PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

PARTICIPATION OF THE NERVOUS SYSTEM IN THE PATHOGENESIS OF ACUTE TOXIC PULMONARY EDEMA

S. M. Leites and N. P. Smirnov

From the Department of Pathological Physiology (Chairman Prof. S. M. Leites) All Union Institute of Experimental Endocrinology (Director Prof. E. A. Vasyukova) Moscow

(Received December 24, 1955. Presented by Academician A. D. Speransky)

The results of a number of investigations* testify to the fact that in the pathogenesis of acute pulmonary edema, an essential role is played by a pathological reflex. The receptors of various sections of the internal medium of the organism form the afferent section of the nervous reflex arc. The center of the arc is situated in the trunk section of the brain below the quadrigeminal bodies [1, 3, 5], and is under the control of the cerebral cortex [3, 4]. A number of investigators consider the sympathetic routes to be the efferent section of the arc [3, 6], and have advanced the idea that hormones of the posterior pituitary [6] are included in routes of the humoral chain.

The question of the participation of the vagus in the efferent section of the arc is not sufficiently clear; some investigators [3], deny this participation and stress the importance of the vagus only as a conductor of the afferent impulses; others [1, 2, 6, 7] do not allow the exclusion of the importance of the vagal efferent impulses in the development of pulmonary edema.

While investigating the role of the pituitary-suprarenal system in the pathogenesis of acute pulmonary toxic edema, we conducted a number of experiments, the results of which are of definite interest in the study of the question concerning the participation of the nervous system in the development of this pathological process.

EXPERIMENTAL METHODS

In the experiments rats were used (89 control and 91 experimental). In the animals of the control groups pulmonary edema was induced by intraperitoneal administration of a 6% solution of ammonium chloride on the basis of 0.6 ml to 100 g animal body weight. In the animals of the experimental groups, the development of edema was investigated after introduction of solutions of novocain, benzene and atropine (doses and times of administration are shown in the table). The rats were killed (if they did not die earlier) 1 hour after the administration of ammonium chloride; on the trachea of the animal, was placed a ligature and the lungs were weighed. The degree of development of edema was determined according to the magnitude of the so-called pulmonary coefficient (ratio of weight of lungs in grams to 100 g of weight of rat). Normally, the pulmonary coefficient does not exceed 0.7-0.8. The number of animals with developing edema of the lung in the control and experimental groups was also taken into account.

* The literature concerning them is given in the monographs of A. V. Tonkikh [6] and G. S. Kan [3].

EXPERIMENTAL RESULTS

The results of the experiments are set out in the table. As is clear from the table, upon simultaneous intraperitoneal administration of a 0.6 ml 1% solution of novocain and 6% solution of ammonium chloride, the development of edema was seen in fewer experimental animals (38.4%) than in the control group (68%).

Influence of Intraperitoneal Introduction of Novocain, Benzene and Atropine on the Development of Toxic Edema of the Lungs in Rats

Preparation introduced	Number of animals				Value of pulmonary coefficient in animals with pulmonary edema (numerator – average findings; denominator – limits of fluctuation		Change in weight of lungs in animals of the experimental group with pulmonary edema in comparison with the control, in %
	Participating in experiments		With developing edema of the lungs				
	Control	Experimental	Control	Experimental	In control animals	In experimental animals	
0.6 ml 1% solution novocain (simultaneous with NH_4Cl	25	26	17	10	1.500 0.85–2.6	1.124 0.90–1.6	— 25.1
0.6 ml 1-2% solution of novocain (5 minutes before introduction of NH_4Cl)	22	23	17	9	1.436 0.88–2.0	1.227 0.90–2.5	— 14.6
1 mg benzene per 100 g (30 minutes before introduction of NH_4Cl	12	12	8	7	1.284 0.82–2.0	1.239 0.82–1.8	— 3.8
1 mg atropine per 100 g (30 minutes before introduction of NH_4Cl	15	15	13	9	1.452 0.8–2.3	1.167 0.88–1.8	— 19.7
20 mg atropine per 100 g (30 minutes before introduction of NH_4Cl	15	15	14	3	1.656 0.92–2.1	0.977 0.86–1.0	— 41.1

Footnote. Toxic edema of the lungs was produced by intraperitoneal introduction of 0.6 ml 6% solution of ammonium chloride (NH_4Cl) per 100 g.

In the animals of the experimental group with developing edema the degree of inflation was on average 25.1% less than in the control group. A similar effect was observed with intraperitoneal injection of 0.6 ml 1--2% solution of novocain 5 minutes before the introduction of ammonium chloride (in the experimental group 39.1% of the animals with developing edema and in the control 77.2%). The degree of inflation of the lungs in the animals with developing edema in this experimental group was higher than in the previous one.

Thus, one can say that the blockade of the neuroreceptor apparatus inhibits the development of toxic edema of the lungs. This corresponds to the findings of G. S. Kan [3], concerning the preventive effect of the cervical novocain blockade in relation to diphosgenic and adrenalin pulmonary edema and concerning a similar effect upon intravenous introduction of novocain in relation to adrenalin pulmonary edema.

Intraperitoneal administration of the sympatholytic benzene 30 minutes before ammonium chloride did not, in our experiments, exert any influence on the frequency of onset of edema or on the degree of inflation (see table). Atropine introduced intraperitoneally 30 minutes before injection of ammonium chloride exerted a distinct retardation effect both on the onset of edema and on the degree of inflation in those animals in which, despite the introduction of atropine, edema occurred nevertheless. This effect was very pronounced on introduction of atropine in a dose of 20 mg/100 g of animal weight (the rats showed resistance to the effect of atropine); in the experimental group the edema developed in only three rats out of 15, and in 14 in the control

group: the degree of markedness of the edema in three animals of the "atropine" group was 41.1% less than in the control.

The results of our experiments with benzene and atropine do not correspond to the findings of G. S Kan. In three experiments on cats, G. S. Kan noted the preventive effect of benzene on the appearance of pulmonary edema, caused by hydremic plethora. He also noted the absence of the atropine effect on adrenalin edema in rabbits. It is possible that this discrepancy is due to the variability of the forms of edema, and to different species of the experimental animals.

The results of our investigations confirm the role of a pathological reflex in the pathogenesis of acute toxic pulmonary edema, and suggest that the fibers of the vagus may serve as the efferent route of this reflex in several forms of edema.

LITERATURE CITED

[1] Bykov, K. M., Rikkl, A. V., Chernigovsky, V. N., and Potapova, V. M., Voenno-Mor. Vrach 1943, No. 2, pp. 34-36.

[2] Desintskaya, M. M., Malov, G. A., and Shishkina, G. M., Works of the Astrakhan Med. Institute, Jubilee Collection (Stalingrad, 1938), pp. 34-42.

[3] Kan, G. S., The Nervous System and Acute Pulmonary Edema* (Leningrad, 1953).

[4] Serebrovskaya, I. A., Byull. Eksptl. Biol. i Med. Vol. 33, No. 3, pp. 27-30, (1952); No. 5. pp. 45-49; Arkh. Patol 1955, No. 1, pp. 67-68.

[5] Speransky, A. D., Lobar Pneumonia* (Moscow, 1942), pp. 3-17.

[6] Tonkikh, A. V., Nervous and Humoral Factors in the Genesis of Pneumonia and Pulmonary Edema*, (Moscow, 1949).

*In Russian.