CHANGES IN THE CIRCULATION PRODUCED BY GRADUAL OCCLUSION OF THE PULMONARY ARTERY

John H. Gibbon Jr., … , Mary Hopkinson, Edward D. Churchill

Research Article

CHANGES IN THE CIRCULATION PRODUCED BY GRADUAL OCCLUSION OF THE PULMONARY ARTERY

By JOHN H. GIBBON, Jr., MARY HOPKINSON, AND
EDWARD D. CHURCHILL

(*From the Surgical Laboratories of the Massachusetts General Hospital and the Harvard Medical School, Boston*)

There appears a striking lack of similarity between observations that record the effects of slow compression of the pulmonary artery in animals and the phenomena that may follow a partial occlusion of the same artery in man by a massive embolus.

Cohnheim's (1) description of the effects of slowly produced pulmonary stenosis is so classical that it is worthy of quotation particularly as other experimental studies have simply confirmed his findings. The experiments of Cohnheim recorded simultaneously the pressure in the right auricle and femoral artery. A ligature was passed about the pulmonary artery and slowly tightened. Even when the constriction was carried to a marked degree there was not "*the slightest change in the femoral curve or in the manometer in the jugular. A change occurs only when the stenosis is carried beyond a certain point. The arterial pressure then undergoes a steep and sudden descent*, while at the same time the level of the venous manometer rapidly rises; and, if the ligature be not loosened, life is in extreme danger." This finding is used by the author to illustrate his concept of the ability of the heart to accommodate itself to increased work until a point is reached "when the resistance becomes so considerable that the cardiac contractions are no longer capable of completely overcoming it," and " the *circulation is instantly at an end. An intermediate state* where the blood stream, though not quite normal, continues; where at each systole the heart still throws a certain quantity of blood into the arteries, though not the former normal, average amount, and thus maintains the arterial and venous pressures at levels lower and higher respectively than is normally the case; such an intermediate state, that is to say, as we become acquainted with in connection with increased pericardial tension, *does not exist here.* The physiological heart-muscle can meet the demands on its work, or it cannot meet them; in the former case, we have a regular physiological circulation, in the latter, death."

The abrupt failure of the circulation under these circumstances has been described repeatedly. Haggart and Walker (2) produced occlusion of the pulmonary artery by slowly approximating the jaws of a clamp. As in Cohnheim's experiments, no effect upon systemic blood pressure or

cardiac output was observed until a certain point was reached; then the blood pressure and cardiac output fell precipitately to zero and the animal died unless the clamp was instantly released. The end point appeared so definite that these observers could predict from the number of turns of the clamp just when it was to occur. Moore and Binger (3), using a similar method, obtained identical results.

It is true that death from pulmonary embolism in man may occur with the dramatic suddenness that is registered in these experiments. The effect of complete occlusion of the pulmonary artery by an embolus can be nothing else but an immediate cessation of cardiac output and death. Not infrequently, however, instead of dying immediately, the patient lives for several hours and autopsy confirms the diagnosis of the presence of a large clot of blood partially obstructing the main stem of the artery. During the interval between embolism and death, the symptoms shown by the patient are those commonly associated with diminishing cardiac output, lowered arterial pressure, peripheral vasoconstriction, and anoxemia. In addition, increasing distention of the veins has been noted (4).

The fact that it is possible to reproduce in experiment a state of affairs comparable physiologically to that observed at the bedside was mentioned briefly in connection with a study directly concerned with the function of the pericardium (5). It is believed that the finding deserves some elaboration, however, and in the following studies we have recorded in detail the changes in arterial and venous pressures and cardiac output following partial occlusion of the main stem of the pulmonary artery. It is shown that the prolonged period of reduced cardiac output observed in man can be reproduced in the experimental animal, and that death occurs not necessarily from precipitate failure of an overloaded right heart, but from a gradual withdrawal of blood from active circulation. This blood accumulates in the venous side of the circulatory system where it is trapped by the obstruction to the outflow from the right side of the heart. Death under these circumstances occurs as it does in hemorrhage or shock—not primarily from cardiac failure, but from the effects of a reduced volume of circulating blood.

EXPERIMENTS

The experiments were performed oh cats anesthetized by the intraperitoneal injection of a 10 per cent solution of sodium barbital, 4.5 cc. per kilogram of body weight. The injection was made about forty-five minutes before the experiment was started. Drinker heart preparations (6) were used in the majority of the experiments. Cats so prepared breathe naturally with the heart exposed in the open pericardium sutured to the wall of the chest. In a few instances the pulmonary artery was exposed by removing a portion of the sternum, and artificial respiration was maintained throughout the experiment by intermittent intratracheal

insufflation. The mean carotid pressure was recorded in the usual manner with a mercury manometer. The venous tracing was obtained by the method described by Lewis and Drury (7). A solution of heparin was given intravenously to prevent clotting.

Graduated compression of the pulmonary artery was accomplished by means of a clamp which has been described in an earlier publication (5). It is very similar to the one used by Haggart and Walker, but is capable of finer adjustments.

The commonly described effect of gradual occlusion of the pulmonary artery may be reproduced with this clamp and is illustrated in Figure 1.
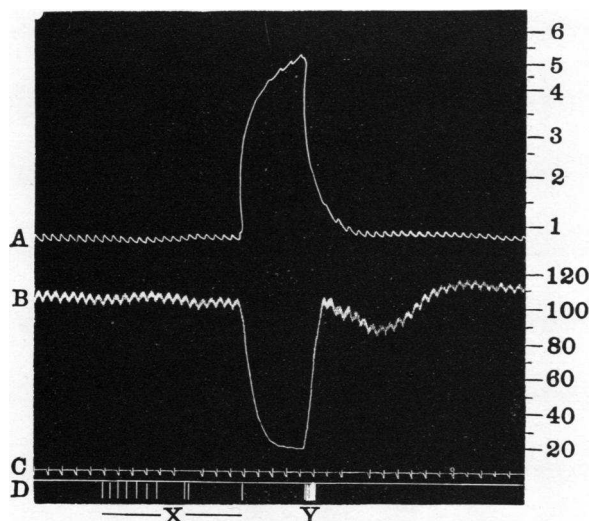

FIG. 1. KYMOGRAPHIC TRACING ILLUSTRATING THE EFFECT OF COMPARA-
TIVELY RAPID COMPRESSION OF THE PULMONARY ARTERY

A, venous pressure in centimeters of water recorded from the superior vena cava. B, arterial pressure in millimeters of mercury recorded from the left carotid artery. C, time in five second intervals. D, signal marker. The pulmonary artery was compressed during the time interval X and released at Y.

In this experiment (Number 7) the pericardium was opened and the clamp adjusted about the pulmonary artery just above the pulmonary valves. The artery was then gradually compressed by successive turns of the screw approximating the jaws of the clamp 0.635 mm. at a time. Circulatory failure occurred suddenly during the course of this compression with an abrupt rise in venous pressure and a sharp fall in arterial pressure. This sudden failure of the circulation occurring in the course of gradual occlusion of the pulmonary artery is identical with that reported by other workers (1, 2, 3).

However, it was found that gradual compression of the pulmonary artery could be made to produce a slow fall in arterial pressure and a
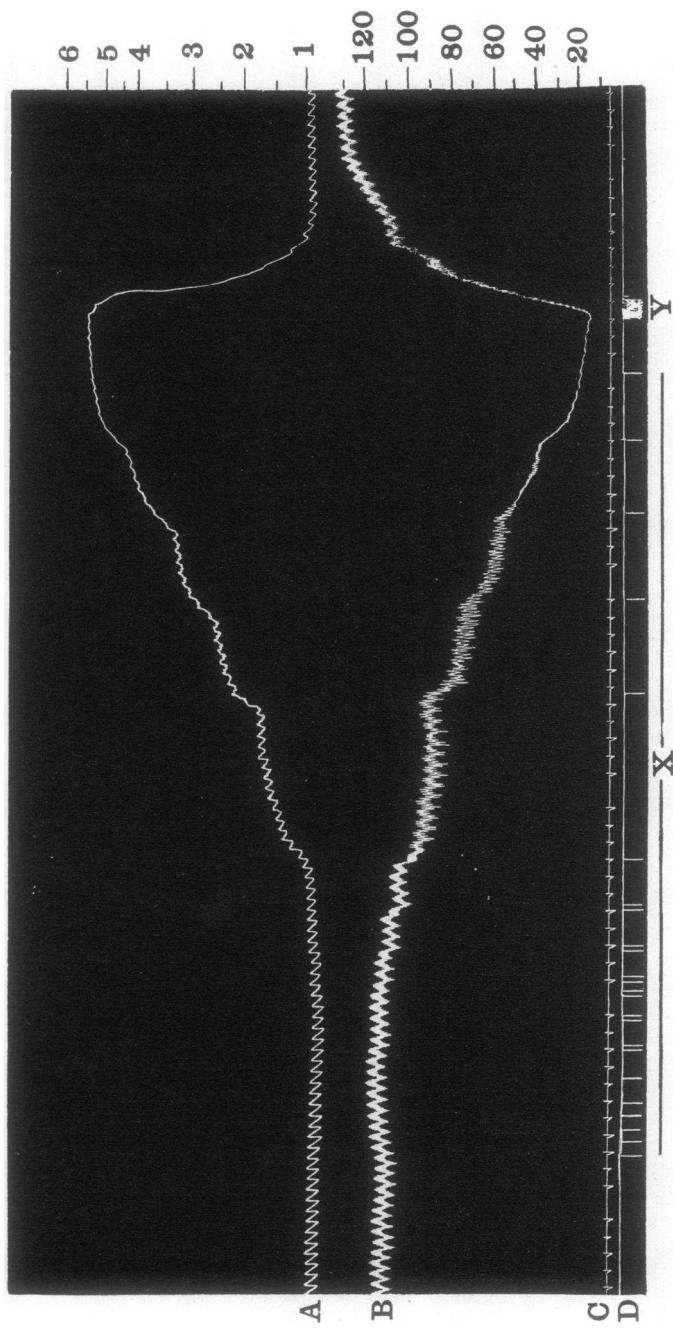
FIG. 2.   KYMOGRAPHIC TRACING ILLUSTRATING THE EFFECT OF MORE GRADUAL COMPRESSION OF THE PULMONARY
ARTERY

A, B, C, D, as in Figure 1.   During the time interval *X* the clamp about the pulmonary artery was tightened.   The
successive increments of compression were very small and a slow fall in arterial and a slow rise in venous pressure
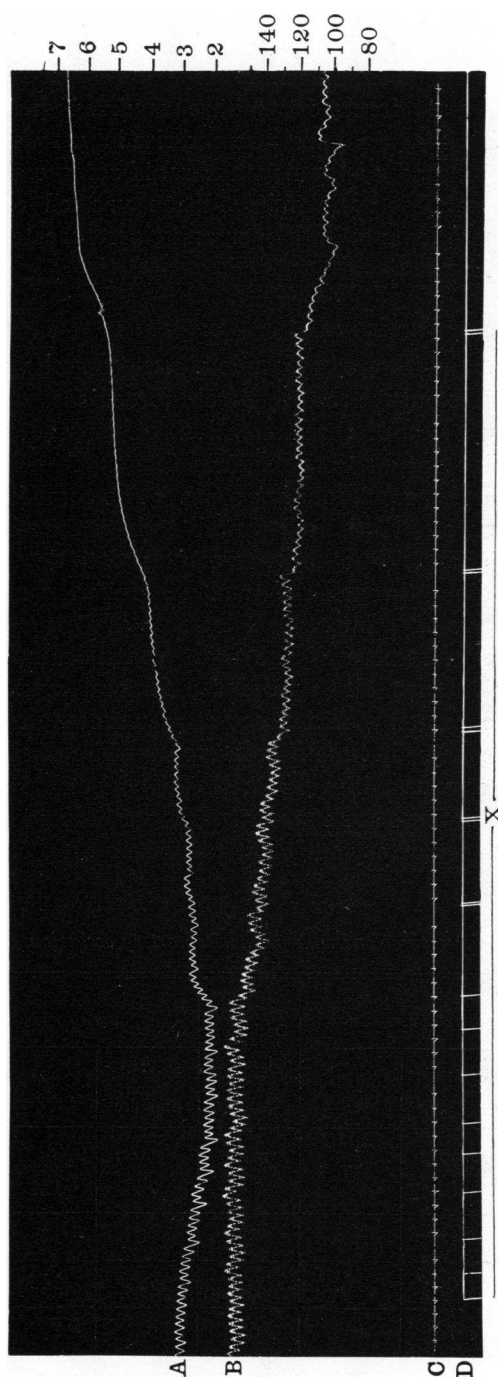resulted.   At *Y* the clamp was completely released.

FIG. 3. KYMOGRAPHIC TRACING ILLUSTRATING THE EFFECT OF GRADUAL COMPRESSION OF THE AORTA

A, B, C, D, as in Figure 1. During the time interval X the clamp about the aorta was gradually tightened. The effect upon arterial and venous pressures is similar to that noted during compression of the pulmonary artery (Figure 2). The slight fall in venous and the slight rise in arterial pressure which can be observed during the initial degrees of compression were noted in many other experiments.

corresponding rise in venous pressure, provided it was carried on with sufficient *finesse*. Figure 2 is another section of the kymographic record of Experiment 7. Here the successive increments of compression were reduced to 0.079 mm. and circulatory failure occurred gradually as evidenced by the slow fall in arterial pressure and rise in venous pressure. Similar results have been noted during slow and rapid compression of the aorta (Figure 3). These observations have been verified eighty-two times in forty-seven experiments in both open and closed chests and with Drinker heart preparations.

Determination of cardiac output

It seemed likely that the lowered systemic blood pressure was caused by a diminution in cardiac output resulting from forced accumulation of the blood on the venous side of the circulation. To prove this point determinations of cardiac output were made in five experiments before and during compression of the pulmonary artery. The compression was continued in each instance until the systemic blood pressure had fallen at least 10 mm. Hg. The Fick method was employed to determine the minute volume flow of blood through the lungs. Drinker heart preparations were used in all five experiments. The samples of mixed venous blood were obtained by puncture of the right ventricle under direct vision. Arterial samples were taken from the femoral arteries. The tracheal cannula was connected with a closed oxygen metabolism system containing Krogh valves, a soda lime chamber and a Krogh spirometer. The fall of the spirometer gave a direct indication of oxygen consumption.

The results obtained in these five experiments are tabulated in Table I. Occlusion of the pulmonary artery sufficient to cause a drop in systemic

TABLE I

Cardiac output determinations with pulmonary artery occlusion

Date	Weight of cat	Before partial occlusion of pulmonary artery		Occlusion of pulmonary artery	During partial occlusion of pulmonary artery		
		Systemic blood pressure	Cardiac output		Systemic blood pressure	Cardiac output	Decrease in cardiac output
1930	*kgm.*	*mm. Hg*	*cc. per minute*	*per cent*	*mm. Hg*	*cc. per minute*	*per cent*
October 29........	2.84	83	179		72	124	31
October 31........	2.85	126	430	88	90	145	66
November 3......	3.47	105	394	87	78	205	48
November 5......	3.55	78	488	61	62	292	40
November 6......	2.50	68	391	83	56	230	41

blood pressure of more than 10 mm. Hg was accompanied by a decrease in cardiac output varying between 31 and 66 per cent. As might be expected, there was no close relationship between the degree of occlusion of the artery, the fall in systemic blood pressure and the decrease in cardiac output. However, the most marked occlusion produced the greatest fall in blood pressure and the largest decrease in cardiac output, while the smallest drop in blood pressure was associated with the smallest decrease in cardiac output.

Degree of occlusion produced by clamp

In order to estimate the degree of occlusion produced by their clamp Haggart and Walker (2) compressed a section of a rubber tube and by inking the distorted end reproduced its sectional area on paper. From the measurements of these ink impressions they drew a curve from which the degree of occlusion of the pulmonary artery could be estimated. It is obvious that the accuracy obtained with such a method is not great.

The degree of occlusion of the artery was estimated with far greater accuracy in the following manner. The clamp was adjusted about the pulmonary artery at the start of each experiment so that the plane of the jaws of the clamp was at right angles to the long axis of the artery. Then the jaws were approximated until the distance between them corresponded to the diameter of the artery during systole. That is, they just touched the external surface of the artery with each heart beat. At the end of the experiment, the jaws were approximated until the artery was completely occluded. The distance traversed by the lower movable jaw of the clamp from its first position to its last corresponds to the original internal diameter of the artery. The original cross sectional area of the artery may then be computed by the formula $O = \pi R^2$ in which O represents the cross sectional area and R the original internal radius of the artery as measured by the clamp.

An elastic tube subjected to a uniform internal pressure will assume the shapes shown in Figure 4 when compressed by the clamp. By measuring a series of such figures stamped with the inked end of a rubber tube Haggart and Walker derived a curve from which they computed the degree of occlusion of the compressed artery. The formula used was $O = \pi r^2 + 2rl$, in which O is the cross sectional area, r, the radius of the lateral curvatures at either side of the compressed artery, and l, the transverse distance across the artery from the end of one curved edge to the beginning of the other (Figure 4, Diagram C). Now the factor r can be computed at any point in the compression because it equals one-half the difference between the original diameter and the distance through which the lower jaw of the clamp has moved. But assuming the circumference of the artery to be constant, l can also be computed by the

formula: $l = \dfrac{2\pi R - 2\pi r}{2}$. Then substituting for l in Haggart and Walker's formula we have : $O = \pi r(2R - r)$, O representing the area of cross section, R, the original internal radius of the artery, and r, one-half of the difference between $2R$ and the distance which the movable jaw of the clamp has moved toward the fixed jaw.
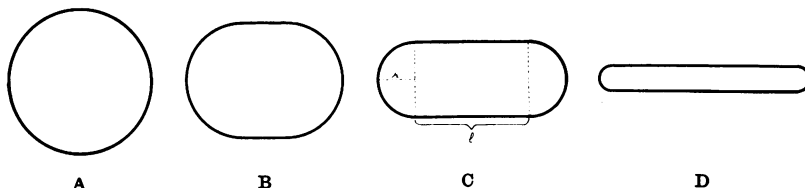

FIG. 4.   DIAGRAMS OF THE CROSS SECTION OF THE PULMONARY ARTERY

A, before compression by the clamp, B, C, D, successive stages of compression.

The last formula makes it possible to determine directly the area of cross section of the artery with any degree of compression.   The accuracy of these computed areas depends chiefly upon the care employed in placing the clamp on the artery.

In fourteen experiments determinations were made of the original cross sectional area of the pulmonary artery, the area at which the first definite lowering (10 mm. Hg) of the systemic blood pressure occurred and the area at which any further compression resulted in death of the animal. It was found that the systemic blood pressure was not definitely lowered until from 61 to 86 per cent of the artery had been occluded and that the compression was not fatal until from 84 to 96 per cent of the artery had been occluded.   In one instance compression was fatal when only 73 per cent of the artery had been occluded.   In this experiment the animal had a large pneumothorax, which undoubtedly contributed to the circulatory failure.   The variations in the figures in these fourteen experiments are probably to be accounted for by the variations in blood loss and length of the experiment with resultant differences in the ability of the right heart to overcome a partial occlusion of the pulmonary artery. The values given are all higher than the estimated degree of occlusion at which Haggart and Walker noted abrupt cardiac failure.

It is of interest to note the mechanical principles that give rise to the artifact of a finely determined end point at which circulatory failure takes place when a coarsely adjustable clamp or ligature is employed to occlude the artery.   The pulmonary artery may be regarded as a flexible tube subjected to a pressure uniformly distributed upon its internal surface and the jaws of the clamp as two parallel planes compressing the tube between them.   A cross section of such a tube will assume the shapes illustrated in Figure 4 as the two parallel planes approach one another.

It is evident from these diagrams that a one millimeter approximation of the jaws of the clamp when the arterial lumen resembles Diagram *D* will cause a much greater reduction in cross sectional area than a similar approximation when the lumen is of the form shown in Diagram *B*. Figure 5 is a graphic illustration of this fact.   It represents the per cent
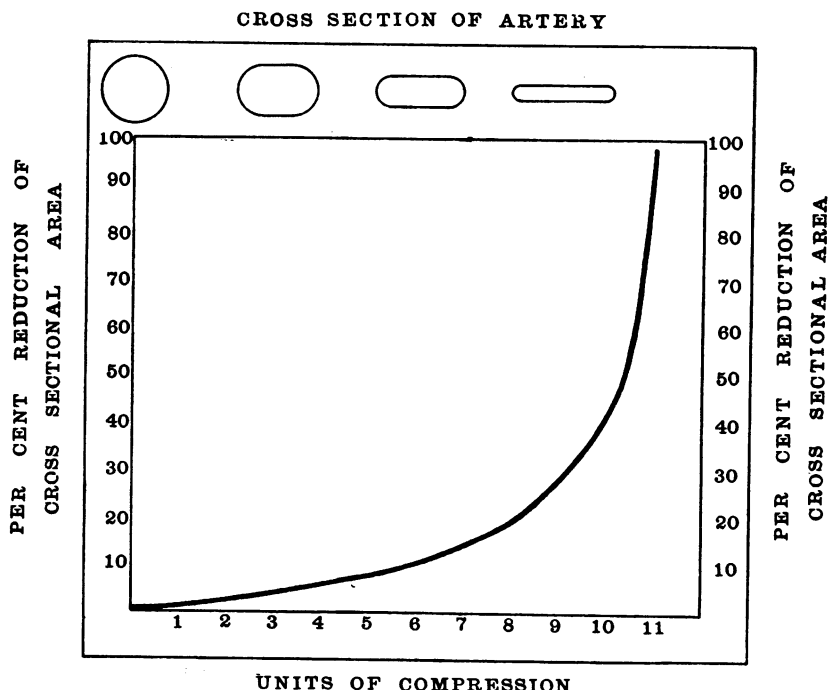

FIG. 5.   GRAPH OF CHANGES IN THE CROSS SECTIONAL AREA OF THE PUL-MONARY ARTERY DURING COMPRESSION BY THE CLAMP IN EXPERIMENT 15

Each unit of compression represents an approximation of the jaws of the clamp equal to 0.635 mm.   The diagrams above the graph represent cross sections of the pulmonary artery at 0, 3, 6, and 9 units of compression.

reduction in each preceding cross sectional area of the pulmonary artery occasioned by an 0.635 mm. approximation of the jaws of the clamp. Each of the first five approximations produces less than a 10 per cent diminution in the immediately preceding sectional area.   Approximation by a similar increment just before complete occlusion of the artery produces a 98 per cent reduction in area.   Thus, unless the clamp is capable of very fine adjustments, cardiac failure will appear to occur abruptly during a slow and gradual compression (Figure 1) although in reality it takes place when the diminution in the cross sectional area of the pulmonary artery becomes markedly increased by each turn of the clamp.

By well known hydraulic principles this rapid decrease in cross sectional area causes a sharp increase in the resistance to blood flow.   A

demonstration to this effect was obtained by experiments with the excised pulmonary artery. In fourteen experiments the pulmonary artery and adjacent portion of the right ventricle were excised after the death of the cat. A glass tube having approximately the same internal diameter as the pulmonary artery was then inserted through the right ventricle and tied into the artery so that it projected just beyond the pulmonary valves. The cannula was connected with a water reservoir designed to deliver water at a constant pressure. The rate of flow through the pulmonary artery was determined by timing with a stop watch the collection of 500 cc. of water in a graduated glass cylinder. The clamp was adjusted about the pulmonary artery in much the same manner as it had been in the living cat. The rates of flow with a constant pressure in the water reservoir were determined at various degrees of occlusion of the artery.

Figure 6 is a graph of the results obtained by this method in one experiment. The same pulmonary artery was used from which the areas in Figure 5 were computed. The sharp decrease in rate of flow as com-
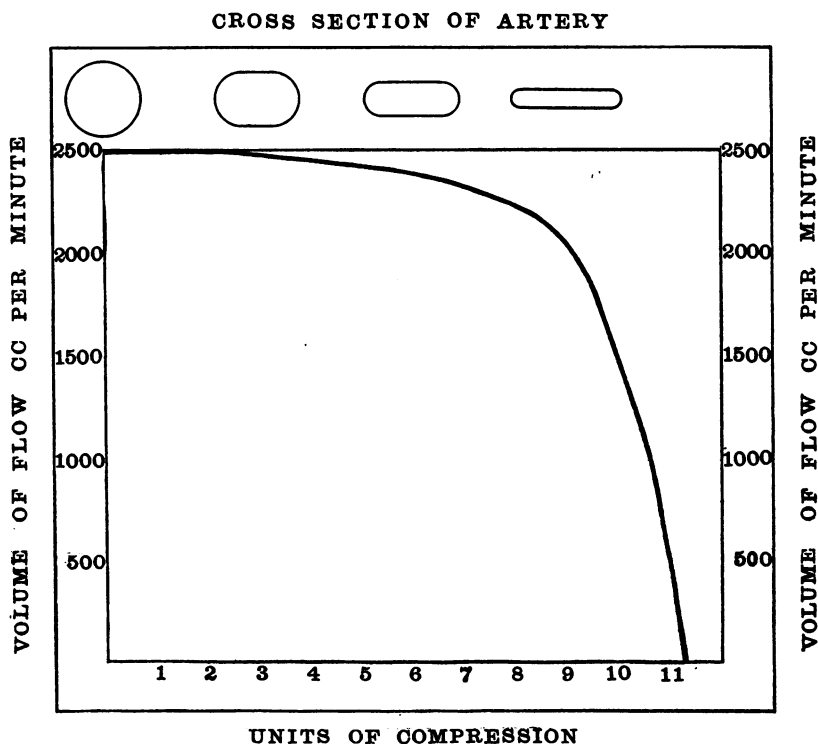

FIG. 6.   GRAPH OF CHANGES IN RATE OF FLOW THROUGH THE EXCISED PUL-
MONARY ARTERY DURING COMPRESSION BY THE CLAMP
Cross sections of artery and units of compression as in Figure 5.

plete occlusion of the artery was approached corresponds to the sharp diminution in the cross sectional area seen in Figure 5.   In fact, by inverting Figure 6, the curves are almost superimposable.   The same abrupt diminution in rate of flow was observed in the other thirteen experiments. As all other factors in these experiments were constant, the rate of flow varied inversely as the resistance offered by the clamp.   This gives experimental confirmation of the sharply increasing resistance offered by the clamp already deduced from a consideration of calculated cross sectional areas.   It is apparent, therefore, that the abrupt circulatory failure noted during a supposedly gradual occlusion of the pulmonary artery or aorta can be ascribed to the use of a method which in reality produces a sudden and large reduction in the calibre of the vessel after a certain point is reached.

CONCLUSIONS

1. Obstruction of the pulmonary artery up to 60 per cent of its cross sectional area is without significant effect upon the arterial or venous pressures.

2. A reduction in cardiac output attended by a fall in blood pressure and rise in venous pressure occurs when the occlusion lies between 60 and 85 per cent.

3. The circulation fails not primarily from cardiac insufficiency but due to the fact that blood collects on the venous side of the system by reason of the obstruction to the outflow from the right heart.

4. The obstruction is fatal when 85 to 100 per cent of the pulmonary artery is occluded.

BIBLIOGRAPHY

1. Cohnheim, J. F., Lectures on General Pathology.   London, The New Sydenham Society, 1889, vol. 1, p. 54 et seq.
2. Haggart, G. E., and Walker, A. M., Arch. Surg., 1923, vi, 764.   The Physiology of Pulmonary Embolism as Disclosed by Quantitative Occlusion of the Pulmonary Artery.
3. Moore, R. L., and Binger, C. A. L., J. Exp. Med., 1927, xlv, 655.   Observations on Resistance to the Flow of Blood to and from the Lungs.
4. Giertz, K. H., and Craford, C., Acta Chirurg. Scandinav., 1929, lxiv, 121.
5. Gibbon, J. H., Jr., and Churchill, E. D., J. Clin. Invest., 1931, x, 405.   The Mechanical Influence of the Pericardium upon Cardiac Function.
6. Drinker, C. K., J. Exp. Med., 1921, xxxiii, 675.   A Useful Heart Method.
7. Lewis, T., and Drury, A. N., Heart, 1923, x, 301.   Observations Relating to Arterio-Venous Aneurysm.   I. Circulatory Manifestations in Clinical Cases with Particular Reference to the Arterial Phenomena of Aortic Regurgitation.