# CHANGES IN PULMONARY HEMODYNAMICS IN ACUTE PULMONARY EDEMA

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An analysis of the differences in origin of clinical and experimental forms of acute pulmonary edema show that in the overwhelming majority of cases an increase in the permeability of the pulmonary membranes and disruption of the pulmonary hemodynamics are the inciting pathogenetic factors [3]. In pulmonary edema which is accompanied by significant disturbances in pulmonary circulation it is usually particularly difficult to separate the action of both factors.

The development of pulmonary edema in such instances is usually explained by the increase in pulmonary capillary pressure, which, however, may mask the effect of permeability disturbances.

As shown by studies from our laboratory, chloramine- and adrenalin-induced pulmonary edema occurs on the basis of disturbance in the pulmonary membrane permeability [3, 7] and depends in large measure on the status of different sectors of pulmonary innervation, in particular its sympathetic innervation [1, 2, 5, 6].

The aim of the present paper was to study the hemodynamic conditions in the pulmonary circulation during the development of these types of pulmonary edema.

## METHODS

Pulmonary edema was produced in 19 adult mongrel dogs by injection of chloramine or adrenalin (5 mg/kg) into the femoral vein. Under pentothal anesthesia (30 mg/kg intravenously) and using succinyl choline (3 mg/kg intravenously) and with control of respiration, the thorax was opened on the right in the sixth intercostal space. The femoral arterial and pulmonary branch arterial pressures were recorded with mercury manometers. A polyethylene probe (external diameter about 3 mm) was introduced into the segmental artery of one of the pulmonary lobes to a wedge position. Another such sound was placed in the lobar vein. Both probes, filled with physiological saline containing added heparin (1:4000), were connected to water manometers to record the pulmonary "capillary" and venous pressures. Heparin was administered intravenously in a dose of 500-700 units/kg. In 6 dogs, at 7 days to 3 months prior to the experiment, both stellate ganglia were removed through an anterior transpleural approach. Animals which did not die at the end of 1 h from the time chloramine or adrenaline was administered were killed with air emboli. The pulmonary coefficient (p. c.)* and dry pulmonary weight† were used as parameters of the presence and degree of pulmonary edema. At the time of autopsy the position of the probes in the pulmonary vasculature was ascertained.

## RESULTS

All ten control dogs to whom chloramine was administered died at 10-35 min after the injection. All these demonstrated clearcut signs of pulmonary edema: p. c. 20.4-32.6, dry lung residual 11.78% (in healthy dogs the p. c. is 6.0-10.0 and the dry residual 19.0 to 22.0%).

* Weight of lungs (in g)/body weight (in kg).
† In per cent of wet tissue weight.

TABLE 1. Mean Values of the Highest Arterial Pressures (in mm of Hg) Recorded in the Systemic and Pulmonary Circulations in Healthy Dogs and Dogs with Stellate Ganglia Removed, Before and After Injection of Chloramine (I, II) and Adrenaline (III, IV)

| Series | No. of dogs | Femoral artery | Pulmonary artery | Pulmonary "capillary" | Pulmonary veins |
|---|---|---|---|---|---|
| I (Healthy dogs): | 10 | 112 / 162 (135%) | 18 / 66 (367%) | 8,4 / 13,3 | 5,8 / 8,1 |
| II (with extirpation of stellate ganglia): | 5 | 116 / 139 (120%) | 26 / 44 (170%) | 9,0 / 9,8 | 5,3 / 6,2 |
| III (Healthy dogs): | 3 | 126 / >300 (>248%) | 19 / 49 (258%) | 5,1 / >33,6 | 3,6 / >32,9 |
| IV (with extirpation of the stellate ganglia): | 1 | 126 / >300 (>248%) | 38 / 62 (163%) | 8,1 / 16,1 | 5,4 / 13,6 |

Note. In the numerator: initial pressure; in the denominator: the highest pressure after chloramine injection.

In 5 dogs in which both stellate ganglia were removed, death was induced by air embolism 1 h after the chloramine injection. In none of these did definite signs of pulmonary edema appear (p. c. was 10.4-16.9 and dry residual 18.46-22.37%).

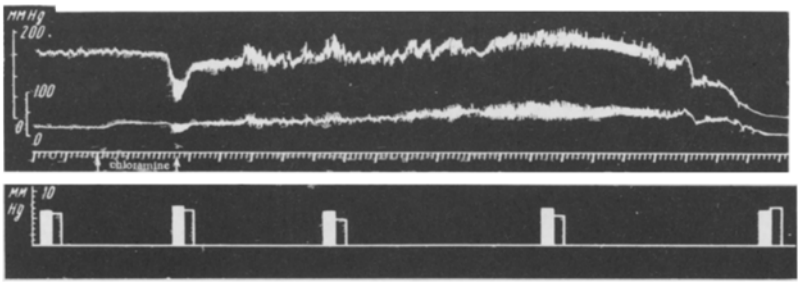
Injection of chloramine in 7 out of 10 healthy dogs produced a fall in systemic arterial pressure of 18-84 mm Hg within 1-3 min. In the other 3 dogs a rise in pressure of 10-36 mm Hg was observed within 1-2 min after injection, and only after this rise did a decrease occur, following which the pressure again exceeded the starting level by 16-96 mm Hg, then falling to zero. The mean maximal rise in pressure was 135% of the initial value (Table 1).

In all 10 dogs the pulmonary arterial pressure at 1-3 min after chloramine injection already exceeded the initial value by 4-39 mm Hg. Thence, as a rule, it remained high (at 23-76 mm Hg above the starting value) until the animal died. In 3 dogs the pulmonary arterial pressure during the experiment was higher than the starting level, falling slightly in a short time. The rise in the pulmonary arterial pressure in all 10 dogs was significant (a mean of 367% over the initial value) and, (in absolute values) sometimes even exceeded the pressure rise in the femoral artery. There was no temporal time relationship between variations in the arterial pressure in the greater and lesser circulations. The pulmonary hypertension produced after chloramine injection, evidently, develops not only as a result of the transfer of blood from the peripheral vessels to the lungs, but mainly as a consequence of an active vascular action of the pulmonary by itself. The pulmonary vasoconstriction as an effect of chloramine is more pronounced and more persistent than systemic vasoconstriction.

The pulmonary "capillary" pressure, which was recorded by the wedge probe, was markedly increased after chloramine injection in 2 dogs out of 7 (Table 2, No. 1 and 2).

The pulmonary venous pressure after chloramine injection varied within a negligible range (±3-4 mm Hg). This indicated that left ventricular failure did not occur and significant spasm in the pulmonary venules did not take place. The kymogram illustrated in the figure denotes a typical picture of the changes in pulmonary hemodynamics following chloramine injection.

Thus, chloramine produces moderate hemodynamic changes in the systemic circulation and significant pulmonary hypertension. The reason for the latter, evidently, is spasm of the pulmonary bed, predominantly in the precapillary section. The injection of chloramine in amounts which invariably produce pulmonary edema is not accompanied by a significant rise in filtration pressure.




Change in the hemodynamics after chloramine. Dog No. 7. Killed 20 min after injection of a 10% solution of chloramine in dose 0.6 ml/kg. P. c. 30.9, dry weight 12.78%. Significance of the curves (from top to bottom) femoral artery pressure, pulmonary artery pressure, time marker (10 sec). Black bars—pulmonary capillary pressure; white bars—pulmonary vein pressure.

In only 1 out of 7 dogs did the "capillary" pressure reach the critical level (26.8-28.3 mm Hg), although in the remaining 6 gross pulmonary edema occurred.

In dogs deprived of both stellate ganglia, the direct reaction of the systemic vasculature to the injection of chloramine was a fall in arterial pressure by 16 to 60 mm Hg in 4 out of 5 cases. A rise then set in (maximal 40 mm Hg) but in none of the 5 dogs reached the limits characteristic for animals with intact innervation. Pulmonary arterial hypertension in animals of this group was also less marked than in controls, despite a statistically valid higher initial pulmonary artery pressure level (see Table 1). A rise in "capillary" and venous pressure did not occur in all animals and was very insignificant. It may be thought that the pulmonary arterial hypertension produced in healthy animals by chloramine is mediated by the sympathetic innervation of the lungs, the greater part of which passes through the stellate ganglia. These ganglia do not have such importance for the peripheral vascular bed, and, therefore, their extirpation prevents a pressure rise to a much lesser degree in the systemic circuit than in the pulmonary vessels.

After intravenous injection of adrenalin the femoral arterial pressure exceeds 300 mm Hg already by the first or second minute. By the fourth minute the pressure has dropped to 190-236 mm Hg. The pulmonary arterial pressure likewise rises rapidly and forcefully (to 24-40 mm Hg). However, in no experiment did it rise so much as in the majority of dogs following chloramine injection. In all animals a very significant rise in "capillary" pressure (24.9, 32, and over 44 mm Hg) was observed. The pulmonary venous pressure also increased rapidly and significantly. (22.2, 32.5, and greater than 44 mm Hg.) Evidently, adrenalin produces a more marked constriction in the pulmonary veins and increase in blood flow through bronchopulmonary anastomoses [4].

Adrenaline was given to 1 dog 7 days after removal of the stellate ganglia. In this animal the same hypertension in pulmonary and systemic arteries was produced as in the healthy dogs. However, the rise in "capillary" pressure and pulmonary vein pressure was considerably less than in animals with intact nervous systems (see Table 1). There was no marked plethora and pulmonary edema in these dogs at death 1 h after the injection of adrenaline (p. c. 7.9, lung dry weight 19.64%).

Thus, changes in pulmonary hemodynamics after adrenalin injection differ significantly from those produced by chloramine and in great degree may promote the development of pulmonary edema. However, out of 3 dogs to whom adrenalin was given, minimal signs of pulmonary edema (p. c. 17.4, dry lung weight 17.67%) were detected in only one, against a background of marked plethera and hemorrhage into the pulmonary tissue. The "capillary" pressure in this animal, which died at 59 min post injection, exceeded 44 mm Hg. In 2 other dogs, killed at 1 h post adrenalin injection, no pulmonary edema developed, although the "capillary" pressure reached the critical level and even exceeded it (see Table 2).

The increase in the pulmonary coefficient after adrenalin injection was related to the marked pulmonary plethera. The absence of overt pulmonary edema in all 3 dogs, despite the administration of large doses of adrenalin which regularly produced edema in other species of animals, is found in accordance with the data of other authors [8, 9]. And so, the hemodynamic changes in the lesser circulation which accompany the injection of chloramine and adrenalin promote the development of pulmonary edema but do not appear to be the decisive factor.

TABLE 2. Maximal Level of "Capillary" Pressure, Pulmonary Coefficient and Value of Dry Lung Weight in Dogs after Injection of Chloramine and Adrenalin

| No. of dogs | Injected substance | Maximal level of "capillary" pressure (in mm H g) | p. c. | Dry residual weight (in %) |
|---|---|---|---|---|
| 1 | Chloramine | 28.3 | 28.0 | 11.90 |
| 2 | " | 22.2 | 30.8 | 11.90 |
| 3 | " | 9.0 | 25.0 | 13.85 |
| 4 | " | 12.9 | 24.1 | 13.48 |
| 5 | " | 6.4 | 31.2 | 11.62 |
| 6 | " | 7.7 | 15.9 | 13.93 |
| 7 | " | 6.8 | 30.9 | 12.78 |
| | Adrenalin | 24.9 | 17.2 | 23.20 |
| | " | > 44.0 | 17.4 | 17.67 |
| 10 | " | 32.0 | 13.4 | 21.61 |

Elevation of the filtration pressure does not act as the necessary determinant of the initiation of pulmonary edema, even if it develops against a background of significant disturbance to the pulmonary circulation. The results of the above experiments suggest that disturbance of the permeability of the pulmonary membrane plays an important role in both experimental forms of pulmonary edema.

## SUMMARY

Experiments were made on dogs to study the hemodynamic changes following intravenous injections of chloramine and adrenaline. Chloramine injections were followed by the development of a severe pulmonary edema in all of the dogs. In most of them, however, the capillary pressure in the pulmonary circulation increased, but insignificantly. The great increase in the pulmonary capillary pressure following adrenaline injection did not culminate in the development of edema or caused very slight edema. The conclusion is drawn that increase of filtration pressure is not an indispensable decisive factor for the development of pulmonary edema, even if it is concurrent with considerable disturbances in the pulmonary circulation.

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