THE INFLUENCE OF THE FUNCTIONAL CONDITION OF THE CENTRAL NERVOUS SYSTEM ON THE DEVELOPMENT OF TOXIC EDEMA OF THE LUNGS AND PLEURISY

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The genesis of toxic edema of the lungs and pleurisy, among other diseases, is not yet sufficiently understood. Several researchers believe the pathogenesis of these pathologic processes to be based on injury to the nervous system [2-6].

The purpose of this work was to find new evidence supporting and elaborating the neurogenic theory of the pathogenesis of pulmonary edema and pleurisy. Our aim was to determine the influence of the functional condition of the central nervous system and change in the relative strength of the nervous excitation-inhibition processes on the development of toxic pulmonary edema and pleurisy.

EXPERIMENTAL METHOD

The investigations were conducted on dogs and cats. Pharmacological substances were used to alter the functional condition of the central nervous system: somnifacients (Bromural, Adalin and Medinal), sodium bromide, caffeine and Phenamine. Acute pulmonary edema and pleurisy were induced by the administration of a sodium iodide solution.

The experimental animals were first given one of the above pharmacological substances, perorally administered, and then an intravenous injection of sodium iodide in a dilution of 1:2, or, sometimes, 1:4. We conducted parallel observations on control animals which were intravenously injected with sodium iodide in the same doses and dilutions used for the experimental animals.

To define the degree of pulmonary edema and pleurisy, we observed the condition of the animals, made macroscopic and microscopic studies of lung preparations* and determined the changes in the pleural cavities. We also determined the weight of the lungs and the amount of fluid in the pleural cavities. The blood was examined in several experiments to determine the hemoglobin content and number of erythrocytes.

EXPERIMENTAL RESULTS

In the first series of experiments, we studied the effect of somnifacient substances and sodium bromide on the development of pulmonary edema and pleurisy induced by the administration of sodium iodide. One hundred and forty-four dogs and ten cats were used in the experiments with somnifacient substances. The effect of sodium bromide was tested on 24 dogs.

* The histological preparations were prepared by the usual method. Pieces of lung were passed through alcohols of varying strengths and xylene, then embedded in paraffin. The sections were stained with hematoxylin-eosin and with van Gieson's stain.

TABLE 1

Results of the Experiments with Somnifacient Substances, Sodium Bromide and Sodium Iodide

Experiment				Control			
Number of animals	Animals received per 1 kg weight	Average weight of lungs (in g per kg animal weight)	Number of pleurisy cases	Number of animals	Animals received per 1 kg weight	Average weight of lungs (in g per kg animal weight)	Number of pleurisy cases
20	0.6 g Bromural and 2 ml NaI	18.1	2	10	2 ml NaI	25.9	5
12*	0.5 and 0.6 g Adalin and 2 ml NaI	20.1	3	12	2 ml NaI; stimulation of vagosympathetic trunk and 2 and 3 ml NaI	27.2	7
40	0.6 g Bromural; stimulation of vagosympathetic trunk and 2 and 3 ml NaI	19.5	6	40		24.7	25
6	0.01 sodium bromide and 0.5 ml NaI	10.8	0	6	0.5 ml NaI	20.2	3
6	0.1 g sodium bromide and 0.5 and 1 ml NaI	18.5	3	6	0.5 and 1 ml NaI	15.3	2

* Two of the dogs (one experimental and one control) did not die.

Bromural and Adalin were administered to 32 dogs. The sodium iodide solution was injected as soon as sleep or narcosis developed. The 22 control dogs received only the sodium iodide solution. Autopsies were performed on all the animals which died (Table 1).

Table 1 shows that the average weight of the lungs and the incidence of pleurisy was less in the animals which had received Bromural or Adalin than in the control animals. Macroscopic and microscopic examinations of the lungs confirmed these data (Figs. 1, 2). The blood change (pyknosis) was greater in the control animals.

Analogous results were obtained in the experiments with cats given Medinal in a dose of 0.5 g/kg weight before being injected with sodium iodide.

In the doses administered, therefore, the somnifacients Bromural and Adalin in the dogs and Medinal in the cats inhibited the development of pulmonary edema and prevented pleurisy.

These data prompted us to determine the effect of somnifacients on the development of toxic edema of the lungs and pleurisy against a background of change in the functional condition of the central nervous system.

Experiments conducted earlier in collaboration with K. F. Berkgaut [1] demonstrated that stimulation of the vagosympathetic trunk to the neck with an ammonium hydroxide solution promotes the development of pleurisy and pulmonary edema in dogs poisoned with sodium iodide. In this present work, we performed experiments in which Bromural was administered before and after stimulation of the vagosympathetic trunk and injection of the sodium iodide solution.

Bromural was administered to 40 dogs. After sleep or narcosis had developed, the animals were given a centrally directed injection in the right vagosympathetic trunk of a 50% ammonium hydroxide solution in a dose of 0.1-0.2 ml. Then the sodium iodide solution was administered to the dogs. Stimulation of the vagosympathetic trunk was done the same way in the control dogs (40), before the sodium iodide solution was administered. Autopsies were performed after the death or sacrifice of the animals.

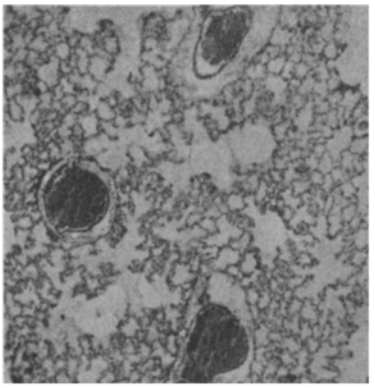

Fig. 1. Change in dog's lung tissue following administration of Bromural and injection of sodium iodide solution. Plethora. Slight perivascular edema. Magnification: ocular 1 ×, objective AA. Stained with hematoxylin-eosin.

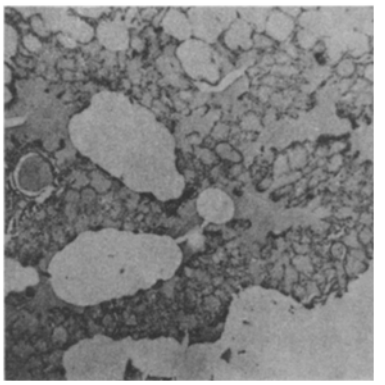

Fig. 2. Change in dog's lung tissue following injection of sodium iodide solution. Alveolar edema. Atelectasis and emphysema. Magnification: ocular 1 ×, objective AA. Stained with hematoxylin-eosin.

The results shown in Table 1 indicate that the average weight of the lungs and the incidence of pleurisy was less in the experimental than in the control animals. The autopsies disclosed stasis and edema in the lungs of only a few experimental animals, while these changes were more pronounced and consistently observed in the control animals. The control animals also showed greater pyknosis of the blood.

The investigations conducted on 10 dogs to which Bromural was administered after stimulation of the vagosympathetic trunk and the injection of sodium iodide showed that, in a dose of 0.5 g/kg animal weight, the preparation did not affect the development of pulmonary edema and pleurisy. In a dose of 0.7 g/kg weight, however, Bromural prevented the development of these processes.

Therefore, under conditions of stimulation of the vagosympathetic trunk, the administration of Bromural did affect the development of pulmonary edema and pleurisy in dogs poisoned with sodium iodide.

By inducing inhibition in the central nervous system, then, somnifacients change its functional condition and thereby prevent the development of edema of the lungs and pleurisy.

On the basis of these data, we set up experiments with sodium bromide, a substance which induces concentrated inhibition in the central nervous system.

Sodium bromide was administered in "small" (0.01 g/kg) or "large" (0.1 g/kg) doses to twelve dogs (Table 1). Then the sodium iodide solution was injected when the dogs were asleep or in a somnolent condition. The control animals received only the sodium iodide solution. Autopsies were performed after the death or sacrifice of the animals.

As Table 1 shows, no pleurisy was found in the animals which had received the "small" dose of sodium bromide, and the average weight of the lungs was within the normal range. Pleurisy was observed in the control animals, and the average weight of the lungs considerably exceeded the normal. The macroscopic and microscopic examinations of the lungs showed no edema in any of the experimental animals. Considerable edema of the lung tissue was observed in the control animals.

In the animals which had received the "large"dose of sodium bromide, pleurisy was found more frequently and the average weight of the lungs was considerably more than in the control. The macroscopic and microscopic examinations of the lungs showed a greater degree of pulmonary edema in 3 of the experimental animals than in any of the control, while the pulmonary edema found in the other 3 animals was analogous to that observed in the control.

TABLE 2

Results of the Experiments with Phenamine, Caffeine and Sodium Iodide

Experiment				Control			
Number of animals	Animals received per 1 kg weight	Average weight of lungs (in g per kg animal weight)	Number of pleurisy cases	Number of animals	Animals received per 1 kg weight	Average weight of lungs (in g per kg animal weight)	Number of pleurisy cases
15	0.0003 and 0.0008 g Phenamine and 0.5, 0.75, 1, 1,5 and 2 ml NaI	20.7	8	15	0.5, 0.71, 1, 1,5 and 2 ml NaI	28.4	13
15*	0.001, 0.002 and 0.005 g Phenamine and 1, 2 and 3 ml NaI	25.9	12	15	1, 2 and 3 ml NaI	19.6	6
4	0.0015 g caffeine and 0.75 and 1 ml NaI	27.4	4	4	0.75 and 1 ml NaI	31.7	4
6	0.01 g caffeine and 0.75 ml NaI	22.9	4	6	0.75 ml NaI	13.5	1
6	0.1 g caffeine and 0.75 ml NaI	14.3	1	6	0.75 ml NaI	21.0	3

* One of the experimental and 3 of the control dogs did not die.

The "small" dose of sodium bromide, therefore, prevented the development of pulmonary edema and pleurisy in the animals following the administration of sodium iodide, while the "large" dose either had no effect on these processes or intensified them.

Consequently, the development of pulmonary edema and pleurisy in dogs poisoned with sodium iodide is affected by the inhibition induced by the administration of sodium bromide as well as by that induced by the administration of somnifacients.

A second series of experiments was conducted to determine the effect of Phenamine and caffeine on the development of pulmonary edema and pleurisy induced by the administration of sodium iodide.

Phenamine was administered in "small" (0.0003 and 0.0008 g/kg) or "large" (0.001, 0.002 and 0.005 g/kg) doses to 30 dogs. Then the sodium iodide solution was injected. Autopsies were performed after the death or sacrifice of the animals.

The data in Table 2 show that the incidence of pleurisy and the average weight of the lungs were less in the animals which had received Phenamine in "small" doses than in the control animals. Macroscopic and microscopic examinations of the lungs disclosed pulmonary edema in some of the experimental and all of the control animals.

In the "large" doses, Phenamine promoted the development of pleurisy and edema of the lungs, causing the weight of the latter to increase. Alveolar edema, a typical change induced in the lungs by the action of the "large" doses of Phenamine, was less pronounced in the control animals.

Therefore, the development of pulmonary edema and pleurisy in dogs poisoned with sodium iodide is inhibited by "small" doses of Phenamine, but intensified by "large" doses of this substance.

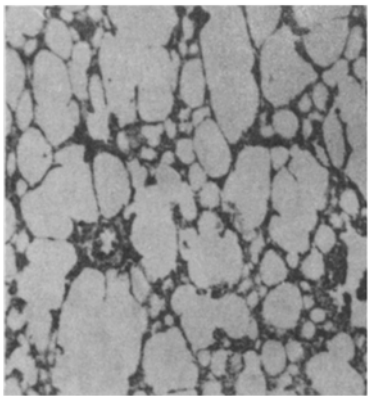

Fig. 3. Normal lung tissue of a dog after the administration of a "large" dose of caffeine and the injection of the sodium iodide solution. Magnification: ocular 8 ×; objective 10 ×. Stained with hematoxylin-eosin.

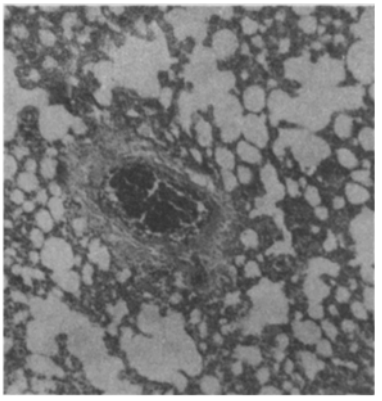

Fig. 4. Lung tissue of a dog after the administration of the sodium iodide solution. Stasis. Perivascular edema. Magnification: ocular 8 ×; objective 10 ×. Stained with hematoxylin-eosin.

Experiments with caffeine were performed in which the preparation was administered in "small" (0.0015 g/kg), "medium" (0.01 g/kg) and "large" (0.1 g/kg) doses to 16 dogs before the injection of sodium iodide. Autopsies were performed after the death or sacrifice of the animals. The results are given in Table 2.

Table 2 shows that the "small" dose of caffeine inhibited the development of edema of the lungs, the average weight of which was less than in the control, but did not affect the development of pleurisy. Macroscopic and microscopic examinations of the lungs showed pulmonary edema to be less pronounced in the experimental animals than in the control.

In the "medium" dose, caffeine intensified pulmonary edema and promoted the development of pleurisy. The macroscopic and microscopic investigations showed the changes in the lungs of the experimental animals to be much greater than in those of the control.

The "large" dose of caffeine inhibited the development of pulmonary edema and pleurisy in dogs poisoned with sodium iodide. This was confirmed by the microscopic findings (Figs. 3 and 4).

In the "medium" dose, therefore, caffeine intensifies the development of both pulmonary edema and pleurisy, in the "small" dose, inhibits pulmonary edema but does not affect the development of pleurisy and in the "large" dose, inhibits the development of both these changes induced by the administration of sodium iodide.

The results of our experimental study of pulmonary edema and pleurisy can be summarized by the statement that change in the functional condition of the central nervous system affects the development of these processes. The balance between the principal nervous processes, excitation and inhibition, is particularly significant in this connection. The experiments have shown that therapeutic substances which influence these processes can by so doing inhibit or promote the development of pulmonary edema and pleurisy.

This is further confirmed by the results of the experiments in which the vagosympathetic trunk was stimulated before and after the development of Bromural-induced inhibition in dogs poisoned with sodium iodide.

Therefore, regulation of the balance between the inhibition and excitation processes in the central nervous system can play an important part in the prevention of pulmonary edema and pleurisy. Clinicians treating pulmonary edema and pleurisy should, then, take into account the role which we have shown the central nervous system to play in the development of these diseases.

SUMMARY

The author studied the effect of the functional condition of the central nervous system and especially of the changes in the correlation of the main nervous processes – excitation and inhibition – on the development

of toxic edema of the lungs and pleurisy. The changes in the functional state of the central nervous system were produced by the administration of sodium bromide, caffeine, and Phenamine (Benzedrine); stimulation of the vagosympathetic trunk was also used. Acute edema of the lungs and pleurisy were induced by sodium bromide administration. The results of experiments have demonstrated that alteration of the functional condition of the nervous system, particularly of the correlation of the excitation-inhibition processes,had a definite influence on the development of toxic edema of the lungs and pleurisy.

LITERATURE CITED

1. K. F. Berkgaut and M. M. Desnitskaya, in: Jubilee Collection of the Scientific Transactions of the Astrakhan Medical Institute [in Russian] (1946) No. 8, p. 65.
2. K. M. Bykov, et al., Voen-Morsk. Vrach 2, 2, 34 (1943).
3. A. D. Speranskii, in: Lobar Pneumonia [in Russian] (Moscow, 1942) p. 3.
4. A. V. Tonkikh, Neurohormonal Factors in the Genesis of Pneumonia and Pulmonary Edema [in Russian] (Moscow, 1949).
5. V. Buchtala, Fortschr. Röntgenstr. 73, 702 (1950).
6. A. A. Luisada and S. J. Sarnoff, Am. Heart J. 31, 282 (1946).