OBSERVATIONS ON RESISTANCE TO THE FLOW OF BLOOD TO AND FROM THE LUNGS.

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PLATES 24 AND 25.

INTRODUCTION.

Previous studies (1–4) have led us to the view that the cause of rapid and shallow breathing which results from multiple emboli in the arterioles and capillaries of the lungs must be sought for in the secondary vascular changes following embolism. Neither the presence of the embolic material *per se* nor the chemical changes found in the blood can be regarded as the direct cause of the modified type of breathing. The phenomenon appears to be related in some manner to the diminution of the pulmonary vascular bed, to the resistance to the flow of blood through the lungs or to the state of congestion and edema of the lungs. It has already been shown (2) that obstruction to the larger branches of the pulmonary artery by the intravenous injection of seeds of various sizes results in a condition quite different from that due to capillary obstruction. The functional abnormalities in breathing thus produced were found to result wholly from the condition of oxygen want. That blocking the capillary bed should have a different effect from blocking some of the larger branches of the pulmonary artery is not hard to understand. The first might be described as an "effective blockade" in which the blood passing through the lesser circulation must necessarily meet resistance. In blocking some of the larger branches, however, the blood has an alternative route to follow, and such resistance may not be encountered.

The probability that resistance to flow of blood through the lungs would result in heightened pressure in the pulmonary artery and perhaps the right heart was borne out by the work of Haggart and Walker

(5) and of Wiggers (6).   It occurred to us that such pressure changes might result in stretching of the walls of the pulmonary artery or of the right ventricle and that this might induce afferent stimuli which could occasion reflex changes in respirations.   No experimental evidence for this assumption, however, can be adduced from this work, and the results here published, though perhaps negative from the point of view of explaining the origin of rapid and shallow breathing, are of themselves of interest, we believe, and have helped us with an understanding of the problem.

EXPERIMENTAL.

Dilatation of the Pulmonary Artery and Right Ventricle Following Obstruction to the Arterioles and Capillaries of the Lungs.

Without indulging in the artificial conditions necessarily prevailing in cardiac oncometry an effort was made to determine what changes occurred in the state of dilatation of the pulmonary artery and right ventricle after obstructing the flow of blood through the lungs by the intravenous injection of a suspension of potato starch grains.   This was done by careful x-ray photographs made of the heart during injection of starch suspensions.   A comparison of the photographs made under uniform conditions before and after the onset of rapid and shallow breathing shows a marked area of bulging at the base of the heart on the left side and a flaring out of the shadow cast by the right side of the heart.   This was clearly shown in two experiments (Nos. 1 and 2).   The x-ray photographs in Experiment 1 taken before and after the onset of rapid breathing following starch injection are reproduced in Fig. 1.   The bulge at the left side of the base is plainly to be seen, as well as the flare in the shadow cast by the right side of the heart. At the time of the first picture the dog was breathing at the rate of 16 per minute; at the time of the second the respiratory rate was 64. The area of the cardiac shadow, measured by a planimeter, averaged 43.4 sq. cm. before the injection of starch as compared with 48.4 sq. cm. after.   And the maximum transverse diameter of the cardiac shadow before embolism was 6 cm. as compared with 6.7 cm. after.

Like results were obtained in Experiment 2, in which x-ray photographs showed similar bulging at the left base of the heart and flaring

of the right border. By taking a series of x-ray plates during the experiment it was shown that these changes occurred synchronously with the acceleration of respirations. These facts are made plain by the two curves shown in Text-fig. 1 in which the lower represents
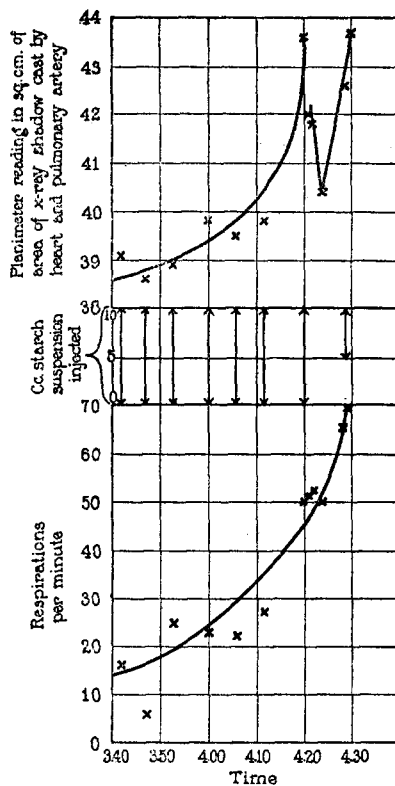
TEXT-FIG. 1. Lower curve: Ordinates, respirations per minute; abscissæ, time. Upper curve: Ordinates, area in sq. cm. as measured by a planimeter of x-ray shadow cast by the heart and pulmonary artery; abscissæ as in lower curve. The length of each arrow represents the volume of starch suspension injected at the time specified in the abscissæ.

respiratory rate per minute at the times specified in the abscissæ, and the upper, the area of the cardiac shadow in sq. cm. as measured by a planimeter. The arrows represent the times at which suspensions of starch were intravenously injected. The two curves will be

seen to vary synchronously and in the same direction. The break at the end of the upper curve may be regarded as a temporary recovery of muscular tone overcome by the injection of an additonal 5 cc. of starch suspension.

The planimeter measurements recorded here and in Experiment 1 were made by tracing the whole dense shadow cast by the heart, including the bulge at the left base which was suspected of being caused by the dilated pulmonary artery. By tracing the ventricular shadow alone from arbitrary points after the method of Levy (7) and Stewart (8), it was found that the increase in area was far less marked than it was when the bulge was included in the tracing. Direct inspection of the photographs shows the heart after embolism to be wider and shorter than before.

By carefully splitting the sternum without loss of blood in a dog* breathing at the rate of 56 per minute following starch embolism (Experiment 3) and maintaining the same respiratory rate by interrupted, intratracheal insufflation, after the chest had been opened, it was shown beyond doubt that the shadow of the bulge at the left base of the heart previously alluded to was cast by a greatly dilated pulmonary artery. This structure stood out a tense, bulging, sausage-like mass, three or four times its normal size.

The experimental facts thus far presented, we believe, prove that *obstruction to the capillaries and arterioles of the lungs results in an increase in the area of the x-ray shadow cast by the heart, and that this increase is the result partly of a widening of the transverse diameter of the ventricles, but chiefly of a marked bulging of the pulmonary artery. The changes in the heart and pulmonary artery were shown to occur synchronously with the acceleration of respiratory rate.*

The hypothesis on which we proceeded, and which was found to be faulty, was that the dilated pulmonary artery sent out impulses which reflexly accelerated respirations. Though the results of these experiments are in a sense negative, by eliminating false causes, they largely clarify our problem.

Experiments were devised with an eye to obstructing the blood flow to the lungs proximal to the pulmonary parenchyma itself so that

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* The animal was anesthetized with barbital-sodium.

any changes in breathing could be attributed wholly to the cardio-vascular effect, unclouded by pathological changes in the lungs. Two methods were used to accomplish this end: (1) the exposed heart method of Drinker; (2) a new method which will be described in detail below.

Experiments with the Drinker Exposed Heart Preparation.

By the technique devised by Drinker (9) the heart of a cat was exposed through a window cut into the sternum and the thorax closed by stitching the split pericardium to the edges of the window. The heart thus everted and supported on its pericardial sling, could be observed and its great vessels manipulated at will while the animal breathed without the aid of artificial respiration. To obstruct the flow of blood through the pulmonary artery, or one of its branches, a clamp and ligature were placed about it, after the method described by Haggart and Walker (5), in such a manner that progressive tightening of the ligature resulted in progressive diminution of the calibre of the vessel until it was completely occluded.

This experiment was performed on two cats anesthetized with barbital-sodium. In one of them (No. 4) the clamp was placed on the left branch of the pulmonary artery, in the other (No. 5) on the main trunk of the artery. Since the results of these two experiments are in complete agreement with those of Haggart and Walker (5) they will not be given in detail. In Experiment 4, in which the left branch of the pulmonary artery was suddenly occluded, no change occurred in the animal's respirations. In Experiment 5, in which the main trunk of the pulmonary artery was gradually compressed, no change in respiratory rate or depth occurred until a point was reached when respirations ceased entirely.

Because all of our previous studies on the effect of pulmonary embolism on breathing had been made on dogs, it was determined to repeat the last two experiments on dogs instead of cats. This, however, brought us face to face with a real difficulty. The Drinker exposed heart preparation, though admirable in the cat, cannot be used satisfactorily in dogs because of the depth of the dog's thoracic cavity, and the difficulty to effect a tight closure between the pericardial edges and the chest wall. Moreover, it seemed desirable to devise a

method in which the thoracic cavity was not restricted in size and one which could be used, if need be, in experiments made without anesthesia, on animals previously prepared by sterile, survival operations.

The method finally achieved was the following: A thin walled, flat rubber bag measuring 1.8 × 5.5 cm. communicating with a 30 cm. length of rather heavy walled rubber tubing (3 mm. in cross-section with a 2 mm. bore) was passed under the previously exposed and freed pulmonary artery.* By surrounding this rubber bag or cuff with a stocking of closely woven silk, to the four corners of which ligatures were attached, the rubber bag could be fastened in position about the vessel. The silk covering prevented overdistension of the bag on inflating it, and assured a uniform compression on the vessel, similar to that produced by the ordinary blood pressure cuff. Inflation of the bag was made through the patent end of the rubber tubing. The pressure in the cuff could be accurately controlled by the use of a mercury manometer. Fig. 2 illustrates the bag in place before the ligatures were fastened. When this is done, the bag forms a closely fitting cuff surrounding the vessel wall. Inflation immediately compresses the vessel. It was found that a pressure of 150 mm. Hg was more than sufficient to obliterate the lumen of the artery. As has been said, the method could be used in survival experiments in which the pulmonary artery or one of its branches could be occluded without the use of anesthetics, and after the effect of operative trauma had subsided. Fig. 3 is a photograph of such a survival experiment (No. 6) to be referred to below. The rubber tube, projecting through the chest wall, through which the bag is inflated, is shown in the picture.

Effect on Respiration of Compression of the Left Branch of the Pulmonary Artery in the Anesthetized Dog.—Dogs anesthetized by the intravenous injection of barbital-sodium were operated on, with the aid of artificial respiration, an incision into the pleural cavity being made through the 4th left interspace. Spreading the 4th and 5th ribs gave free access to the left branch of the pulmonary artery after the upper and middle lobes of the left lung had been carefully retracted downward and packed out of the field. The left branch of the pulmonary artery was surrounded by the pneumatic cuff described above and the chest wall closed by approximating the spread ribs with three stout ligatures after proper distention of the lungs. In closing the thorax, the free end of the rubber tube which communicates with the cuff was permitted to project through the chest wall.

* When one of the two main branches of the pulmonary artery was compressed. a somewhat smaller bag was used, *viz.*, 0.8 × 4.2 cm.

The effect on breathing of compressing the left branch of the pulmonary artery was noted in a series of experiments. The results obtained are similar to the cat experiment (No. 4) cited above. Blocking the circulation to the left lung produces essentially no immediate (2 minutes to 2 hours) effect on respiratory rate. Five animals showed a slight drop in rate, -1, -3, -3, -1 and -2, respectively. One animal showed no change. Eight animals showed a slight increase in rate, $+2$, $+6$, $+1$, $+5$, $+1$, $+3$ and $+1$. Whereas the average postoperative control rate was 22.5 per minute, the average rate after compression of the pulmonary artery was 24.2 The periods of compression, during which the respiratory rates were observed, varied from 2 minutes to 2 hours. Anoxemia was prevented from arising in these experiments by allowing the animals to inhale oxygen.

From these observations it can be definitely concluded that *restriction of the pulmonary vascular bed by nearly half does not result in rapid and shallow breathing.*

In two of this series of experiments (Nos. 7 and 8), the carbon dioxide tension and hydrogen ion concentration of the serum were studied before and after excluding the left lung from the circulation.

In Experiment 7 there was an increase of nearly 10 mm. Hg in $p\mathrm{CO_2}$ with a corresponding drop in pH from 7.34 to 7.27. In Experiment 8, however, the $p\mathrm{CO_2}$ fell from 54.05 mm. Hg, before clamping the left branch of the pulmonary artery, to 50.35 mm. Hg after, and the pH rose from 7.29 to 7.32. Tables I and II give the analytical data of these two experiments.

No constant effect, therefore, on the $\mathrm{CO_2}$ tension or pH of the serum is to be anticipated from suddenly shutting off the circulation to the left lung.

Effect on Respiration of Gradual Compression of the Main Trunk of the Pulmonary Artery in the Surviving Unanesthetized Dog. Protocol of Dog 6.—(See Fig. 3.) February 3, 1926, a white and black, male setter, weighing 14.5 kilos, was given ether by cone after a preliminary injection of morphine. When the dog was fully relaxed a rubber tube was inserted into the trachea. Artificial respiration and anesthesia were maintained by forcing an air-ether mixture intermittently into the lungs at a pressure of 20 mm. Hg. The dog was placed on its right side, with fore legs extended. Thorax was shaved and skin scrubbed with soap, water and alcohol. The chest was opened by resecting the 5th rib from its costochondral junction laterally for a distance of about 3 inches. By a self-

retaining mechanical retractor the edges of the wound were held apart and the left lung was retracted from the field by a cotton pad moistened with warm, physiological saline solution. A vertical incision was then made in the anterior surface of the pericardium directly over the pulmonary artery, from the point at which

TABLE I.

Experiment 7.

Time	Procedure	Respira-tions	[CO_2]	pCO_2	pH
		per min.	*mM*	*mm.*	
1.41	Postoperative control period. Cuff in place but deflated. Dog breathing oxygen throughout experiment	20	27.56	50.40	7.34
1.46	Cuff inflated to 150 mm. Hg				
2.10		26			
2.40		24			
3.25		26	28.45	59.60	7.27

TABLE II.

Experiment 8.

Time	Procedure	Respira-tions	[CO_2]	pCO_2	pH	O_2 capacity	O_2 content	O_2 satura-tion
		per min.	*mM*	*mm.*		*mM*	*mM*	*per cent*
2.14	Postoperative control period. Cuff in place but deflated. Dog breathing oxygen throughout experiment	24	26.76	54.05	7.29	8.97	8.88	99
2.17	Cuff on left branch of pulmonary artery inflated to 150 mm. Hg							
2.52		25	26.71	50.35	7.32	9.02	9.10	101
2.52	Cuff deflated							
3.24		25	26.63	49.35	7.33	9.17	9.06	98.8

the pericardium is reflected from the great vessels downward for a distance of 2 inches.

The edges of the pericardium were retracted by temporary ligatures. The pulmonary artery was freed from the aorta by blunt dissection and the cuff tied snugly in place. After approximating the edges of the pericardium, the wound

was closed in layers, the tube connecting with the cuff being led through the incision as far as the platysma muscle, then beneath this muscle, to make its exit through the skin at a point on the dorsolateral aspect of the chest, 3 inches distant from the wound. This was an added precaution taken against the possibility of infection working its way in from the outside. Silk ligatures and sutures were used throughout.

The dog made a splendid recovery and on February 9, 1926, appeared well and acted normally. The only sign of infection was a slight, odorless discharge, which could be expressed about the tube at the point of its exit in the skin. Weight on this date, 13 kilos. The dog had shown a very decided disinclination toward food, but there had been some improvement in this respect over the immediate postoperative period.

February 9, 1926. On four separate occasions the tension in the cuff was gradually raised to the point of producing respiratory failure, without any increase in respiratory rate. Each break was characterized by identically the same symptoms. The dog would suddenly become restless, lift up its head and then begin to whine. This was immediately followed by muscle rigidity, and the respirations, which had become irregular, abruptly ceased. Immediate deflation of the cuff restored the animal to its normal state within a few seconds. The results obtained during the first and second compressions on this date are shown in Tables III and IV.

Similar results were obtained in another dog (No. 10) of this series. In this experiment it was observed at operation that inflation of the rubber cuff resulted in a marked dilatation of that portion of the pulmonary artery proximal to the cuff.

The conclusion can now be definitely drawn that *resistance to the flow of blood to the lungs obtained by sudden or gradual compression of the pulmonary artery, in both the cat and the dog, though it results in dilatation of the pulmonary artery and of the right chambers of the heart, does not give rise to rapid and shallow breathing as do multiple emboli of the pulmonary capillaries and arterioles, but produces practically no change in respirations until syncope and respiratory failure suddenly occur.* From this it is likewise concluded that the markedly accelerated and shallow respirations following embolism of the pulmonary capillaries and arterioles are not the result of a reflex stimulus arising in the dilated heart or pulmonary artery.

Effect of Gradual Compression of the Pulmonary Veins on the Heart and Respirations.—It remained to discover what effect impeding the return of blood from the lungs to the heart would have on the respira-

TABLE III.

Dog 6.

February 9, 1926. Sudden Compression of Pulmonary Artery in an Unanesthetized Dog.

Time	Tension in cuff	Respiratory rate	Pulse rate	Remarks
a.m.	*mm. Hg*	*per min.*	*per min.*	
11.30	0	19	135	Dog quiet
11.35	0	19	168	
11.36	0	16	124	
11.39	0	18		
11.40	100±	0		Cuff abruptly inflated. Respirations ceased. Cuff released
11.41	0	20		
11.43	0	20	124	

TABLE IV.

Dog 6.

February 9, 1926. Gradual Compression of Pulmonary Artery in an Unanesthetized Dog.

Time	Tension in cuff	Respiratory rate	Pulse rate	Remarks
p.m.	*mm. Hg*	*per min.*	*per min.*	
3.22	0	20		Dog quiet
3.23	0	22		
3.24	0			Inflation begun
3.25	40	24		
3.30	36	20	152	
3.32	50	21	147	
3.35	47	24		
3.38	62	24		
3.43	74	23		
3.45		24	145	
3.49	85	24	176	
3.52	106	26–0		Respirations ceased
3.58	0	20		

tory rhythm. Multiple embolism of the pulmonary capillaries and arterioles, we know, results in a condition of congestion and edema of

the lungs. That this change in structure might be responsible for the altered function was long suspected. Drinker, Peabody and Blumgart (10) showed that compression of the pulmonary veins in the cat resulted in a diminution in lung volume as measured by the volume of air which could enter the lungs under a uniform pressure. This diminution was attributed to the state of engorgement induced in the pulmonary capillaries. When the resistance to the outflow of blood was sufficiently severe and prolonged a condition of pulmonary edema arose. Their work included no functional studies on respiration, as
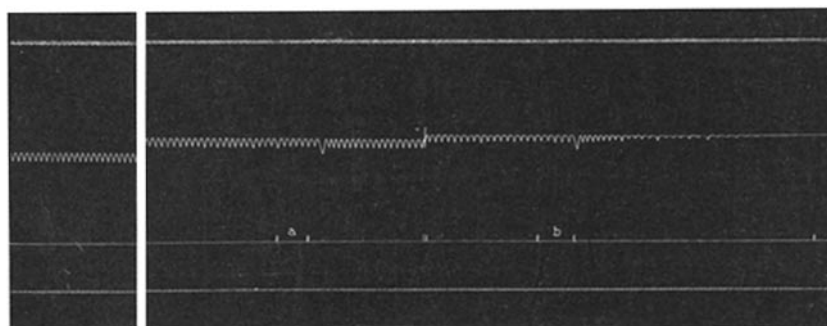

TEXT-FIG. 2. Graphic spirometer tracing made by cat in Experiment 11. The first portion of tracing was taken during the control period. The second portion of the tracing was taken toward the latter part of the experiment in which the pulmonary veins were being progressively compressed by a ligature. At *a* and *b* the ligature was still further tightened. The intervening respiratory rates may be seen in Text-fig. 3.

the animals (cats) were curarized and, therefore, not breathing spontaneously.

We again availed ourselves of the Drinker exposed heart preparation, and in a series of experiments on cats, we gradually compressed the pulmonary veins and observed the effect on the heart and on the respirations. To our surprise exactly the same "all or none" relationship obtained as in compression of the pulmonary artery. Gradually increased pressure exerted by a clamp and ligature on the pulmonary veins leads, after a certain point, to acute dilatation of the heart, followed by cessation of respiration. In no experiment, even when pressure was exerted for many minutes at the point just before respira-

tory failure occurs, did respirations become rapid and shallow. In
Text-fig. 2 a graphic tracing is shown of the respirations and heart
beat during gradual compression of the pulmonary veins in a cat. The
first part of the record is the control period with the ligature in place
but slack. It corresponds to the first bracketed zone in Text-fig. 3.
The second portion of the record represents heart rate and respirations
toward the end of compression corresponding in time to the second
bracketed zone in Text-fig. 3. The intervening portion of the graphic
spirometer tracing is omitted, but the rate may be seen in Text-fig. 3.
During this whole second period the heart was blue and markedly
dilated. Respirations will be seen to continue at about uniform rate
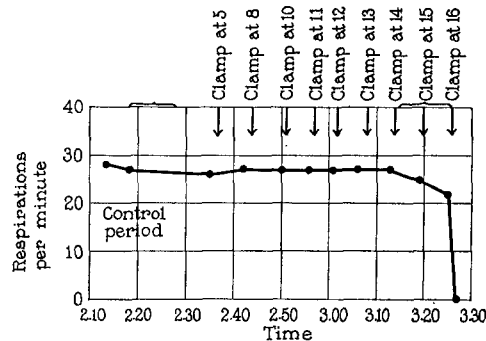
TEXT-FIG. 3. The respiratory rate of the cat in Experiment 11. The bracketed
areas in the curve correspond in time to the two sections of the graphic tracing
shown here (Text-fig. 2).

and depth until they more or less suddenly cease. This observation
was repeated in two other cats in which it was shown that release of
the ligature was promptly followed by return of the heart to its nor-
mal appearance and the respirations to the control rate and depth.
*In no experiments did rapid and shallow breathing develop as the result
of gradual compression of the pulmonary veins or, in other words, of
increased resistance to the flow of blood from the lungs.* It was, unfor-
tunately, impossible to compress the pulmonary veins in the dog be-
cause, as has been said, this animal is anatomically unsuited to the
Drinker exposed heart technique; nor is the pneumatic cuff method
applicable, so obscurely and closely packed are the veins as they enter
the posterior auricular wall.

DISCUSSION.

Since this paper constitutes the last of this series of experimental studies on respiration it may be well, even at the cost of redundancy, to consider again our findings, and what lessons are to be gleaned from them. The work was originally undertaken with a hope of understanding more clearly the mechanism and significance of that type of breathing frequently encountered in patients suffering from lobar pneumonia,—breathing characterized by being both rapid and shallow. Such disordered respiration is known to be accompanied often by oxygen want, and the point has been raised that it may indeed be responsible for oxygen want which, in turn, through its influence on the respiratory center, may perpetuate the disordered type of breathing and lead eventually to the exhaustion and ultimate collapse of the respiratory organ system.

Our work began some years ago with a quantitative study of the degree of pulmonary involvement which occurred in lobar pneumonia (11). By measuring the so called "functional residual air," or that volume of air enclosed in the lungs at the end of a normal, quiet expiration, we arrived at a more or less quantitative estimation of the degree of pulmonary involvement. It was found in general that this function varied with the clinical course of the disease, that after crisis the volume of the functional residual air rapidly increased, and that it remained either stationary or decreased as long as the active infection persisted. No unequivocal correlation, however, could be arrived at between lung volume, so measured, and the type of breathing. Occasionally rapid and shallow respirations were seen to persist for a considerable length of time after the disease process had become arrested. Nor did the state of anoxemia seem to be responsible for the accelerated respirations. In most patients in whom oxygen inhalation relieves the existing state of anoxemia, as determined by oxygen analysis of the arterial blood, rapid respirations still persist.

There seemed to be a hitherto unconsidered element responsible for the disordered breathing and for various reasons this was assumed to be one of a nervous reflex nature. The work of Porter and Newburgh (12) showed that the dyspnea associated with experimental lobar pneumonia in dogs could be checked by sectioning the vagus

nerves or blocking them with cocaine. Dunn (13) discovered the interesting fact that multiple embolism of the pulmonary arterioles and capillaries in goats resulted in very rapid and shallow breathing which could at once be stopped by double vagotomy. Our studies began where Dunn's left off. We found that this phenomenon was inherently related to obstruction of the capillaries and arterioles. When the larger branches of the pulmonary artery were obstructed a similar disorder of breathing resulted, but this was found to be wholly the result of oxygen want and could accordingly be arrested or prevented by oxygen inhalation. Anoxemia of this origin was demonstrated to be due to a relative change in rate of blood flow through the pulmonary vessels. Obstruction of the finer vessels, though often associated with anoxemia, was not in this respect the responsible factor for the disordered breathing, since rapid and shallow breathing persisted even after relief of oxygen want.

What then was the cause of rapid and shallow breathing due to capillary embolism? To this problem we addressed ourselves and it was found far more difficult in its solution than had been anticipated. Indeed a proper understanding of it has depended upon the exhibition of a large amount of so called negative evidence.

We know that capillary obstruction is associated with a diminution in the volume of the "functional residual air" which is probably dependent upon the secondary state of edema, atelectasis and congestion which arises. It seemed reasonable to believe that this pathological condition of the lung, which could give rise to oxygen want, might likewise be responsible for a retention of carbon dioxide, or an increase in the pressure of CO_2 and the concentration of hydrogen ions in the blood. These changes were, in fact, found but that they are not the cause of the disordered breathing is strongly indicated by the fact that rapid and shallow breathing may occur after embolism without any increase in pCO_2 or fall in pH. We know, too, that the actual presence of the embolic material is not responsible for the accelerated breathing in the sense of its being a local irritant, though the inhibitory effect of vagotomy or vagal freezing first made us suspect this to be true. The fact that starch emboli do not produce rapid and shallow breathing solely by acting as local irritants is shown by these two considerations: (1) a considerable amount of embolic mate-

rial may be present without any influence upon the normal respiratory rhythm; (2) emboli may be present in the capillaries and arterioles of one lung sufficient ordinarily to produce rapid breathing without however, any alteration in normal breathing unless the circulation to the other lung is cut off or has been disturbed by a previous period of obstruction. These last facts suggested that the phenomenon was in some manner related to (1) a restriction of the pulmonary vascular bed, (2) resistance to the flow of blood through the lungs or (3) the state of congestion and edema of the lungs. The first two of these possibilities might easily be related to an extra burden on the heart, resulting in an increased pressure in the pulmonary artery and right side of the heart with a subsequent dilatation of these tissues. The demonstra-stration by Levy (7) of an increased heart size in pneumonia was thought perhaps to be a germane phenomenon. It has been shown in this paper that dilatation of the pulmonary artery and right heart does in fact occur when the arterioles and capillaries of the lungs are obstructed. And it was tentatively hypothecated that the dilatation of the pulmonary artery and right heart resulting from obstruction to the finer vessels of the lungs occasioned impulses which reflexly accelerated respirations. Evidence has been brought forth in this paper to show that this hypothesis is erroneous and that reduction of the pulmonary vascular bed, at least by half, produces no change in breathing. Moreover, both resistance to the flow of blood to and from the lungs though followed, when of sufficient grade, by dilatation of the pulmonary artery and right heart, does not give rise to rapid and shallow breathing. The result of such resistance is an "all or none" phenomenon in which respirations continue at their normal rate and depth until they more or less suddenly cease completely.

We are left then to a consideration of the third possibility enumerated above, namely, that rapid and shallow breathing of the kind here described is the result of the particular lesion produced in the lungs, namely, congestion and edema.

How this acts to produce accelerated breathing still remains more or less a mystery: whether directly through irritation of vagal nerve ending; whether as the result of marked encroachment on lung volume; or whether through changes in elasticity of the lung, which to be sure we have not been able to demonstrate in the embolized lung at autopsy.

The first of these three possibilities seems to us at present to be the most likely. It is tempting to theorize but perhaps unwise to befog an already complicated subject by unproven hypotheses. Certainly congestion of the lungs, reduction in lung volume and impaired elasticity of the pulmonary parenchyma are all three intimately associated phenomena, and are present in many of the clinical states in which disordered breathing is a prominent symptom.

SUMMARY AND CONCLUSIONS.

1. Embolism of pulmonary arterioles and capillaries produced by the intravenous injection of starch grains results in a dilatation of the pulmonary artery and the right chambers of the heart. This has been demonstrated both by x-ray studies and direct inspection.

2. The dilatation of the pulmonary artery and heart occurs synchronously with the acceleration of respirations.

3. Dilatation of these structures produced by other means, such as obstruction to the flow of blood to and from the lungs, by gradually clamping either the pulmonary artery (cat and dog) or pulmonary veins (cat) does not, however, give rise to rapid and shallow breathing.

4. The effect of these maneuvers on respiration does not become apparent until respirations suddenly cease.

5. Neither does sudden restriction of the pulmonary vascular bed by clamping the left branch of the pulmonary artery give rise to rapid and shallow breathing, though this procedure may cause an increase in CO_2 tension and in hydrogen ion concentration of the blood.

6. Since rapid and shallow breathing is *not* the result of (1) anoxemia, (2) increased pCO_2 and hydrogen ion concentration of the serum, (3) restriction of pulmonary vascular bed by nearly half, (4) increase in resistance to the flow of blood to and from the lungs, (5) the presence of starch grains in the lungs acting as a local irritant, it must be the result of the secondary pathological changes which occur in the pulmonary parenchyma following embolism.

7. The nature of these changes, congestion and edema, has been discussed elsewhere. Whether they operate directly on nerve endings or through their influence on lung volume and tissue elasticity is not certain.

8. Various important clinical analogies have been emphasized.

BIBLIOGRAPHY.

1. Binger, C. A. L., Brow, G. R., and Branch, A., *J. Clin. Inv.*, 1924, i, 127.
2. Binger, C. A. L., Brow, G. R., and Branch, A., *J. Clin. Inv.*, 1924, i, 155.
3. Binger, C. A. L., and Moore, R. L., *J. Exp. Med.*, 1927, xlv, 633.
4. Binger, C. A. L., Boyd, D., and Moore, R. L., *J. Exp. Med.*, 1927, xlv, 643.
5. Haggart, G. E., and Walker, A. M., *Arch. Surg.*, 1923, vi, 764.
6. Wiggers, C. J., *Physiol. Rev.*, 1921, i, 239.
7. Levy, R. L., *Arch. Int. Med.*, 1923, xxxii, 359.
8. Stewart, H. J., *J. Clin. Inv.*, 1927, iii, 475.
9. Drinker, C. K., *J. Exp. Med.*, 1921, xxxiii, 675.
10. Drinker, C. K., Peabody, F. W., and Blumgart, H. L., *J. Exp. Med.*, 1922, xxxv, 77.
11. Binger, C. A. L., and Brow, G. R., *J. Exp. Med.*, 1924, xxxix, 677.
12. Porter, W. T., and Newburgh, L. H., *Am. J. Physiol.*, 1916, xlii, 175; 1917, xliii, 455.
13. Dunn, J. S., *Quart. J. Med.*, 1920, xiii, 129.

EXPLANATION OF PLATES.

PLATE 24.

FIG. 1, a and b.   X-ray photograph of dog's heart taken in Experiment 1. Tube distance 2 meters.   In a the dog was breathing 16 times to the minute, the area of the shadow as measured by a planimeter being 43.4 sq. cm.   In b after a starch suspension had been injected intravenously, respirations were 64 to the minute, and the area of the shadow is 48.4 sq. cm.

PLATE 25.

FIG. 2. Operative field with pulmonary artery exposed and cuff in place ready for ligation.

FIG. 3. Dog 6, 8 days after operation, showing tube, which communicates with cuff surrounding the pulmonary artery, projecting through the chest wall.
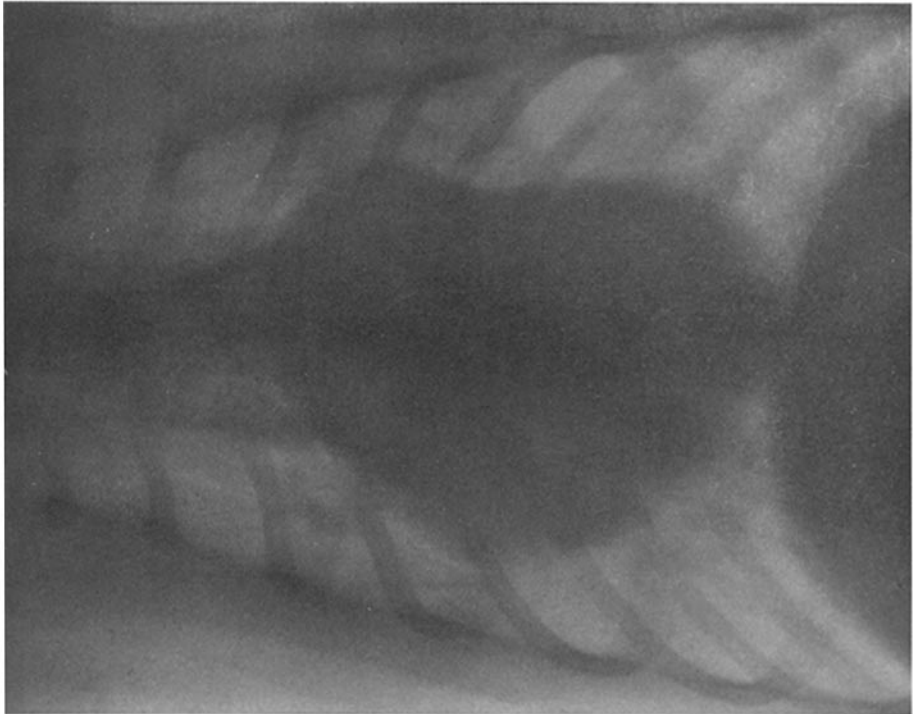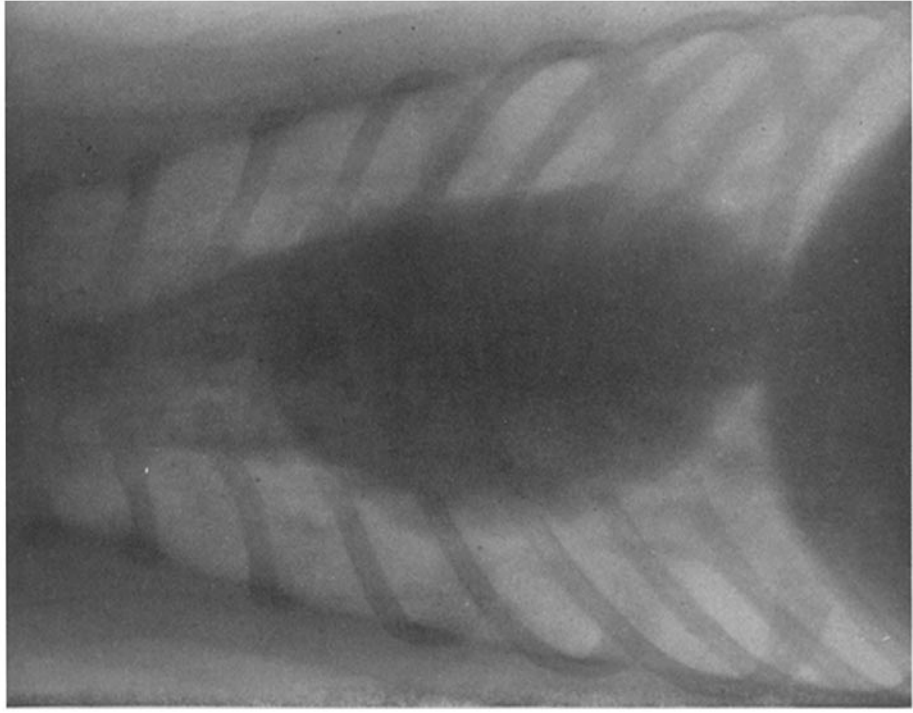
FIG. 1, b.

FIG. 1, a.

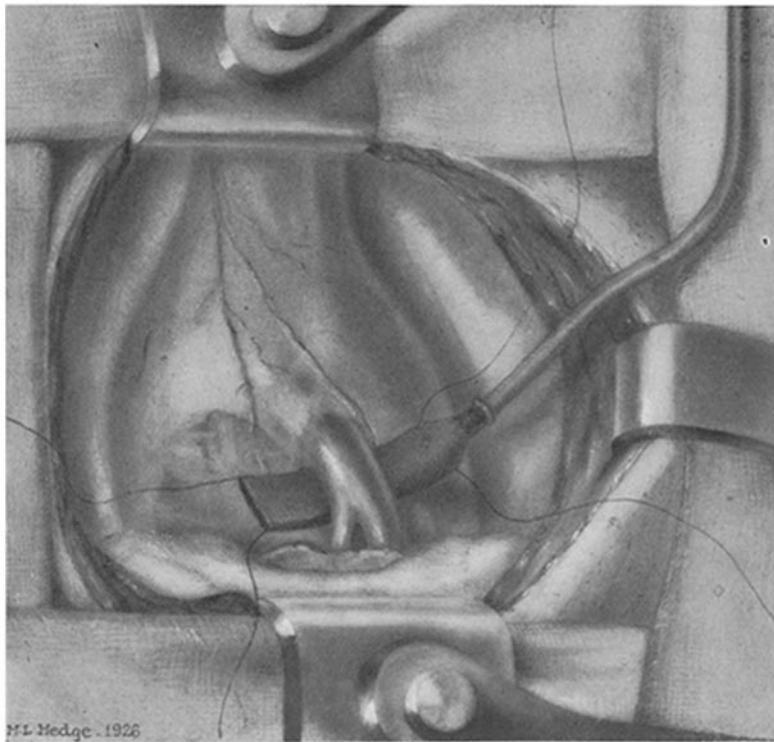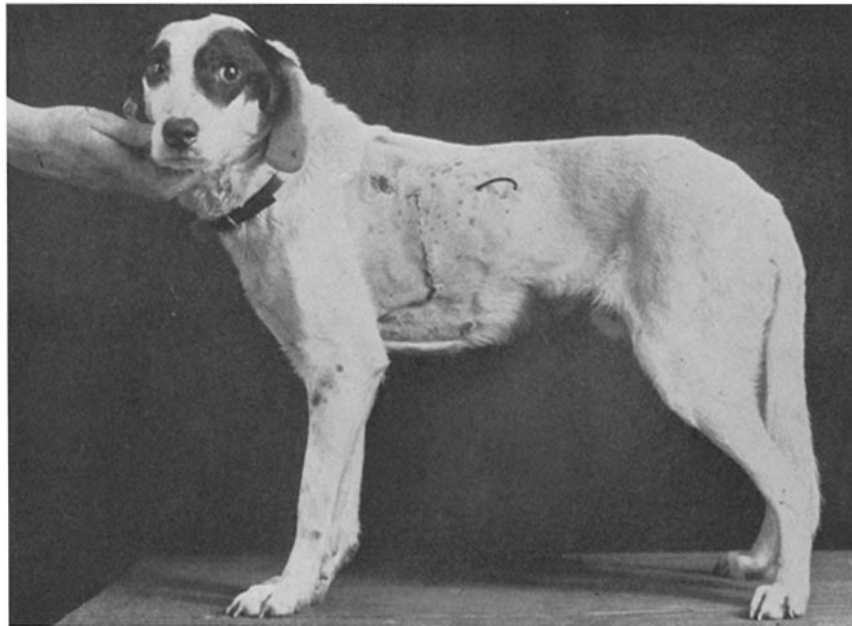(Moore and Binger: Blood flow to and from lungs.)

FIG. 2.

FIG. 3.

(Moore and Binger: Blood flow to and from lungs.)