Respiratory Burns with Special Reference to Pulmonary Edema and Congestion

By Domingo M. Aviado, Jr., M.D., and Carl F. Schmidt, M.D.

The functional changes in respiration, circulation, blood composition and blood temperature were investigated in anesthetized dogs that were subjected to the inhalation of steam. The pathogenesis of the accompanying pulmonary congestion and edema was analyzed by measurements of: (a) pulmonary blood flow, (b) pressures in pulmonary artery and vein, (c) pulmonary blood (P32) volume, (d) electrical (AC) resistance of the lungs, and (e) edema fluid of the excised lung. The peculiarities of the pulmonary circulation that were demonstrated by bleeding and blood infusions explain the difficulties of correcting the congestion that regularly preceded thermal edema.

The susceptibility of the lungs to various forms of injuries is attested by the numerous publications on blast injury,\(^1\) phosgene poisoning,\(^2\) and dust inhalation.\(^3\) The subject of respiratory burns has been conspicuously neglected. The available publications consist entirely of pathologic reports of suspected clinical cases\(^5\) -\(^7\) and of experimental burns.\(^8\) It is the primary aim of this report to analyze the important functional changes resulting from steam inhalations particularly those of respiration, circulation, blood temperature and blood constituents. Pulmonary congestion and pulmonary edema were so prominent in this investigation that attempts were included to understand, in greater detail, the behavior of the pulmonary circulation by radioactive technics\(^9\) -\(^10\) and by electrical resistance measurements.\(^11\) -\(^12\) These methods have revealed certain interesting characteristics of the lung circulation that were further explored for therapeutic possibilities of this, so far, fatal, thermal edema.

Methods

Dogs under morphine (2 mg. per kilogram) and chloralose (50 to 100 mg. per kilogram) were used exclusively. A metal tracheal cannula was inserted and connected to the manifold represented in figure 1. By opening and closing the appropriate stopcocks, the animal was allowed to inhale room air or steam at atmospheric pressure. The following measurements were taken repeatedly before, during and after each inhalation: (a) temperature of the blood in the abdominal aorta by inserting through one femoral artery a polyvinyl catheter containing a copper constantan thermocouple (40 S. W. G.), the electromotive force developed being measured by a (Rubicon) galvanometer; (b) electrocardiogram; (c) carotid arterial pressure by a mercury manometer or by a Lilly electrical capacitance manometer;\(^13\) (d) respiration by pneumograph and by collecting expired air in a spirometer; (e) analysis of femoral arterial blood (Paritol\(^1\) as anticoagulant) for oxygen and carbon dioxide content,\(^14\) total hemoglobin,\(^15\) plasma hemoglobin,\(^16\) plasma specific gravity expressed as plasma protein\(^16\) and hematocrit.\(^17\)

The following additional measurements were taken in a selected number: (f) cardiac output estimated by the standard direct Fick method including catheterization of the pulmonary artery and analysis of expired air\(^18\); (g) measurement (by a saline manometer) of pressures in a cannulated pulmonary lobar artery and a lobar vein with the chest subsequently closed over the connecting tubes; (h) measurement of volume of blood in the lungs by means of radioactive erythrocytes,\(^19\) described briefly

* The Paritol was kindly supplied by Dr. Joseph Seifter, Wyeth Institute of Applied Biochemistry, Philadelphia.
in figure 13; and (i) pulmonary electrical resistance described in detail below under Part III-A.

All animals were autopsied and the lungs were further analyzed by (a) gross examination; (b) histologic section; (c) weighing for per cent moisture based on wet and dry weights; and (d) chemical analysis for blood content and edema fluid content, described in detail in the appendix. The analyzed lungs were also obtained from perfusion experiments described in figure 12.

Results and Discussion

Part I. Pathologic Physiology of Steam Inhalations

Steam was selected in this investigation following the suggestion by Moritz, Henriques and McLean* that moist heat is more effective than dry heat in inducing pulmonary burns. The following preliminary experiments were designed to study events in an intact dog, with full realization that lung burns normally coexist with burns of the upper respiratory passages and of the skin.

Skin burns were induced in three dogs by flushing steam into a metal chamber harboring the whole body excluding the head. Such a procedure was always accompanied by a prominent hyperpnea, bradycardia and carotid hypertension, which started before any rise in arterial blood temperature. The reflex nature of these early effects was further demonstrated by noticing a similar response when the burn was limited to one hindleg with its circulation occluded temporarily. The sensory impulses from the leg were not transmitted entirely by the spinal nerves because the response could still be elicited after cutting the sciatic, obturator and femoral nerves. The sensory sympathetic fibers evidently participated in the stimulation of respiration and circulation following burns of the skin.

As soon as steam was allowed to enter the respiratory passages in three other dogs, the response was strikingly different. Nasal inhalation of steam caused a marked inhibition of respiration. When steam was forced into the upper respiratory tract (by a tracheal cannula directed towards the nose), the inhibition of respiration was not as impressive as when steam was administered to the lower tracts of the same dog (by a second tracheal cannula directed towards the lungs). Although almost all of the experiments that will now be described consisted of direct tracheal steam inhalation, the functional changes can be regarded as fairly typical of those encountered when an anesthetized intact animal is allowed to inhale heat, particularly steam.

A. Blood Temperature. The outcome in the 18 dogs that were subjected to tracheal steam inhalation is summarized in table 1. All dogs died within two hours after injury. There was no correlation between the duration of inhalation (12 to 120 seconds) and the time of death chiefly because the amount of steam inhaled was limited by the respiratory response.

The estimation of the uptake of steam by measuring arterial blood temperature brings into consideration not only the amount of steam inhaled, but also the efficiency of the circulatory system to conduct the heat absorbed from the alveolar spaces. The maximum rise in aortic blood temperature ranged from 0.3 to 12.6° C. A close comparison of these rises and the survival of the dogs (table 1) did not show any relation. It was therefore apparent that the amount of injury and its outcome can

* Silicon Rubber (Type SR150) was supplied by Mr. Elbridge Stockwell, Jr., of the Stockwell Rubber Co., Philadelphia.
Table 1.—Summary of Dogs Subjected to Tracheal Steam Inhalations, Arranged in the Order of Duration of Survival

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Date 1931</th>
<th>Weight (Kg.)</th>
<th>Burn Sec.</th>
<th>Max. rise in Bl. Temp. (C.)</th>
<th>Death (mins. after burn)</th>
<th>Tracheal Fracture (mins.)</th>
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Circulatory Deaths

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Respiratory Deaths

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Pulmonary Edema

Fig. 2. Blood temperature of aorta following steam inhalations. The circles connected by dotted line represent mean temperature in 14 dogs.

not be judged by aortic temperature changes alone.

The temperature curves were interesting in other respects. After the quick rise and slow fall, the arterial temperature was stabilized in three minutes to a new level that averaged about half a degree higher than the control (fig. 2). In two dogs, this higher level was manifested by additional thermocouples introduced into the pulmonary artery, the left ventricle and the rectum. Oxygen consumption at this time was not higher than before burns so that increased metabolism was not a plausible explanation. The fever started too early to be explained by a systemic response as encountered after severe injuries and infections. The cause was suggested by extending the observations of blood temperature before the tracheotomy. Blood temperature remained constant, but the insertion of the cannula caused a gradual rise averaging 0.6 C. per hour. It was inferred that the omission of the upper passages interfered with normal pulmonary heat loss, and that burning the trachea and lungs interfered even more. Other examples of corresponding impairment of respiration and circulation as a result of lung burns will be mentioned below.

B. Respiratory and Circulatory Events During Inhalation. The most consistent effects during steam inhalation were apnea, bradycardia, and a rise in carotid blood pressure (fig. 3). They were often interrupted in a minute or so by polypnea and tachycardia. No single mechanism could entirely explain them. At least three were identified:

1. Respiratory reflexes from the lungs: The apnea was originated by a reflex mechanism, because (a) it could not be elicited after vagotomy, and (b) it started before there was a noticeable rise in arterial temperature. The latter observation suggested further that the receptors were not far from the lungs and consisted of one or all of the following groups: (a) sensory receptors in the respiratory passages, (b) stretch receptors in the alveolar wall, and (c) pressoreceptors and drug receptors in the pulmonary veins. Although these reflexes could not definitely be implicated, the known stimuli to each group (ammonia inhalation,
lung inflation, veratridine injection, respectively) became ineffective when tested after the inhalation of steam. The permanent damage to these receptors is reflected by two other observations. Subsequent inhalations did not cause an apnea (fig. 3). The slow and deep breathing which followed the apnea and which persisted long after the initial steam inhalation, simulated the effects of vagotom y and continued after cutting both vagi.

2. Reflexes causing bradycardia: The slowing of the heart rate during inhalation started as abruptly as the apnea but was distinct from motor stimulation and by direct peripheral action. In most instances the peak in carotid pressure was accompanied by other signs of medullary stimulation, namely tachycardia and polypnea.

The exposure of the entire pulmonary circulation to heat caused hemolysis more extensive than that encountered in peripheral burns. Plasma hemoglobin values were as high as 1.0 Gm. per 100 cc. initially and dropped slowly to lower levels (table 5*). The maximum hemolysis encountered in each dog was related neither to the severity of respiratory and it. As long as the vagi were intact, repeated inhalations could still cause bradycardia but no apnea. Identification of the receptors involved was not possible in these preparations.

3. Medullary stimulation: The carotid hypertension coincided very closely with the rise and fall of blood temperatures before and after vagotomy. This rise in blood pressure was due to a generalized vascular constriction because cardiac output during this response was lower than the control value (table 2). No other attempt was made to distinguish between constriction caused by central vaso-

circulatory effects, nor to the early onset of death which will now be described.

C. Early Deaths: Circulatory and Respiratory Failures. Five of the 18 dogs died of circulatory failure within three minutes after lung burns. Blood pressure fell to zero, while the animal continued breathing (fig. 3). Vagotomy in two dogs effectively eliminated the severe bradycardia, but the resulting tachycardia did not cause the blood pressure to recover. The death was not caused by vagal

Fig. 3. Apnea, bradycardia and carotid arterial hypertension after first steam inhalation. The second inhalation caused less prominent respiratory inhibition and immediate circulatory failure. Other pertinent data of dog 399 are in tables 1, 3, and 5.*

* At the request of the editor, tables 5 and 6 are being omitted but will be supplied on request.
influences. For some unknown reasons, these burns had severely damaged the circulatory system.

The other three early deaths were characterized by primary cessation of respiration. Low arterial blood oxygen saturation was characteristically present before burning probably because of difficulties in closure of the chest. The even lower oxygen saturations after the burns did not stimulate respiration as in a normal animal. The resulting depression signified a respiratory center and/or chemoreceptors that could not compensate properly for anoxemia.

The early respiratory deaths were characterized further by the appearance after death of froth in the tracheal and bronchial passages. The remaining 10 dogs that are described in the next section, developed froth before death and presented an opportunity to study the pathogenesis of pulmonary edema.

Part II. Pathogenesis of Thermal Edema

The first appearance of fluid in the tracheal cannula regularly occurred within half an hour after the inhalation. A conspicuous sign at this time was an increased respiratory minute volume chiefly due to an increased depth with the rate constant and was characterized by visible participation of the accessory muscles of respiration (fig. 4). The other measurements helped in understanding the causes of the hyperpnea. Blood oxygen saturations remained essentially normal and carbon dioxide content was decreased until just before the animal died. A central stimulation by known chemical stimulants therefore was unlikely. Vagotomy in two dogs did not interfere with the hyperpnea. The only re-
maining possibility was that the hyperpnea was a reflex that was activated by edema and was mediated by the sensory sympathetic nerves. The existence of such receptors has been suggested by others.20–23

As soon as edema started, death was inevitable within two hours. The tracheal fluid was found to have a specific gravity equal to about 80 per cent of that of plasma. The accumulation of fluid and plasma protein in the lung parenchyma was further reflected by an increasing hemocrit, blood hemoglobin content, and plasma specific gravity (table 5*). As expected, blood oxygen content and saturations became low enough to explain the fatal outcome.

A. Changes in Pulmonary Circulation. The mechanism of pulmonary edema was studied by the radioactive measurements of pulmonary blood volume. Four dogs showed an increase in pulmonary blood volume amounting to 60 to 80 per cent of control value (table 2). This increase is not due to increased pulmonary flow because cardiac output always fell after pulmonary burns. It therefore involved the stagnant blood rather than flowing blood. The cause of this congestion was further investigated by measuring pulmonary vascular and cardiac pressures.

There are three ways of producing pulmonary congestion with decreased pulmonary blood flow: (a) Failure of the left side of the heart; this was not present here because left auricular pressure did not rise after burns (fig. 5). The observed increase in pulmonary arterial pressure did not support (b) a dilatation of the pulmonary vessels. On the other hand, it favored (c) a constriction of the pulmonary veins with accumulation of blood in the capillaries and arterioles.

The demonstration that pulmonary congestion always preceded the appearance of tracheal fluid establishes the importance of venous and capillary pressure in the causation of edema and casts doubt upon increased capillary permeability as a sole cause. The amount of pulmonary congestion as measured by the radioactive experiments was influenced by other factors. One dog that died of immediate circulatory failure did not show a rise in counts (table 2). When the other dogs lived long enough to develop edema, the radioactive counts invariably increased. Pulmonary venous constriction was maximum immediately after

Fig. 5. Effects of steam inhalation on respiration, pulmonary arterial pressure, carotid blood pressure and left auricular pressure (top to bottom). Other pertinent data for dog 416 are in tables 1, 2, 3, and 5.*

* At the request of the editor, tables 5 and 6 are being omitted but will be supplied on request.
due to unidentified factors, that were probably acting in vicious cycles.

B. Pathologic Changes in the Excised Lungs. The significant autopsy findings of dogs that were subjected to steam inhalations were confined to the lungs. The gross picture was a constant and characteristic one, as typified in figure 7. The tracheal and bronchial mucosal linings showed marked capillary injection and contained a foamy sanguinous fluid. The lung tissue was boggy, and when cut, revealed multiple small focal areas of hemorrhage centered about the respiratory bronchioles.

Microscopic examination showed that the greatest pathologic changes were centered

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**Fig. 6.** Pulmonary blood radioactivity and carotid blood pressure after steam inhalation until death (D). Other pertinent data for dog 413 are in tables 1 and 2.

**Fig. 7.** Lung excised immediately after death of dog subjected to nasal steam inhalation for one minute. Tracheal fluid appeared in 20 minutes; animal died 65 minutes later. Dog 462, 161. K9., 11-27-51. (The use of color in this illustration is made possible by a grant from Winthrop-Stearns, Inc., to the publication fund of the American Heart Association.)
about the respiratory portions of each lobule showed minimal involvement (fig. 8). The most striking finding was that of edema fluid which occupied the more central alveolar sacs. The adventitial lining of the venules showed a peculiar swelling or “cuffing” by edema fluid (figs. 8, 9, 10). Capillary engorgement with or without the frank extravasation of erythrocytes into the surrounding tissues was prominent (fig. 10). Ruptures of the alveolar walls were seen in some slides (fig. 9).

The morphologic changes largely confirm the importance of congestion in the development of edema. The “cuffing” of the pulmonary veins by edema fluid illustrates further that the veins are affected before edema spreads to alveolar spaces. The instantaneous appearance of congestion and edema can be deduced from the dogs that died immediately after burning without fluid in the passages (fig. 8).

C. Chemical Changes of the Excised and Perfused Lungs. Further confirmation of lung pathology was offered by quantitative measurements of the excised lungs (see appendix and table 3). There were significant differences in total weight and total moisture content between lungs of dogs killed with Nembutal or bled to death, and lungs from the burned dogs. The greater moisture in the burned lungs was due partly to more blood and chiefly to more edema fluid.

Although these measurements on severity of congestion and edema do not help in understanding the reasons for the differences in behavior among the various living dogs, the measurements become more informative when they are compared with measurements obtained from perfused lungs. The excised lung (one side) from a freshly killed dog was perfused for one hour with its own blood at normal arterial pressure (25 mm. Hg) but slightly higher than normal venous pressure (10 mm. Hg). (Method described in fig. 12.) Four such lungs were found to be heavier; they contained more blood, but the normal amount of edema fluid when compared with the corresponding unperfused side. Still another similar group of lungs with additional burning during perfusion, exhibited the usual increased blood volume.
### Table 3.—Chemical Analysis of Excised and Perfused Lungs for Total Weight (Wt.), Per Cent Moisture (Per Cent M), Cubic Centimeters Blood Per 100 Gm. Lung (BVL) and Per Cent Edema Fluid (Per Cent E. F.)

<table>
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<tr>
<th>Dog Side</th>
<th>Body Wt. (Kg.)</th>
<th>Wt.</th>
<th>% M</th>
<th>BVL</th>
<th>% E.F.</th>
<th>Dog Side</th>
<th>Body Wt. (Kg.)</th>
<th>Wt.</th>
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<th>BVL</th>
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<td>467R L</td>
<td>25.0</td>
<td>125.2</td>
<td>80.44</td>
<td>21.20</td>
<td>62.71</td>
<td>488R L</td>
<td>98.30</td>
<td>85.30</td>
<td>15.94</td>
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<td>Average R</td>
<td>67.56</td>
<td>79.56</td>
<td>26.93</td>
<td>55.76</td>
<td></td>
<td>155.36</td>
<td>83.21</td>
<td>16.96</td>
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<td>±32.40</td>
<td>±1.73</td>
<td>±11.94</td>
<td>±9.82</td>
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<td></td>
<td>±65.15</td>
<td>±3.64</td>
<td>±3.33</td>
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<tr>
<td></td>
<td>Average L</td>
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<td>78.91</td>
<td>22.19</td>
<td>58.29</td>
<td></td>
<td>113.98</td>
<td>84.60</td>
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<td></td>
<td>±24.12</td>
<td>±1.70</td>
<td>±9.99</td>
<td>±1.01</td>
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<td></td>
<td>±47.13</td>
<td>±2.67</td>
<td>±3.09</td>
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<td></td>
<td>Perfused Congested Lungs</td>
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<tr>
<td>442L</td>
<td>19.0</td>
<td>31.91*</td>
<td>83.19</td>
<td>15.94</td>
<td>64.69</td>
<td>392R</td>
<td>11.6</td>
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<td>85.60</td>
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<td>446L</td>
<td>29.6</td>
<td>42.05</td>
<td>79.96</td>
<td>27.20</td>
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<td>459L</td>
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<td>81.77</td>
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<td>400R</td>
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<td>75.55</td>
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<td>80.12</td>
<td>26.05</td>
<td>56.77</td>
<td></td>
<td>161.43</td>
<td>87.25</td>
<td>16.83</td>
<td></td>
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</table>

* Represents weight of lower lobe only; weight of entire side otherwise.
but considerably more edema fluid (table 3). Increased capillary permeability by burning is therefore necessary for congestion to lead to edema in the perfused lung.

Summary of Causation of Thermal Edema. At least two factors are actively causing the pulmonary edema after steam inhalations: (a) congestion and (b) increased capillary permeability. The permeability changes were demonstrated in burned perfused lungs but their exact role in intact animals remains to be proven. The prominence of congestion is based on observations in animals with closed chest, and on morphologic and chemical analysis of excised lungs. The immediate congestion is initiated, at least, by pulmonary venous constriction which was the only possible interpretation from the following: increased lung blood (P2) volume, decreased pulmonary flow, increased pulmonary arterial pressure and normal left atrial pressure. The persistence of congestion after pulmonary arterial pressure has become normal means that other factors besides venous constriction were causing the congestion. The "cuffing" of the pulmonary veins with edema fluid (seen histologically) may be one of such factors. The control of pulmonary blood volume was next investigated as an attempt to remedy this congestion.

Part III. Control of Pulmonary Blood Volume

Our present information on pulmonary blood volume is based on direct measurements in perfused lungs,24-26 and on estimates by dye dilution26-28 and by vital capacity29 in man. The radioactive technic has offered an additional means of supplementing our understanding of the pulmonary circulation. The last group of experiments now to be described was designed to elucidate the factors affecting pulmonary blood volume as related to the correction of pulmonary congestion and edema. A concomitant problem was the development of a method to measure the progress of pulmonary edema in the living animal so that any beneficial effect of the selected procedure can be assessed not only on the congestion (by radioactive method) but also on the edema.

A. Detection of Edema by Alternating Current Resistance. One of the greatest difficulties in the study of pulmonary edema is its detection before the relatively late appearance of fluid in the passages. Methods that involve histologic examination become undesirable when continuous observations on a living animal are preferred. The estimation of fluid changes by electrical methods was first applied by Lambert and Gremels in 1926 to the heart-lung preparation.11 Its application to the whole animal with closed chests was undertaken systematically in the following manner:

1. Excised Lung. The original method proposed by Lambert and Gremels required the application of direct current voltage on copper electrodes inserted into the lungs. Polarization of such electrodes in an excised lung was easily demonstrated by noticing one to be polished and the other tarnished. The direct current measurements were indications of an electrolytic electromotive force, which was independent of the position of electrodes. We have minimized polarization by two modifications: (a) using platinum electrodes (size 26), and (b) measuring alternating current resistance with the signal source from an oscillator, an alternating current bridge for balancing the impedance and an oscilloscope as a null point indicator. The alternating current resistance was affected by distance between the platinum electrodes inserted into the lung. For a sample spacing, the resistance beyond a frequency of 20,000 cycles per second remained essentially constant (Fig. 11). This level was selected for all subsequent readings because it represented a reasonable compromise of all other factors, namely, problems of shielding and ease of operation. At this frequency the excised lung was found to be sensitive to the introduction of 5 cc. fluid into the cannulated artery and of 10 cc. air into the trachea, but not to induced temperature changes (Fig. 11).

2. Perfused Lung. The sensitivity of alternating current resistance measurements to air and fluid changes in the lung was further demonstrated in the isolated perfused lung. A dog was bled to death, the right lung was excised, and cannulas were inserted into bronchus, artery and left auricle for negative ventilation and perfusion (Fig. 12). In each of two preparations, stopping arterial flow to reduce the amount of blood in the lung caused an increase in alternating current resistance while the development of edema (by alloxan) caused a fall in resistance. The effects of blood flow changes are important because they emphasize the fact that alternating current resistance is sensitive to fluid changes but cannot distinguish between blood and edema fluid.

3. Intact Dogs. The experience in intact animals confirms the above observations. The chest was opened and the platinum tips were tied into two points of one lobe. With the chest closed, the
respiratory movements were reflected in time and in magnitude on the oscilloscope. Although the movements were difficult to follow, they were an assurance that electrical connections to the lung were complete. The initial values of alternating current resistance ranged from 0.167 to 1.17 ohms, which meant variable spacing among different dogs. The absolute values in each dog were meaningless, hence relative per cent changes were utilized in expressing the results. The control values every three minutes for one hour had a variation of 3 per cent or less. Changes that were greater than this value were regarded as significant.

The pulmonary alternating current resistance measurements obtained from dogs breathing spontaneously are tabulated in table 4. The animals dying after steam inhalation showed a larger percentage fall in values than those dying of other causes (bleeding, asphyxia, Nembutal) without evidences of edema. The utilization of this technic for detecting the exact onset of edema was not successful. Although the resistance dropped immediately after the steam inhalation, it was difficult to exclude the possibility that such changes were due to accompanying congestion. As will next be described, alternating current resistance detected blood volume changes in the lung after bleeding and infusion and it was mainly for this purpose that the measurements proved most useful.

B. Effects of Bleeding and Blood Infusion. The simplest way of reducing blood volume in the lungs was by decreasing the available circulating blood. When an animal was bled in sufficient amounts (by way of femoral artery 15 cc. per kilogram) pulmonary blood radioactivity fell while alternating current resistance increased. This reduction in lung blood volume

* The lung chamber was made by Mr. D. W. T. Cochrane of this laboratory.
remained until the lost blood was replaced. Bleeding in repeated smaller amounts (5 cc. per kilogram three times) did not affect all the measurements significantly although the total blood lost was equal to a larger bleeding. The repeated bleedings happened within a period of 15 minutes so that the entrance of tissue fluids to replace the lost blood seemed improbable. Hematocrit remained essentially constant.

The pulmonary arterial pressure reflected closely the amount of blood lost. It decreased equally after one large bleeding and after three smaller bleedings (fig. 13). The logical explanation for the maintenance of pulmonary blood volume when blood is lost slowly is that blood is shifted from the peripheral depots to the lungs. This compensation was not clearly reflected by pulmonary arterial pressure changes although the dilatation of pulmonary capillaries to accept the shifted blood may coexist with diminished cardiac output to cause a fall in pulmonary arterial pressure. The disappearance of this compensating mechanism after vagotomy suggested a neurogenic factor. Electrical stimulation of peripheral end of vagus before or after bleeding did not change the pulmonary blood measurements. The importance of the vagi in this compensatory adjustment may not depend on pulmonary vasomotor fibers, but may depend on the cardiopulmonary pressoreflex (vagal afferent) fibers that have been shown to participate in the maintenance of peripheral circulation during bleeding.

Table 4.—AC Resistance Measurements: Initial and Terminal Values for Dogs Dying of Pulmonary Edema, and Dogs Dying of Other Causes. Platinum Electrodes Were Tied into Lung Tissue (L-L), Introduced Blindly through Chest Wall into Lung (L-W), or Utilized Pulmonary Arterial Catheter and Chest Wall (A-W)

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Date</th>
<th>Body Weight (cc.)</th>
<th>Method</th>
<th>Cause of Death</th>
<th>Initial Resistance (ohm)</th>
<th>Terminal Resistance (ohm)</th>
<th>% Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>405</td>
<td>7-27</td>
<td>11.1</td>
<td>L-L</td>
<td>Burn</td>
<td>.564</td>
<td>.551</td>
<td>-2.3</td>
</tr>
<tr>
<td>418</td>
<td>8-7</td>
<td>14.1</td>
<td>L-L</td>
<td>Burn</td>
<td>.486</td>
<td>.393</td>
<td>-22.0</td>
</tr>
<tr>
<td>420</td>
<td>8-8</td>
<td>13.0</td>
<td>L-L</td>
<td>Burn</td>
<td>.764</td>
<td>.636</td>
<td>-16.8</td>
</tr>
<tr>
<td>424</td>
<td>8-10</td>
<td>12.3</td>
<td>L-L</td>
<td>Burn</td>
<td>.918</td>
<td>.723</td>
<td>-21.1</td>
</tr>
<tr>
<td>393</td>
<td>7-17</td>
<td>17.0</td>
<td>L-W</td>
<td>Nembutal</td>
<td>.568</td>
<td>.426</td>
<td>-24.9</td>
</tr>
<tr>
<td>395</td>
<td>7-18</td>
<td>14.3</td>
<td>L-L</td>
<td>Bleeding</td>
<td>.610</td>
<td>.323</td>
<td>+18.3</td>
</tr>
<tr>
<td>414</td>
<td>8-2</td>
<td>12.3</td>
<td>L-L</td>
<td>Bleeding</td>
<td>.118</td>
<td>.350</td>
<td>+198.0</td>
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<tr>
<td>422</td>
<td>8-9</td>
<td>18.9</td>
<td>L-L</td>
<td>Nembutal</td>
<td>.184</td>
<td>.350</td>
<td>+198.0</td>
</tr>
<tr>
<td>431</td>
<td>8-16</td>
<td>7.7</td>
<td>L-L</td>
<td>Asphyxia</td>
<td>.655</td>
<td>.662</td>
<td>+1.6</td>
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<tr>
<td>433</td>
<td>8-20</td>
<td>19.3</td>
<td>L-L</td>
<td>Bleeding</td>
<td>1.170</td>
<td>1.000</td>
<td>-14.5</td>
</tr>
<tr>
<td>435</td>
<td>8-22</td>
<td>17.3</td>
<td>A-W</td>
<td>Nembutal</td>
<td>1.050</td>
<td>.945</td>
<td>-10.0</td>
</tr>
</tbody>
</table>

Fig. 13. Continuous recording of lung blood radioactivity (upper) and pulmonary arterial pressure (lower) after repeated small bleeding (100 cc. three times), one large bleeding (300 cc.), and blood infusion. The effects of gelatin, adrenaline and vasoactive substances are included. Measurement of lung blood volume from the pleural surface with a counter (Amperex 150NB) enclosed in an aluminum channel that is protected with a thin rubber membrane to allow complete closure of chest. The radioactivity of the erythrocytes tagged with phosphorus32 (5 cc. blood equilibrated with 0.1 mc. and washed) was registered continuously on a scaler (Technical Associates GS4) attached to an inkwriting oscillograph (Brush Development BL202). All results were expressed as counts per minute (cpm) after correction for background.

Blood infusion caused the converse picture, that is, increased pulmonary radioactivity and decreased alternating current resistance (table 6*). This response was present when the infusion followed a small compensated or a large noncompensated bleeding. A closer analysis of continuous radioactive and pulmonary arterial pressure measurements revealed that the increased radioactivity and increased pulmonary arterial pressure after a blood infusion lasted for several minutes, and outlasted the accompany-

* At the request of the editor, tables 5 and 6 are being omitted but will be supplied on request.
ing rise in carotid pressure. After pulmonary measurements have completely recovered to normal levels, cardiac output was essentially unchanged. It appeared as though the infusion caused a temporary storage of blood in the lung by venous constriction to explain the increased arterial pressure and increased lung blood volume with the cardiac output not higher than expected. This venous constriction was not affected by vagotomy. A similar response of the pulmonary arterial pressure has been reported in man.32

After steam inhalation, bleeding or infusion did not significantly change the already high pulmonary radioactivity. The three burned dogs subjected to repeated bleeding died with usual pulmonary congestion and edema as described in Part II.

Final Comment

The difficulties in treating pulmonary congestion and edema after steam inhalation can be explained on a twofold basis: (a) the compensating mechanism that normally stabilizes lung blood volume, and (b) injury to pulmonary vessels by heat, particularly by direct venous constriction and early “cuffing” of the pulmonary vein. As long as these factors are active, blood-letting does not offer any advantage. The prolonged congestion seen after blood infusion characterizes the pulmonary vessels as being able to store blood so that the contraindication of infusions in respiratory burns and other forms of pulmonary congestion is understandable.

The treatment of the other causative factor, that is, increased capillary permeability remains as an alternative approach in the therapy of pulmonary edema associated with respiratory burns. The problem of detecting early edema in a living animal remains unsolved. Findings in the experiments reported here have suggested a new means to the solution. The radioactive technic is now being extended so that blood volume is measured by P32 tagged erythrocytes while edema fluid is measured by I131 tagged plasma albumin.

Summary and Conclusions

The effects of respiratory burns were investigated in anesthetized dogs. The following functional disturbances were observed:

(a) The most prominent effect of tracheal steam inhalation is an immediate apnea that is followed in a minute by polypnea. This inhibition arises from lung receptors which are permanently damaged after activation by steam.

(b) The bradycardia that accompanies the apnea is also a reflex arising from extrapulmonary receptors, unidentified in these experiments.

(c) The uptake of heat is reflected by a sudden rise in aortic blood temperature. A central medullary stimulation by warm blood is the best explanation for the short-lasting peripheral vasoconstriction, polypnea and tachycardia, which all coincided with the peak of arterial blood temperature rise. The stabilization of temperature at a higher level is caused by the loss of heat-eliminating function of the burned lungs and passages.

(d) Blood hemolysis is more extensive than that encountered in skin burns.

(e) Froth in respiratory passages appears within half an hour after steam inhalation. One prominent accompanying sign is an increased respiratory minute volume. The increased depth is best explained by reflexes mediated by the sympathetic nerves from the lungs. After prolonged edema, anoxia becomes severe and blood analyses show low oxygen content and saturation, high blood hemoglobin, high hematocrit and high plasma specific gravity.

All 18 dogs died within two hours after tracheal steam inhalation. Although the five dogs that died of immediate circulatory failure did not show fluid in the tracheal cannula, congestion and edema were seen grossly and histologically in all the excised lungs. Congestion is a constant accompaniment of thermal edema. Radioactive measurements of lung blood volume show an immediate congestion after burning. This is due to a venous constriction which is the only possible interpre-
tation from increased radioactivity, decreased pulmonary flow, increased pulmonary arterial pressure and normal left atrial pressure. The chemical analysis of perfused lungs for edema fluid shows that increased capillary permeability by heat is a necessary accompaniment for pulmonary congestion to cause edema.

A pulmonary venous constricting mechanism is also initiated by blood infusion such that blood is stored for some time after it is injected intravenously. This response persists after vagotomy.

An attempt to treat pulmonary congestion after steam inhalation by arterial bleeding was unsuccessful partly because of a neurogenic mechanism that stabilizes the pulmonary blood volume at a constant level. Bleeding causes a shifting of blood from the peripheral depots into the lungs.

The electrical resistance method of Lambert and Gremels has been adapted for intact dogs. Several modifications in technic and interpretations are described. The alternating current resistance measures fluid changes in the lung but cannot distinguish between blood and edema fluid. It can measure lung blood volume changes.

A method that can detect early edema in a living animal is still wanting.

APPENDIX

Chemical Analysis for Blood Volume and Edema Fluid in an Excised Lung Principle: The edema fluid is calculated as the difference between total moisture and bloody moisture of the excised lung. This estimated edema fluid includes normal tissue fluid.

**Measurements:**

- \( L_D \) = weight of lung cut proximal to ligated hilus and prevented from drying (Gm.).
- \( L_W \) = wet weight of aliquot portion after whole lung is minced in Waring Blender for 10 minutes (Gm.).
- \( L_D \) = dry weight of \( L_W \) after 24 hours in 150 C. oven (Gm.).
- \( B_w \) = wet weight of accurately measured cardiac blood (Gm./100 cc.).
- \( B_D \) = dry weight of \( B_w \), similarly dried (Gm./100 cc.). (All above weighings were on an analytic balance, expressed to nearest 0.01 Gm.)
- \( H_W \) = hemoglobin content of \( B_w \); duplicate analysis by colorimetric technic\(^{12}\); (Gm./100 cc.).

\[ H_L \] = hemoglobin content of aliquot portion of minced lung by the method originally described by Greenberg and Erickson.\(^{12}\) Dr. Werner Kalow has introduced the following modifications that were found necessary for congested and edematous lung: (a) Instead of cutting small pieces of lung with a pair of scissors, the whole lung was ground into a brei with a Waring Blender thus providing a representative sample; (b) After washing with acetone and adding acid mixture, the acid hematin was most effectively extracted by mechanical shaking of tubes for one hour at room temperature. Duplicate analyses of same lung were found to have a standard deviation of 0.142 Gm., and an average variation of 7 per cent. Results were expressed in Gm. hemoglobin per 100 Gm. lung.

**Calculations:**

\[
\text{Per cent Total Moisture of Lung} = \frac{L_W - L_D}{L_W} \times 100
\]

(Also total moisture Gm./100 Gm. lung).

Blood Volume in Lung (cc. blood/100 Gm. Lung)

\[
\text{Lung} = \frac{H_L}{H_W} \times 100
\]

Per cent Blood Moisture in Lung =

\[
\frac{(B_w - B_D) \times \text{Blood Volume in Lung}}{100}
\]

(also blood moisture Gm./100 Gm. lung).

Edema Fluid in Lung (Gm./100 Gm. Lung) =

\[
\% \text{Total Moisture} - \% \text{Blood Moisture in lung}.
\]

Sample values of normal, edematous and perfused lungs are in table 3.

**ACKNOWLEDGMENTS**

We are deeply grateful to Albert H. Niden, David M. Seymour and Leonard J. Epstein for their patient assistance in the performance of most of these experiments. We also wish to acknowledge the help of Geraldine F. Croft and Helen D. Shelley in the blood and lung analysis, of Joseph E. Paul in the electronic equipment, of Dr. W. C. Yakovac in the histologic examination, and of Dr. W. Kalow in developing the modifications for the analysis of lung hemoglobin.

**REFERENCES**


Respiratory Burns with Special Reference to Pulmonary Edema and Congestion

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