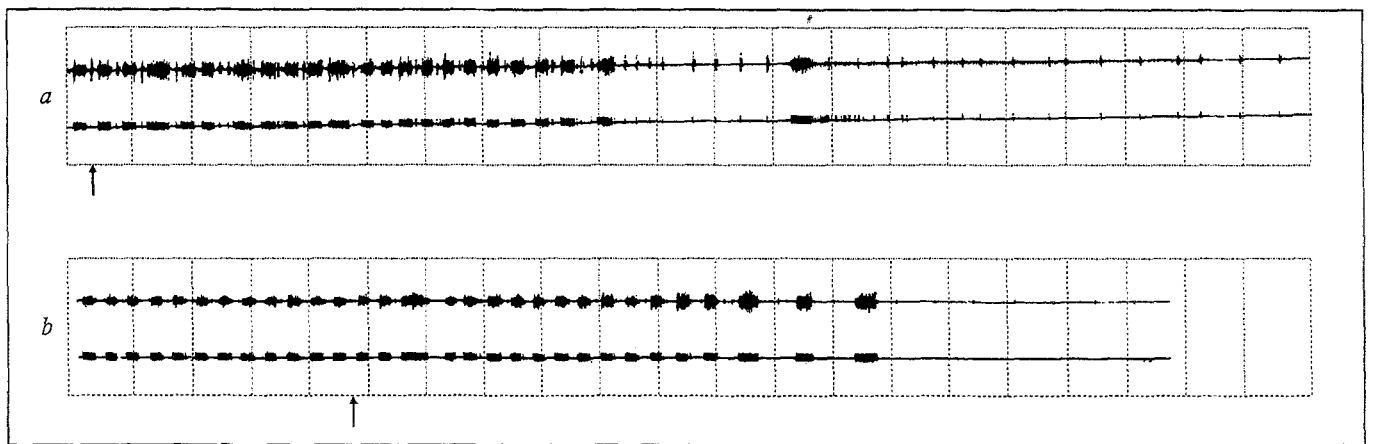

Fig. 2. Differences in cessation of spontaneous rhythmic activity of respiratory center between two rats (*a* and *b*) during inhalation of natural gas. Same designations as in Fig. 1.

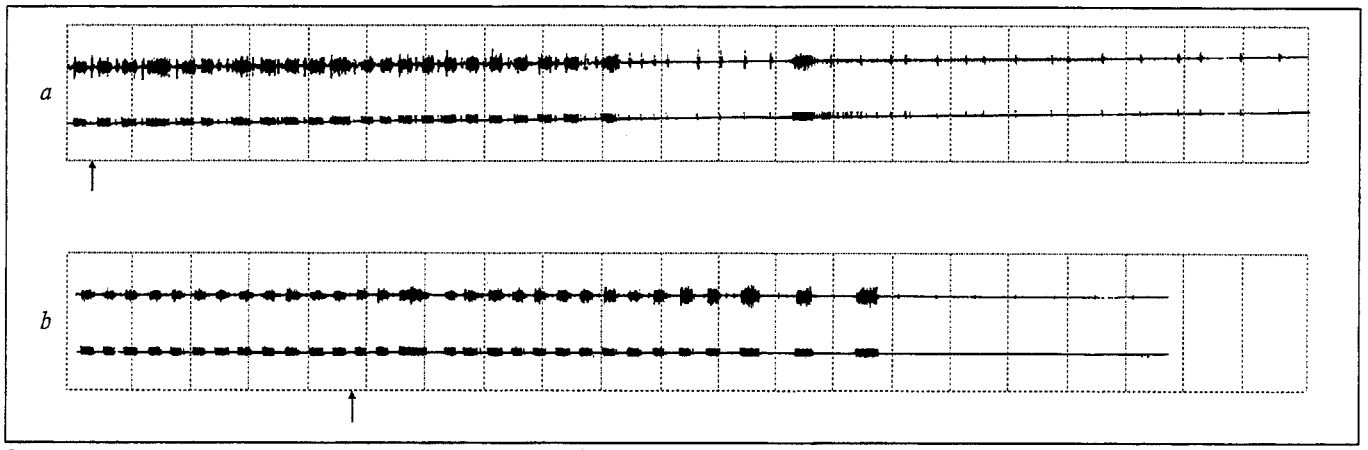

Fig. 3. Variations in activity of a complete (*a*) and a late (*b*) inspiratory neuron during inhalation of natural gas by a rat. The second arrow in *a* marks discontinuation of exposure to the gas. Other designations as in Fig. 1.

relatively long time (10-15 sec) before disappearing completely.

In rats exhibiting a terminal pause, inspiratory neurons were either inactive (Figs. 1 and 2, *a*) or continued to fire throughout the pause and then during the last inspiration (Fig. 3, *b*).

After the cessation of rhythmic breathing, the rate of firing of a neuron that had been firing continuously and with increased frequency at inspiration was somewhat higher as compared to that at expiration, but remained lower than that at inspiration. The phase of increased firing rate was followed by one of progressively decreasing firing rates until complete cessation of impulse discharges (Fig. 4, *a*).

The phase of increased firing rates was most conspicuous with the reticular neurons: the firing rate of such a neuron started to increase even before the termination of rhythmic breathing and was appreciably higher immediately after the cessation of spontaneous respiratory movements (Fig. 4, *b*), but then it fell away to zero rather rapidly, although the reticular neurons ceased to discharge at a later time than did the inspiratory or expiratory neurons.

The observation that respiratory abnormalities arise after the first few inhalations of the gas and lead very rapidly to a complete and irreversible cessation of rhythmic activity of the respiratory center indicates that hydrogen sulfide exerts profound toxic effects on the respiratory neurons. It appears to cause complex metabolic disturbances in the system of these neurons, prompting a search for means of preventing (or inhibiting) the toxicity of this compound.

REFERENCES

1. E. B. Velikanov, M. A. Lebedeva, and L. S. Surkova, in: *Abnormalities of Regulatory Mechanisms and Their Correction* [in Russian], Moscow (1989), Vol. 3, p. 1089.

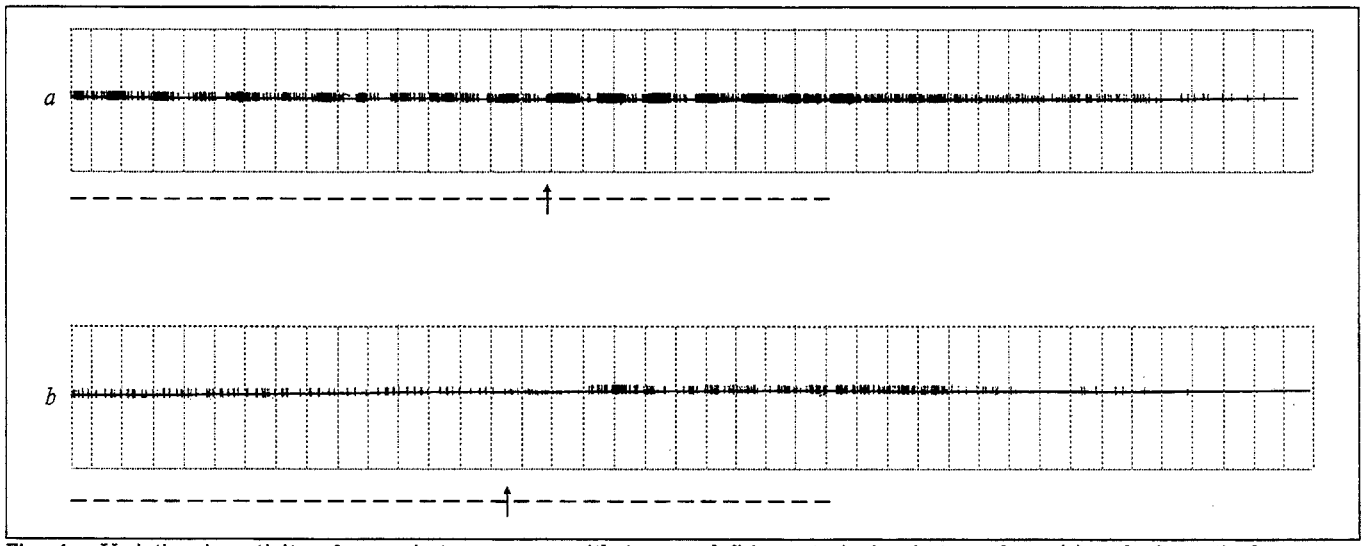

Fig. 4. Variation in activity of a respiratory neuron with increased firing rate in inspiratory phase (*a*) and of a reticular neuron (*b*) during inhalation of natural gas. From the top down: time marks of 1 sec; neuronal activity; marks of inspiratory phase. The arrows indicate the time when inhalation of the gas was started.

2. M. A. Dolgov and V. V. Darsht, in: *Physiology of the Autonomic Nervous System* [in Russian], Kuibyshev (1979), Vol. 1, pp. 176-177.
3. N. I. Kas'yanov, *Klin. Med.*, **46**, № 11, 95-100 (1968).
4. M. I. Sarin, N. V. Sarina, N. D. Topolyanskii, *et al.*, *Klin. Med.*, **50**, № 1, 99-101 (1972).
5. V. A. Safonov, V. N. Efimov, and A. A. Chumachenko, *Neurophysiology of Respiration* [in Russian], Moscow (1980).
6. O. S. Sergeev, *Neuronal Organization of the Respiratory Center in the Medulla Oblongata, and Regulation of Its Activity* (Doctoral dissertation) [in Russian], Moscow (1984).

Respiratory and Circulatory Effects of Inhalation Exposure to Air Mixtures with Low Concentrations of Hydrogen Sulfide-Containing Natural Gas

E. B. Velikanov, N. N. Trizno, I. A. Tarakanov, and V. A. Safonov

UDC 612.1+612.2].06:546.221.1].08

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 116, № 7, pp. 35-38, July, 1993
Original article submitted March 4, 1993

Key Words: *respiration; circulation; hydrogen sulfide; natural gas*

The importance of unraveling the mechanisms by which hydrogen sulfide-containing gases act on living organisms stems from the fact that hydrogen sulfide is highly active both chemically and biologically and can cause serious and even irreparable damage to various organs and systems of the body [2,5]. Although the deleterious effects of hydrogen sulfide-containing gaseous mixtures have been under study for a long time, there is still no agreement among investigators as to how such mixtures act on the vital systems, including the respiratory and cardiovas cular systems. In fact, the available information about the mechanisms of the damaging action of natural gases on these systems is rather fragmentary.

In this study, we measured parameters of pulmonary hemodynamics and respiration in cats inhaling gaseous mixtures with relatively low concentrations of the hydrogen sulfide-containing gas from the Astrakhan condensed gas deposit.

Laboratory for Pathophysiology of Respiration, Institute of General Pathology and Pathophysiology, Russian Academy of Medical Sciences, Moscow; Department of Pathophysiology and Department of Medical and Biological Physics, Medical Institute, Astrakhan. (Presented by S. S. Debov, Member of the Russian Academy of Medical Sciences)

MATERIALS AND METHODS

The study was carried out on 19 nembutal-anesthetized (35 mg/kg i.p.) random-bred cats of both sexes 2-4 kg in weight. Rectal temperature was measured in the cats at the start of the tests and then maintained close to the initial level (±0.5°C) throughout the study period by means of an electric heater. Tracheotomy was performed at the level of the upper third of the trachea; systemic arterial pressure (AP) was measured via a cannula inserted into the femoral artery. In the course of the study, AP, heart rate, breathing rate, and minute volume were recorded with a Russian-made MKh-01 polygraph. Oxygen tension in arterial blood (pO_2) and its reactions (pH) were recorded continuously using a DS67101 flow-through cuvette that contained fixed electrodes and was thermostatically controlled at 37.5°C with a VTS-136 thermostat. Oxygen tension was determined with an E-5046 electrode

0007-4888/93/0007-0801$12.50