THE EFFECT OF PURE OXYGEN INHALATION ON THE LUNGS AND HEART OF WHITE RATS

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The toxic action of oxygen was described by Lavoisier shortly after he discovered the gas. The pathomorphological changes in the lungs have been depicted in detail by a number of authors [2, 3, 6, 9, 10], but as far as we know, the developmental dynamics of the pulmonary and cardiac lesions has not yet been studied. At the same time, this question is of great practical importance.

In this work, we studied the state of the heart and lungs of white rats exposed to toxic levels of oxygen, employing roentgenographic and electrocardiographic methods. A portion of the animals were also autopsied.

EXPERIMENTAL METHOD

Two to four experimental animals were placed in the exsiccators, which were ventilated with oxygen-nitrogen mixtures containing 97.5, 75-80, or 60-70% O_2. The carbon dioxide was removed by a special absorbent. The exsiccators were cleaned every day, and the animals given fresh food; in a number of the cases, the air was analyzed in a Scholander Apparatus.

EXPERIMENTAL RESULTS

In the first series of experiments, we studied the effect of breathing the gaseous mixtures with the high oxygen content.

In the experiments designed to study the toxic effect of the gas mixture containing 60% oxygen, 4 rats were kept in an atmosphere of this mixture for a period of 28 days, and four remained in it for 30 days. In these experiments, we failed to note any kind of changes in the roentgenological picture of the lungs and heart. The same was true for the EKG in these cases.

In the experiment involving the maintenance of the rats under an atmosphere of the gas mixture containing 75-80% oxygen, 3 animals survived up until the end of the experiment, a period of 30 days, and one animal died on the 26th day. We failed to observe any kind of changes in the EKG of these animals, but through a histological examination of the rat that died, performed by V. I. Nikolaeva, a lesion was demonstrated in the form of a myocardial infarct.

In the roentgenograms that were taken during the first 6 days, no essential changes were observed in the organs of the thoracic cavity. Beginning with the 20th day, we noted changes characteristic of congestive phenomena, and consolidation of the lung tissue. In one case, we also observed enlargement of the cardiac shadow.

The clinical picture of the pulmonary and cardiac lesions in the rats that breathed 90-100% oxygen (second series of experiments) markedly differed from that which was seen in association with respiration of the 60-80% oxygen – nitrogen mixture. Under these conditions, as a rule, manifest pathological processes were observed by the end of the 2nd-, beginning of the 3rd experimental day. In this series, a total of 23 rats were studied, the animals inhaling the oxygen for 44-52 hours.

In the course of the first 44 hours, only a mild increase in the transparency of the lung fields was observed in the majority of the animals (14 out of 22), coupled with caudal displacement of the diaphragm as a result of increased lung volume.

Beginning with the 46th hour of the experiment, the pulmonary markings were more apparent, associated with a certain decrease in transparency. The increased markings, as a rule, were more manifest in the caudal divisions.

As we know, pulmonary congestion is responsible for changes such as these. Between the 46th and 52nd hours of the experiment, the roentgenological picture of the lungs usually worsened markedly, and cardiac changes also began. The changes in the lungs were of two types: in some of the animals we observed cloud-like darkenings, fusing with each other in places, within the lung fields (more often in the middle and lower portions of the lungs) (Fig. 1). It is known from practical experience with clinico – roentgenological observations that these changes indicate the presence of sections of consolidation within the lung tissue. In individual experiments, the darkening occupied an entire lobe of the lung.

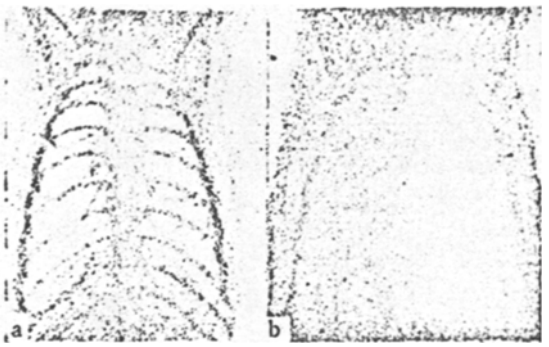

Fig. 1. Roentgenograms of the organs in the chest cage of rat No. 132. a) Before the experiment; b) at 10 minutes after termination of the experiment involving inhalation of 90-100% oxygen for 46 hours. In the roentgenogram of the experiment rat, fusing, cloud-like, darkenings are seen throughout the entire field of both lungs. The size of the heart is increased slightly.

Fig. 2. Roentgenograms of the organs in the chest cage of rat No. 69. a) Before the experiment; b) at 10 minutes after termination of the experiment involving inhalation of 90-100% oxygen for 50 hours. Significant enlargement of the cardiac shadow is seen in the roentgenogram of the experimental rat. In the middle of the right lung field there is an obliquely situated, strikingly homogeneous darkening, characteristic of exudative pleuritis.

In the other animals, in the mid-field of the right lung, the roentgenograms showed an obliquely situated, strikingly homogeneous darkening of triangular form, whose base was closely connected with the shadow of the mediastinal organs. The contour of the darkening were smooth, and it was clearly delineated from the surrounding lung tissue. There is no doubt that this picture reflects an interlobar exudative pleuritis (Fig. 2).

On autopsy, we observed a considerable amount of transparent, protein-containing fluid in the pleural cavity.

The specific gravity of the exudate was determined in three animals, and this figure was used to calculate the protein concentration, which proved to be 3.2, 3.5, and 3.33%. The dry residue of these exudates was equal to 5.65, 6.65, and 5.8% respectively. The protein composition of the exudates was barely distinguishable from the composition in blood serum. Only a slight increase in the albumins was noted, at the expense of the globulins. As was already pointed out, the exudate was transparent, and upon cytological examination of a smear, showed only isolated cells.

Significant changes in the roentgenological picture of the lungs were always accompanied by changes of one type or another in the heart; an increase in its dimensions, leveling out of individual curves. When the cardiac shadow was widened to a considerable degree, its contours were not sharply defined, i.e., they were indistinct. More careful analysis of the roentgenogram showed that the increase in heart size was mainly due to enlargement of the right side.

Although, as a rule, changes were seen in both the heart and lungs at a certain stage in the illness, there was no strict parallel between them. It was possible to distinguish cases where development of pathology occurred predominantly in the lungs or predominantly in the heart (see Figs. 1 and 2).

The results of linear and planimetric measurements of the cardiac shadow's basic parameters, taken from the roentgenograms of rat No. 69, are presented in the table.

This table shows that the cardiac measurements increased up to 2 times as compared with the original picture.

Complete analysis of the EKG's from the rate would have presented major difficulties; thus, we limited the procedure to only a general appraisal of the rhythm and the forms of the waves, not going into a detailed analysis. However, even such a superficial study of the electrocardiographic tracing made it possible to draw certain interesting conclusions.

In 9 of the 11 animals studied, clear EKG changes were noted only at the end of the experiment, by the 3rd to 4th day, when the general condition of the animals underwent a marked deterioration. It was manifested by a gradual decrease in the frequency of the cardiac contractions, and disturbance of the sinus rhythm. Various forms of blockade appeared, including complete atrioventricular block. The EKG took on characteristics of a terminal tracing.

Change in the Dimensions of the Cardiac Shadow in a White Rate Exposed to Toxic Amounts of Oxygen

Time of the investigation	Basic cardiac measurements				
	right half (in mm)	left half (in mm)	diameter	length	area (in mm^2)
Before the trial	5	10	15	21	20
At 10 minutes after the termination of the trial (duration of the trial being 50 hours)	9	12	21	23	32
At 5 hours after termination of the trial	11	14	25	25	40
At 23 hours after termination of the trial	9	11	20	24	30
At 47 hours after termination of the trial	5	9	14	20	18

In the other cases, the EKG changes were focal in character. Against the setting of a normal sinus rhythm, the EKG of the animals showed marked displacement of the S – T interval below the isoelectric line, mainly in lead I, and to a lesser degree, in lead II. In clinical practice, such EKG changes are regarded as signs of a myocardial infarct, with predominant involvement of the left ventricle.

It is interesting that, according to the roentgenological data, the changes primarily involved the right heart. Following removal of the animal from the gas environment containing the elevated oxygen concentration, the EKG quickly normalized. One animal was sacrificed on the 16th day after the experiment, and subjected to a histological investigation by V. I. Nikolaeva. Necrotic changes were found in both the right and left heart, in the process of reversion.

As a rule, the pulmonary and cardiac pathology caused by inhalation of the oxygen did not run a malignant course – the overwhelming majority of the animals we studied recovered from the rather serious lesions. However, in the first hours following termination of the pure oxygen inhalation, it was still often possible to observe further development of the pathological process (see table). The duration of its progression depended on the degree of the lesions, being longer in the more severe cases. The actual time ranged from 2 to 15 hours, after which reversion began. Complete disappearance of the changes observed took from 3 to 80 hours (from 24 to 48 hours in the majority of cases) following termination of the experiment. In the cases where changes took place only in the lungs, restoration of the normal roentgenological picture for the organs of the chest cage occurred more rapidly than when there was combined involvement of the lungs and the heart.

The time interval that we observed in our experiments for the development of the pathological changes in the lungs corresponded to the pathomorphological data that exist in the literature.

In searching the available literature, we were able to find only one reference to the accumulation of exudate in the pleural cavity [1], and we did not encounter any references to cases with predominant cardiac lesions. We have the impression that, in addition to the classic picture of oxygen-induced pathology, there are also atypical pictures, cardiac pathology and exudative pleuritis being among the most prominent.

Apparently, the course of the illness along one or another line is determined by species-specific and individual characteristics of the animals, and also by small changes in the oxygen concentration within the atmosphere. In our experiments, pleuritis developed more often in those cases where the oxygen concentration was close to 100%.

Since the exudate was discovered only in the pleural cavity, and was close to blood plasma in its composition, its accumulation is evidence of massive systemic involvement of the pulmonary circulation.

This is borne out by the data [4] from studies of the outflow of iodine-tagged albumin.

To understand the developmental mechanism of oxygen-induced pathology, it is essential to resolve the question of where the primary pathological process is localized. Does it involve the heart in addition to the lungs, or must the cardiac lesion be regarded as secondary? The data obtained on the relative independence of the pulmonary and cardiac lesions supports the first point of view.

It was already established some time ago [5] that oxygen inhalation leads to changes in the EKG, associated with elevation of vagal tonus (bradycardia, increase in the P – Q interval). There are also indications that respiration of 80-100% oxygen for 2 hours may lead to the development of extrasystoles in humans [8]. The EKG changes that we observed were of a different character – they were apparently related to focal lesions of the cardiac musculature or its vessels. Unfortunately, the histological investigation did not make it possible to resolve this question. The parasthesias and chest pains in humans inhaling oxygen, described by a number of authors [6, 8], suggests the probability of vascular lesions of the heart.

SUMMARY

The state of the heart and lungs was studied in albino rats subjected to oxygen intoxication. Roentgeno- and electrocardiographic methods were used for that purpose. A number of animals were also autopsied. As established, albino rats kept in a 90-100% oxygen atmosphere begin to develop severe effects on the lungs usually by the end of the first 48 hours. If the animal is removed from the oxygen atmosphere after having been kept in it for a period of 48-52 hours these changes disappear without leaving any trace. Inhalation of a gas mixture containing 60-80% of oxygen for a period of up to 30 days provoked but insignificant changes in the roentgenological picture of the lungs and heart.

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