THE EXPERIMENTAL PRODUCTION OF UNCOMPENSATED HEART DISEASE WITH ESPECIAL REFERENCE TO THE PATHOLOGY OF DROPSY.¹

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FOR the past few years the older methods of studying the pathology of œdema by the actual production of dropsy under various experimental conditions have been replaced by the more modern methods of investigating the lymph flow from lymphatic vessels, and of taking the specific gravity of the tissues; the reason for this is, that the processes underlying lymph formation are believed to be the same, to a large extent, as those which are responsible for the production of œdema. The present investigation is therefore, as it were, a reversion to the older methods of study in that it is concerned with the experimental production of œdema.

Without entering into any detailed discussion as to the ultimate factors involved in the production of cardiac dropsy, the present paper is concerned only with the experimental facts relating to the blood pressures in the arteries, veins, and capillaries, which have been found to occur in an animal the subject of uncompensated heart disease.

A brief outline of the principal experiments that have been made with the view of elucidating the pathology of the œdema of venous obstruction will first be given.

There are at the present time three distinct theories with regard to the primary factors concerned in the pathology of the dropsy of venous stagnation:—

1. A secretory theory, according to which the endothelial cells of the capillaries are supposed to have a specific secretory function, and that in dropsy this function is very much increased.

Hamburger (¹) is the chief exponent of this theory. He holds the same views upon lymph formation as does Heidenhain, and believes that in passive œdema the accumulation of waste products in the blood vessels stimulates the capillary endothelium to increased secretion, and that the dropsy does not

¹ The expenses of this investigation have been defrayed, in part, by a grant from the British Medical Association.

depend upon increased pressure in the capillaries or alteration in their walls.

2. A theory which maintains that malnutrition of the tissues and accumulation of waste products are the most important factors in determining the production of œdema, and that a minor part is played by the blood vessels.

Lazarus-Barlow⁽²⁾ originated this theory. He has investigated the œdema of passive congestion by taking the specific gravity of the blood and tissues, and the amount of lymph flow from the lymphatics. He concludes that increased venous pressure *per se* does not cause œdema. He points out that, in all circumstances in which there is œdema, the tissues are deprived of nutriment, or that waste products are not removed, or that both these are combined; and he considers that these are the primary factors concerned in the production of œdema, but he also states that there is no doubt that the vessel walls are altered.

He grants that in uncompensated heart disease there is a rise of venous and a fall of arterial pressure, and remarks that the low arterial pressure leads to starvation of the tissues; the raised venous pressure adds to this, and also prevents the removal of waste products.

He defines œdema production as "an excess of the normal process whereby the nutrition of the tissues and the removal of their waste products are carried out."

3. A mechanical and physical theory, according to which the dropsy depends upon increased venous and capillary pressure, together with an altered condition of the vessel wall, filtration and osmosis playing a most important part in it.

This theory dates its origin to more than two hundred years ago, when Richard Lower⁽³⁾ ligatured the inferior vena cava in the chest in animals and obtained ascites; he also ligatured the jugular veins at their lower ends, and obtained œdema of the head and neck. He therefore concluded that the œdema of heart disease was due to an increase of pressure in the veins and capillaries.

Ranvier⁽⁴⁾ repeated Lower's experiment of ligaturing the jugular veins, but found that œdema was not produced. He also ligatured the inferior vena cava in the abdomen, and cut the sciatic nerve on one side, and then the œdema appeared on the same side as the section, but not on the other side. He finally concluded that the œdema was due to vascular dilatation which, together with ligature of the vein, raised the pressure in the vessels, and so led to an exudation of serum.

Cohnheim⁽⁵⁾ showed that œdema of the leg can be produced by injecting the veins with plaster of Paris, in other words by blocking up all the anastomotic channels.

In order to study the effects of uncompensated heart disease upon the peripheral circulation, Cohnheim experimentally distended the pericardium with oil, and noted the changes in arterial and venous pressures as the intrapericardial pressure was raised. He found that, as the intrapericardial pressure was raised, the pressure in the jugular vein rose, and that in the femoral artery fell; and that, when the pressure within the pericardium had risen to from 240 mm. to 320 mm. of oil, the circulation was stopped, the pressure in the jugular vein being 240 mm. (or higher) of soda solution, and that in the femoral artery from 10 to 15 mm. Hg, the pulsations having ceased. His explanation of the phenomenon was that the rise of pressure in the pericardium interposes an obstacle to the escape of blood from the veins into the heart, and

therefore the blood accumulates in the venous system. He argues that "whatever be the cause of the disturbance of compensation, it cannot have escaped you that its effect on the circulation in general differs in no essential particular from that resulting from the abnormal increase of pericardial tension." He concludes that in uncompensated heart disease the *general* venous pressure is raised and the arterial lowered, and, therefore, the pressure in the capillaries is raised and the velocity of the blood stream diminished, the sluggish stream becoming more venous. In discussing the dropsy of heart disease and of venous stagnation generally, he says that the dropsy depends upon increased capillary pressure together with diminished velocity of blood stream, but, at the same time, adds that we are also "compelled to assume a peculiar influence exerted by the vessel wall." An experiment by Wooldridge⁽⁶⁾ shows the importance of this "influence exerted by the vessel wall." Wooldridge showed that if a solution of tissue-fibrinogen be injected into the circulation, and the femoral vein ligatured, oedema of the leg occurs with hæmorrhages over the upper part of the leg and the lower part of the abdomen.

Starling's⁽⁷⁾ experiments upon lymph formation led him to support the mechanical and physical theory of the production of oedema. He has also investigated the blood pressures in the various regions of the vascular system in uncompensated heart disease.

Following Weber, he considers that the mean systemic pressure in the vessels when the circulation is brought to a standstill (hydrostatic mean pressure) is equivalent to the mean systemic pressure when the blood is circulating (hydrokinetic mean pressure); and that there are two ways of raising the mean systemic pressure, namely, (1) by diminishing the total capacity of the system (vaso-constriction), and (2) by increasing the total amount of fluid in the system (plethora).

Having brought the circulation to a standstill by stimulation of the vagus, he finds that the position of the mean systemic pressure, or neutral point of the system, is situated in the region of the portal vein and at the upper end of the femoral vein. He therefore concludes that heart failure alone cannot raise the mean systemic pressure; and that the effect of heart failure would be a *rise* of pressure in the large veins of the trunk and in the liver, and a *fall* of pressure in the arterial system, and in the capillaries and veins of the intestine as far as the portal vein, and a *fall* of pressure in the capillaries and veins of the limbs as far as the upper end of the femoral vein. He considers that Cohnheim had no right to deduce a general rise of venous pressure on injecting oil into the pericardium, since he only measured the venous pressure in the jugular vein. Starling, therefore, repeated Cohnheim's experiments, taking the arterial pressure and the venous pressures in the inferior vena cava and portal vein. He found that there was a fall of arterial pressure and a rise in pressure in both the inferior cava and portal vein. On letting the oil out of the pericardium, the pressure in the inferior cava rapidly fell to its former level, and the arterial pressure rose even higher than it was before; the portal pressure, before settling to its level before the introduction of the oil, rose to a point more than twice as high as it was at the beginning. Starling concludes that a previous vasomotor constriction was responsible for the height to which the arterial and portal pressures rose after the oil was let out of the pericardium. He therefore states that the mean systemic pressure is raised in uncompensated heart disease owing to vasomotor constriction. In order to find out whether this rise of mean systemic pressure can extend back to the capillaries, he repeated his former experiments, placing the limb in a plethysmograph, and he found on raising the intrapericardial pressure that the limb diminished in volume. Applying these results to uncompensated heart disease, Starling differs from Cohnheim in that he considers that there is a rise of venous pressure in the large veins of the trunk and in the liver, but in the intestines and limbs there is a fall of venous and capillary pressure. He also

points out that there might be a rise of capillary pressure if plethora existed in heart disease, but that there is no evidence to prove this; that hydræmia is present, but not hydræmic plethora.

With regard to the manner in which œdema is brought about, he considers that the low capillary pressure leads to increased absorption from the connective-tissue spaces; there is hydræmia, and this, as Cohnheim has proved, if long continued, will injure the vessel wall, so rendering it more permeable; the stagnation of blood leads to absence of a proper renewal of oxygen and nutrient material to the capillary wall; the dropsy is entirely conditioned by the state of the capillary wall, and the very slight increase of capillary pressure, such as occurs in a dependent part, will cause œdema.

It may be stated here that Leonard Hill's⁽⁸⁾ views, and also those of other observers, concerning the equivalence of the hydrostatic and hydrokinetic mean pressures of the vascular system by no means coincide with those of Weber. For his arguments against this equivalence, and also against the assertion that contraction of the arterioles diminishes the total capacity of the system, the reader is referred to Schafer's *Physiology*.

Hill maintains that—(1) "The vascular system is not filled to distension" owing to the great capacity of the veins, so that "the whole of the blood within the body can pass into the roomy reservoirs of the veins, and yet the walls of the veins will scarcely be thrown into tension."

(2) "That various pressures can occur in different parts of it, when the heart is in arrest."

(3) "That a reduction in the total capacity of the system need not raise the mean pressure of the whole."

The first point, therefore, which has to be settled in discussing the pathology of cardiac dropsy is whether there is a *general* rise of venous pressure, or a rise in the large veins of the trunk only, and a fall in the more peripheral parts of the venous circulation, and also whether this pressure remains high whilst dropsy is being produced.

METHOD OF INVESTIGATION.

The principle which has been adopted is the same as that employed by Cohnheim, namely, to interfere with the diastolic filling of the heart. The method which has been used consists in constricting the pericardium by means of sutures, so that the free expansion of the chambers of the heart during diastole is prevented, and the blood tends to accumulate in the venous system. It will be seen later (p. 82) that constriction of the pericardium does not act solely by preventing the free diastolic filling of the heart, and also that it differs in several important particulars from Cohnheim's experiments.

The other alternative would have been to interfere with the emptying of the heart, or, in other words, with the heart in its capacity as a force pump. Experiment, however, has shown that the heart, with its muscle in all respects intact, can so perfectly accommodate itself to increased work which is presented to it, that it will overcome an increasing resistance opposed to it up to a certain point, and thus maintain the arterial and venous pressures at their normal heights; beyond this point, however, when the heart cannot completely overcome the resistance, it suddenly fails and the circulation stops. There

is no intermediate condition, in which the arterial pressure falls and the venous pressure rises according to the amount of resistance opposed to the heart, as is seen when the diastolic filling of the heart is interfered with.

This difficulty has also been encountered in the present series of experiments, the majority of the animals dying outright from a too severe constriction, or, on the other hand, completely recovering, probably on account of stretching of the pericardium, or owing to the constriction not being tight enough, and the heart therefore being able to adjust itself to existing circumstances. An intermediate condition of uncompensation has, however, been hit in a certain proportion of the cases at the expense of much waste of time.

The best method of estimating the *amount* of constriction is to take the degree of fall of the arterial pressure as a guide; but here again it is difficult to determine how much of the fall is directly due to the constriction and how much is due to the shock which must necessarily accompany so severe an operation.

Further difficulties are encountered with reference to the blood pressures, because they vary so much under different circumstances (artificial respiration, morphia, variations in depths of anæsthesia) that it is extremely difficult to get an *absolute* reading of the average blood pressures, and two readings at different times would not be the same unless the animal was placed under identical conditions on each occasion. On the other hand, *relative* changes of blood pressure, occurring as the immediate result of certain experiments, are more reliable, as whether the initial pressure is up to its average level or above or below it, is not a matter of much importance.

The present investigation was commenced in January 1902, and completed in February 1903. The experiments have been repeated several times, and fifteen of those, illustrating the required points, are now described. These experiments naturally fall into three groups:—

GROUP I.—Those in which the pericardium is constricted and the animal allowed to recover in order to determine whether dropsy results.

GROUP II.—Those in which the pericardium is constricted and the result upon the arterial and venous pressures noted, the animal being killed at the conclusion of the experiment.

GROUP III.—Those in which the subsequent changes, if any, in the arterial and venous pressures, whilst dropsy is being produced, are observed.

In the experiments described under Group II., from $\frac{1}{4}$ to $\frac{1}{2}$ gr. of morphia was injected and the animal was anæsthetised with ether; in this way a very perfect anæsthesia was produced. In those of Groups I. and III., ether alone was used. The animals employed in all cases were cats. The position in all the experiments was supine, with the limbs stretched out and the back of the head resting on the table. The skin having been shaved and disinfected, a

longitudinal incision was made on the *right* side of the chest, and the skin and underlying muscles held aside by weighted retractors; the chest was opened by an incision in the sixth intercostal space, and the sixth and seventh ribs drawn apart by weighted retractors. A longitudinal fold of parietal pericardium was taken up in Spencer Well's forceps, and a continuous suture of silk was introduced so as to unite the two layers of the fold along the side of the closed blades of the forceps next to the heart. The forceps were then removed, the sixth and seventh ribs united by interrupted sutures, and the muscles and skin then stitched up. The whole operation was of course conducted under strict antiseptic precautions.

Another method described below was also employed:—

The *left* side of the chest was opened as described above and the apex of the parietal pericardium seized in Spencer Well's forceps and cleared from fat. The pericardium was stitched as described above; or a double ligature was passed through it behind the forceps, leaving a loop on one side and two free ends on the other, each free end was then passed round to the loop side and one end passed through the loop; the ligature was then drawn tight and tied.

The advantage of taking the pericardium in forceps first is, that the degree of constriction can be more easily adjusted so as to produce a certain fall of arterial blood pressure than if the stitches are introduced one by one. In some cases where the animal was killed at the end of the experiment the forceps alone were used to cause the constriction of the pericardium.

During the operation artificial respiration was maintained by means of bellows communicating with a bent piece of glass tubing which was passed into the larynx. The air was blown through a bottle containing ether, and a short-circuiting tube was used, so that the ether could be cut off and pure air used for inflating the lungs at any moment. In this way the animal could be kept perfectly anæsthetised to the same degree without any trouble whatever, and the operation of tracheotomy was rendered unnecessary.

In Group III. experiments the blood pressures were taken whilst the operation was being carried out, and the alterations in these were noted; the blood pressures were taken later on when the animal was suffering from uncompensation. On each occasion the animals were under exactly the same conditions.

The arterial blood pressure was taken in either the carotid or the femoral artery. A mercurial manometer with a millimetre scale attached was used. The manometer was connected by pressure tubing with a glass cannula, and these were filled from a side tube by means of a pressure bottle with 25 per cent. MgSO_4 solution. (One-thirteenth the weight of mercury.)

The venous pressures were taken in the inferior vena cava, the cannula being introduced into the external iliac vein; at the upper end of the external jugular, the cannula being introduced into the posterior auricular vein and pushed down to the opening of the latter into the jugular; in the lower end of the femoral vein just immediately above the foot, the cannula being introduced into a side branch as in the case of the external jugular; in the portal vein, the cannula being introduced into a splenic vein or into a mesenteric vein. A manometer with similar connections to the arterial manometer described above was used, and was filled with a 25 per cent. solution of MgSO_4 .

RESULTS OF EXPERIMENTS.

GROUP I.—In these experiments the pericardium was constricted, and the animal was allowed to recover, dropsy resulting.

EXPERIMENT A.—*Jan. 8, 1902.*—Cat. Weight, 2720 grms. Anæsthetised with ether; intubation of larynx and artificial respiration. Chest opened and four Lembert's sutures introduced into right side of pericardium. Recovered. 9.—A little swelling under the lower jaw; cat seems languid. 10.—The swelling is more marked, and extends round the eyes and under the ears; respirations, 96 per minute. 12.—Animal died.

Post-mortem.—Œdema of subcutaneous tissues in front of neck, extending down to the chest and upwards under the chin, round the ears, the upper and lower lips, and the eyelids. The back of the neck and the remaining subcutaneous tissues quite normal. About 12 c.c. of slightly blood-stained serum in each pleural cavity and a small amount in the peritoneal cavity. No signs of inflammation anywhere. The right ventricle of the heart was slightly grooved by the stitches in the parietal pericardium. Wound quite healthy, a little surrounding œdema.

EXPERIMENT B.—*Jan. 30, 1902.*—Cat. Anæsthetised with ether. Intubation of larynx and artificial respiration. Chest opened and apex of parietal pericardium ligatured as described above. Recovered. 31.—Animal died.

Post-mortem.—Œdema of subcutaneous tissues of front of shoulders and neck, extending almost up to chin, and especially collected round the external jugular veins. Œdema of mediastinum. A little fluid in each pleural cavity. No signs of inflammation anywhere. Wound quite healthy; a little surrounding œdema.

EXPERIMENT C.—*June 19, 1902.*—Cat. Weight, 2350 grms. Placed in cage to collect urine. 20.—Passed 230 c.c. of urine, no albumin, in the twenty-four hours. Anæsthetised with ether; intubation of larynx and artificial respiration. Chest opened and pericardium stitched, the upper end as near the auriculo-ventricular groove as possible. Recovered. 21.—No urine passed. 22.—100 c.c. of urine in the twenty-four hours. Trace of albumin. 23.—40 c.c. of urine in the twenty-four hours. Trace of albumin. Respirations, 45. The animal put under ether in order to take the blood pressures, died of asphyxia.

Post-mortem.—Œdema of front of neck, especially round external jugular veins and extending on to front of chest.

Pleural cavities.—50 c.c. of very slightly blood-stained serum in the right pleural cavity. In twenty-four hours a loose rusty-coloured coagulum separated, the resulting fluid being quite clear, and straw-coloured. 30 c.c. of similar fluid in the left pleural cavity, depositing a similar coagulum. In both cases the fluid boiled practically solid.

Peritoneum.—23 c.c. of slightly milky serum, which in twenty-four hours deposited a very loose and small coagulum.

Mediastinum.—Œdema of the mediastinum extending up into the neck.

No signs of inflammation anywhere. Wound quite healthy; a little surrounding œdema.

From these experiments it is apparent that constriction of the pericardium produces the clinical picture of uncompensated heart disease—dropsy, diminished amount of urine and dyspnoea. Whether albumin in the urine is also produced cannot be absolutely decided, because the mere administration of ether sometimes produces a trace of albumin in the urine. A much more frequent result of the operation is for the dropsy to be limited to the serous cavities and mediastinum, as is seen in the following experiment:—

EXPERIMENT D.—*Jan. 20, 1903.*—Cat. Weight, 4000 grms. Anæsthetised with ether. Pressure in the femoral artery (normal respiration) 160 mm.

Hg. The cat stopped breathing, and the blood pressure began to fall and reached 60 mm. Hg. Intubation was rapidly performed, and artificial respiration was commenced, after which the pressure rose to 80 mm. Hg. The chest was opened and the apex of the pericardium tied, the arterial pressure falling to about 40 mm. Hg. When breathing normally the pressure had risen to 100 mm. Hg. 21.—130 c.c. of urine passed containing a cloud of albumin. Respirations, 40. Took 320 c.c. of milk. 22.—130 c.c. of urine passed. Respirations, 40. Has taken 100 c.c. of milk. Put under ether arterial pressure, 135 mm. Hg.; intubated, and right side of pericardium stitched, the pressure in the femoral artery then fell to 50 mm. Hg. On normal respiration the pressure in the femoral artery was 80 mm. Hg. Death in about four hours.

Post-mortem.—10 c.c. of very slightly blood-stained serum in the peritoneal cavity. A few c.c. of blood-stained serum in each pleural cavity. Œdema of the mediastinum. No subcutaneous œdema, and no sign of inflammation anywhere.

In this case the fluid present was no doubt a result of the first operation.

It is also evident from the experiments contained in this group that, in the absence of any special effect of gravity upon the circulation, the dropsy of heart disease first manifests itself in the serous cavities and in the mediastinum.

GROUP II.—In these experiments the pericardium was constricted and the immediate effect upon the arterial and venous pressures was recorded; in some of the cases the experiment was kept in progress for over one hour in order to determine if the pressures remained constant.

The animals were in all cases killed at the end of the experiment.

EXPERIMENT A.—*March 7, 1902.*—Cat. Weight, 2350 grms. Morphia, $\frac{1}{4}$ gr. administered. Anæsthetised with ether. Tracheotomy and artificial respiration. Cannula was pushed up the femoral vein into the external iliac vein in order to take the pressure at the lower end of the inferior vena cava. Another cannula was inserted into the carotid artery. The sixth left intercostal space was incised, and the apex of the pericardium was cleared from fat. At this moment the pressures were—carotid 90 mm. Hg; inferior vena cava, 55 mm. MgSO_4 solution. The pericardium was constricted with forceps, and at once the pressure became—carotid, 30 mm. Hg; inferior vena cava, 145 mm. MgSO_4 solution. The systolic elevations were much smaller than before, and a presystolic elevation was evident in the vein. A further portion of pericardium was taken up in the forceps, and the carotid pressure then fell to about 10 mm. Hg, the systolic elevations practically ceasing; meanwhile the venous pressure continued to rise until it attained the height of 230 mm. MgSO_4 solution. The pericardium was now released, and at once the carotid pressure shot up to about 100 mm. Hg, and the pressure in the vena cava fell to its original level. The animal was now killed.

EXPERIMENT B.—*March 17, 1902.*—Cat. Weight, 1730 grms. $\frac{1}{3}$ gr. morphia given. Anæsthetised with ether. Tracheotomy and artificial respiration. Cannulae inserted into the external iliac vein and carotid artery as in the previous experiment, and the chest was opened as before. In this case, however, ligatures were tied round the apex of the pericardium, instead of its being seized in forceps.

The pressures obtained were as follows:—

At commencement of operation.—Carotid, 120 mm. Hg; inferior vena cava, 69 mm. MgSO_4 solution.

After first ligature.—Carotid, 70 mm. Hg; inferior vena cava, 100 mm. MgSO_4 solution.

After second ligature (nearer heart than first).—Carotid, 40 mm. Hg; inferior vena cava, 120 mm. MgSO_4 solution.

After third ligature (still nearer heart).—Carotid, 20 mm. Hg; inferior vena cava, 140 mm. MgSO_4 solution.

In a few moments the heart began to fail, the systolic elevations becoming irregular and finally spasmodic, the heart ceasing in diastole.

The two preceding experiments show that whether the pericardium is constricted by means of forceps or ligatures the immediate effect upon the peripheral circulation is exactly the same as on the introduction of oil into the pericardium, namely, a fall of arterial pressure and a rise of venous pressure, the output of the heart during systole being diminished. If the constriction is released, the pressures return to normal, the arterial for a time exceeding this; if the constriction is increased beyond a certain point the heart, fails and ceases in diastole.

EXPERIMENT C.—*May 27, 1902.*—Cat. Weight, 3150 grms. No morphia was given, as it is much easier in the absence of morphia to get the animal to breathe naturally after the operation. Anæsthetised with ether. Cannulæ introduced into the femoral artery and external iliac vein.

Pressures.—Femoral artery, 94 mm. Hg; inferior vena cava, 58 mm. MgSO_4 solution.

Pressures after intubation and artificial respiration.—Femoral artery, 80 mm. Hg; inferior vena cava, 75 mm. MgSO_4 solution.

Pressures after chest opened and apex of pericardium cleared.—Femoral artery, 80 mm. Hg; inferior vena cava, 75 mm. MgSO_4 solution.

A ligature tied round apex of pericardium.

Pressures subsequently.—Femoral artery, 50 mm. Hg; inferior vena cava, 120 mm. MgSO_4 . The chest was stitched up, and in a few minutes the animal was breathing naturally.

One hour later, with the animal breathing naturally, the pressures were:—

Femoral artery, 52 mm. Hg; inferior vena cava, 68 mm. MgSO_4 solution. The animal was now killed.

The result of this experiment shows that although there is a preliminary rise of venous pressure synchronous with the fall of arterial pressure, the *venous pressure subsequently falls practically to its normal level* in the course of an hour or so; and, moreover, this fall of venous pressure is not due to relaxation of the pericardium, because in that case the arterial pressure would rise to its original level with the fall of venous pressure. It is, however, practically unchanged.

EXPERIMENT D.—*February 6, 1903.*—Cat. Weight, 3000 grms. Anæsthetised with ether; tracheotomy and artificial respiration. Cannula in right femoral artery; cannula introduced into a branch of the left femoral vein, just above the foot, and pushed down till it just reached the opening of the branch into the main trunk.

Pressures at the beginning of the operation.—Artery, 110 mm. Hg; vein, 140 mm. MgSO_4 solution.

1. *Pericardium Constricted with Forceps.*

The pressures at once altered as follows, the presystolic pulsation in the vein, together with the rises in pressure synchronous with insufflation of the lungs being very evident:—

		Artery.	Vein.
		50 mm. Hg.	175 mm. MgSO ₄ solution.
In	... 5 minutes	50	160
"	5 "	40	155
"	10 "	48	150
"	5 "	60	148
"	5 "	70	150
"	5 "	78	146
<hr/>			
	35 "		

2. *Pericardium further Constricted.*

		Artery.	Vein.
		60 mm. Hg.	164 mm. MgSO ₄ solution.
In	... 5 minutes	60	155
"	5 "	70	148
"	5 "	70	143
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	15 "		

3. *Pericardium Constricted still further.*

		Artery.	Vein.
		50 mm. Hg.	150 mm. MgSO ₄ solution.
In	... 5 minutes	48	145
"	10 "	50	140
<hr/>			
	15 "		

The pericardium was now released, and at once the pressures became—

		Artery.	Vein.
		80 mm. Hg.	100 mm. MgSO ₄ solution.
In	... 3 minutes	80-90	95
"	5 "	90-100	85
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	8 "		

4. *Pericardium again Constricted.*

		Artery.	Vein.
		40 mm. Hg.	120 mm. MgSO ₄ solution.
In	... 5 minutes	50	150
"	30 "	50	130
"	15 "	46	123
"	5 "	50	130
"	5 "	52	130
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	1 hour		

The pericardium was now released, and at once the pressures became—

Artery.	Vein.
80 mm. Hg.	80 mm. MgSO ₄ solution.

The animal was then killed.

EXPERIMENT E.—*May 7, 1902.*—Cat. Weight, 3570 grms. $\frac{1}{4}$ gr. morphia. Anæsthetised with ether. Tracheotomy and artificial respiration. Cannula in

left carotid; another was introduced into a branch of the femoral vein, just above the foot, and pushed down till it reached the opening of the branch into the main trunk.

Pressure at beginning of operation.—Carotid, 100 mm. Hg; vein, 140 mm. MgSO_4 solution.

The pericardium was constricted with forceps, and at once the pressures became—carotid, 62 mm. Hg; vein, 195 mm. MgSO_4 solution.

In forty minutes the pressures were—carotid, 40 mm. Hg; vein, 145 mm. MgSO_4 solution.

Normal saline solution was now run into the external jugular vein; both the arterial and venous pressures rose rapidly, and in five minutes pressures were—carotid, 72 mm. Hg; vein, 410 mm. MgSO_4 solution.

The arterial pressure would not rise any higher, and the injection was therefore stopped.

Half an hour later the pressures had fallen to what they were after the pericardium was constricted—carotid, 58 mm. Hg; vein, 195 mm. MgSO_4 solution.

The pericardium was now released, and at once the pressures assumed practically their normal levels—carotid, 90 mm. Hg; vein, 152 mm. MgSO_4 solution.

The animal was now killed.

It is quite evident from the two preceding experiments that the rise of venous pressure is not limited to the trunk, *but occurs also in the limbs*, when the flow of venous blood into the heart is obstructed; and also that the venous pressure falls to its normal level again as it does in the inferior vena cava.

The small rises of venous pressure which occur synchronously with each insufflation of the lungs, and also the presystolic elevation shown in the venous manometer, are of themselves sufficient evidence that the wave of increase of venous pressure does not stop at the upper end of the femoral vein, but extends right to the periphery of the limbs.

The last experiment also demonstrates the fact that, by increasing the volume of blood or producing hydræmic plethora, it is not possible to raise the arterial pressure to its normal level or to keep up the venous pressure.

It is also seen that after the venous pressure has fallen to what it was before the constriction, if the latter is released the venous pressure falls still lower, whilst the arterial rises not quite to its former level. These facts appear to indicate that the fall of venous pressure is not due to the relaxation of the pericardium or to vasomotor action, and, moreover, that the initial vasomotor action, so well seen in the first experiment of this group, tends to pass off; they also seem to demonstrate that the veins undergo a process of stretching before the increased pressure to which they have been subjected, *and that the fall of venous pressure is chiefly due to dilatation of the veins*, especially the large veins of the trunk which are nearest to the seat of obstruction, and are therefore subjected to a somewhat greater strain.

The contraction of the limbs occurring in Starling's experiments, and which he interprets as resulting from a fall of venous pressure,

seems rather to indicate the initial vasomotor constriction which undoubtedly occurs.

With regard to the pressure in the capillaries, it is entirely a matter for speculation whether it rises, falls, or remains normal when the venous pressure is raised and the arterial lowered; but this is a matter of very little moment, as the venous pressure remains high for so short a time. The essential point is, that when the venous pressure has fallen to its normal level, the arterial pressure remaining low, the *capillary pressure must be low*.

EXPERIMENT F.—*February 5, 1903.*—Cat. Weight, 3230 grms. Anæsthetised with ether. Cannulæ in portal vein and femoral artery. Tracheotomy and artificial respiration.

Pressures with Chest opened.

	Artery.	Vein.
...	110 mm. Hg.	100 mm. MgSO ₄ solution.
(1) Pericardium constricted	50 "	120 "
" released	80 "	85 "

The portal vein fell at once to 85, and there was no vasomotor rise at all; the artery did not rise to its former level.

	Artery.	Vein.
(2) Pericardium constricted	40 mm. Hg.	105 mm. MgSO ₄ solution.
In 5 minutes	65 "	108 "
" 5 "	70 "	112 "
" 5 "	80 "	120 "
" 5 "	84 "	122 "

20 "

(3) Pericardium constricted	50 "	125 "
In 5 minutes	40 "	118 "
" 5 "	50 "	125 "
" 5 "	60 "	128 "

15 "

Pericardium released . 100 " 85 " "

The portal vein fell at once in spite of the large rise in the arterial pressure on releasing the pericardium. One minute later—artery, 90 mm. Hg; vein, 88 mm. MgSO₄ solution.

	Artery.	Vein.
(4) Pericardium constricted	30 mm. Hg.	130 mm. MgSO ₄ solution.
In 5 minutes	40 "	127 "
" 5 "	42 "	125 "
" 5 "	46 "	122 "
" 5 "	46 "	120 "
" 5 "	48 "	117 "
" 5 "	52 "	118 "
" 5 "	50 "	115 "
" 5 "	52 "	113 "
" 5 "	52 "	113 "
" 5 "	50 "	110 "
" 5 "	52 "	110 "
" 5 "	48 "	105 "

1 hour

The pericardium was released, and at once the pressures were—

	Artery.	Vein.
...	82 mm. Hg.	60 mm. MgSO_4 solution.
In 3 minutes	80 "	60 " "
" 5 "	80 "	65 " "
(5) Pericardium constricted	12 "	130 " "

The pulsations of the heart were stopped.

	Artery.	Vein.
Pericardium released	80 mm. Hg.	80 mm. MgSO_4 solution.
		At once.

The animal was killed.

EXPERIMENT G.—May 1, 1902.—Cat. Weight, 2700 grms. Morphia, $\frac{1}{3}$ gr. Anæsthetised with ether. Cannulæ in carotid and also in portal vein. Tracheotomy and artificial respiration.

Before constriction of the pericardium the pressures were—carotid, 70 mm. Hg; portal vein, 75 mm. MgSO_4 solution.

The pericardium was constricted by forceps, and at once the pressure became—carotid, 44 mm. Hg; portal vein, 110 mm. MgSO_4 solution.

In twenty minutes the pressures were—carotid, 40 mm. Hg; portal vein, 75 mm. MgSO_4 solution.

Normal saline solution was run into the femoral vein until the portal pressure was 235 mm. MgSO_4 solution, and the carotid pressure was 60 mm. Hg; the injection was then stopped, and the pressure in the portal vein rapidly fell to 110 mm. MgSO_4 solution, and then much more slowly.

In three quarters of an hour the pressures were—carotid, 40 mm. Hg; portal vein, 75 mm. MgSO_4 solution.

The clamp was now released and at once the pressures became—carotid, 60 mm. Hg; portal vein, 65 mm. MgSO_4 solution.

The animal was then killed.

By these experiments one learns that *the portal pressure behaves in the same manner as the other veins* in the body, namely, that there is a preliminary rise of venous pressure and subsequently the pressure falls. In Experiment F., after the first constriction was released, the portal pressure at once fell, and the arterial pressure did not attain its previous height, therefore it follows that vasomotor action is not a necessary consequence of interfering with the heart's action. After the second and third constrictions, the rise of both portal and arterial pressure indicates vasomotor action, but still the portal pressure fell whilst the arterial regained its former level, and therefore one must conclude that, although there may be vasomotor constriction in the liver, the portal pressure may still fall on disencumbering the pericardium, the vasomotor constriction not being able to prevent the rapid emptying of the portal vein. After the fourth constriction the pressure in the portal vein gradually fell, as in the case of the other veins, although the arterial pressure rose, and therefore it is evident that the vasomotor constriction had passed off.

It is extremely doubtful what changes in capillary pressure occur in the intestines and liver at the beginning of the experiments. Heart failure alone without vaso-constriction causes a fall of arterial pressure in the splanchnic area and a rise of portal and vena cava pressure, therefore it may be stated that the pressure in the hepatic

capillaries would be raised, whilst it is doubtful what pressure would obtain in the intestinal capillaries. Vaso-constriction alone (⁹) might cause a slight rise of capillary pressure in the liver, but what its effect upon the pressure in the intestinal capillaries is, is uncertain.

It is probable, therefore, that there is a rise of pressure in the hepatic capillaries, but it is extremely doubtful what would be the pressure in the intestinal capillaries; however, as the experiment proceeds, and when the portal pressure has fallen and the vaso-constriction has passed off, there is no doubt that ultimately *the pressure in the intestinal capillaries is low and in the hepatic capillaries is normal*, as both the portal vein and inferior cava have normal pressures.

EXPERIMENT H.—April 24, 1902.—Cat. Weight, 3140 grms. Morphia, $\frac{1}{2}$ gr. Anæsthetised with ether. Tracheotomy and artificial respiration. A cannula in the carotid and another fine cannula introduced down the posterior auricular vein to the point where it enters the upper end of the external jugular vein.

Pressures on commencing operation with chest opened and apex of pericardium cleared—carotid, 90 mm. Hg; external jugular, 55 mm. MgSO_4 solution.

A ligature was tied round the apex of the pericardium and at once the pressures became as follows—carotid, 44 mm. Hg; external jugular, 105 mm. MgSO_4 solution.

In half an hour the pressures were—carotid, 40 mm. Hg; external jugular, 85 mm. MgSO_4 solution.

In one hour the pressures were—carotid, about 40 mm. Hg; external jugular, about 70 mm. MgSO_4 solution.

The pericardium was released and at once the pressures were—carotid, 60 mm. Hg; external jugular, 50 mm. MgSO_4 solution.

The animal was now killed.

This experiment is merely introduced for the sake of completeness, as it shows that *the same effects upon the circulation occur in the head*, as have already been shown to occur in the limbs and trunk.

To sum up shortly: the results upon the arterial, venous, and capillary pressures obtained in the experiments in Group II. demonstrate that, when the heart fails to maintain its normal systolic output, there is a fall of arterial pressure and a rise of pressure throughout the whole venous system; that soon the venous pressure falls to its normal level, probably owing to distension of the veins; and that, finally, there is a low arterial pressure, a normal venous pressure, and a low capillary pressure, except in the liver where the capillary pressure is normal. It follows from this that the blood flows with a diminished velocity through the capillaries.

EXPERIMENT K.—Feb. 12, 1903.—Cat. Weight, 3150 grms. Anæsthetised with ether. Cannulæ in femoral artery and vein of opposite sides. A cannula was tied into the pericardium and connected by means of a tube to a funnel; the whole was filled with oil, and the tube just above the cannula clipped, so that on releasing the clip the pericardium would be distended with oil, and the pressure of the oil distending the pericardium could be raised or lowered to any level desired by raising or lowering the funnel.

A cannula was inserted into the left femoral vein and connected with a funnel, so that normal saline solution could be transfused into the venous system when required. Tracheotomy and artificial respiration.

Initial pressures when all was ready to start—artery, 130 mm. Hg; vein, 65 mm. MgSO_4 solution.

The oil cannula was unclipped, and the level of the oil in the funnel raised to 120 mm. In about $1\frac{1}{2}$ minute the pressures were—

...	Artery.	Vein.
	60 mm. Hg.	120 mm. MgSO_4 solution.
In 5 minutes	58 "	120 " "
" 5 "	46 "	117 " "
" 5 "	40 "	116 " "
<hr/>		
15 "		

The systolic elevations were now very small indeed, and the arterial pressure continued to fall.

Saline solution was now run into the femoral vein until the venous pressure was 160 mm. in the inferior cava, and the arterial pressure now rose to 60 mm. Hg.

In 3 minutes	Artery.	Vein.
	50 mm. Hg.	120 mm. MgSO_4 solution.
" 3 "	76 "	132 " "
" 2 "	80 "	128 " "
" 5 "	82 "	128 " "
" 5 "	84 "	126 " "
" 5 "	80 "	126 " "
" 5 "	76 "	124 " "
" 5 "	70 "	122 " "
" 5 "	60 "	118 " "
" 3 "	50 "	116 " "
" 2 "	40 "	115 " "
<hr/>		
43 "		

The systolic elevations were again very small, and the arterial pressure continued to fall.

More saline solution was run in until the pressures were—

...	Artery.	Vein.
	90 mm. Hg.	220 mm. MgSO_4 solution.
In 2 minutes	100 "	165 " "
" 5 "	104 "	145 " "
" 5 "	100 "	140 " "
" 5 "	100 "	133 " "
" 5 "	94 "	130 " "
" 5 "	90 "	127 " "
" 10 "	42 "	112 " "
<hr/>		
37 "		

The arterial pressure continued to fall although the venous pressure kept up, and the animal was allowed to die.

This repetition of Cohnheim's experiment shows that, on keeping the pericardium distended with oil for some time, the heart tends to gradually fail. That this failure is due to deficient supply of blood to the heart, and not due to primary heart failure, is shown by the fact

that if the venous pressure is increased by injection of saline solution the arterial pressure rises on account of the increased blood supply to the heart. Both arterial and venous pressures, after a wave of vaso-motor constriction has passed away, continue to fall to the level they were at immediately after the oil was introduced, when the venous pressure remains about the same level, whilst the arterial pressure continues to fall, the systolic output becoming less and less till the heart stops in diastole.

The time the heart takes to fail varies according to the pressure in the pericardium, and also varies somewhat in different animals, but it has occurred in all the animals I have experimented with, and sooner or later the animal dies.

This difference between Cohnheim's oil experiment, in which the venous pressure does not fall, and constriction of the pericardium, in which the venous pressure falls to normal, is easily explained by a reference to the different mode of action of the impediment to the heart in each case.

Cohnheim definitely states that in his experiments the diastolic expansion of the cardiac cavities is not interfered with, but that an obstacle has been opposed to the escape of blood from the veins into the heart. In support of this statement he points out the almost equal elevations of the oil and soda-manometers at every period of the experiment, that the cardiac contractions continue after the circulation has stopped, and also that a rise in the oil manometer not uncommonly marks the moment when the heart stops in diastole.

There is no doubt that the problem resolves itself into a question of equilibrium between the blood in the veins and the oil in the pericardium. The oil surrounds not only the ventricles and auricles but also the lower ends of the thin walled superior and inferior venæ cavæ, which penetrate the pericardium. It therefore follows that if the pressure of the oil around the veins were greater than that of the blood within them they must collapse, and the blood be prevented from entering the heart, although the latter would still continue to contract; but as the pressure of the oil is raised, so the pressure of the blood within the veins rises, by accumulation of the blood within them, owing to the decreased flow into the right side of the heart. Finally, when the pressure of the oil rises beyond the point to which it is impossible for the venous pressure to rise, the veins and auricle collapse and the circulation is at an end. On the other hand, if the venous pressure tends to fall, as, in fact, it does by distension of the veins, the oil tends to collapse the veins, and therefore there is a further accumulation of blood in the latter, which again tends to raise their pressure; consequently, there is a gradual accumulation of blood in the veins at the expense of the arterial pressure which gradually falls until the animal dies.

On the other hand, when the pericardium is constricted, the pres-

sure tends to contract the terminations of the veins, to prevent the free diastolic expansion of the chambers of the heart, and also to embarrass the heart in its action as a force pump. The pressure exerted is not an elastic pressure tending to collapse the veins, but is a rigid and fixed quantity; and therefore when the venous pressure falls to normal, the veins and auricles do not tend to collapse, but the circulation still goes on with a rather lower arterial pressure than it otherwise would have.

This is not possible in Cohnheim's experiment; and *it may be stated generally that, if the maintenance of a high venous pressure is necessary for the continuance of the circulation, death will occur*, because owing to the distensibility of the veins a gradual accumulation of blood in them is necessary to keep up their high pressure, and this can only occur at the expense of the arterial pressure, which gradually falls till life is extinct.

GROUP III.—In these experiments the arterial and venous pressures were taken before the pericardium was constricted, and the changes noted during the operation. The animal was allowed to recover, and the blood pressures were taken subsequently, when dropsy had commenced to appear.

EXPERIMENT A.—*January 13, 1903.*—Cat. Weight, 2550 grms. Anæsthetised with ether. Intubation and artificial respiration. Pressures taken in left femoral artery and left external iliac vein were—femoral artery, 120 mm. Hg; inferior vena cava, 70 mm. MgSO_4 solution.

Pericardium exposed, and the right side stitched up.

At conclusion of the operation the pressures were—artery, 40 mm. Hg; vein, 120 mm. MgSO_4 solution.

Quarter of an hour later.—Artery, 40 mm. Hg; vein, 100 mm. MgSO_4 solution.

14.—Passed 85 c.c. of urine in the twenty-four hours; no albumin. Respirations, 38 to 40 per minute. Anæsthetised with ether.

Pressures were as follow, when breathing naturally—carotid artery, 108 mm. Hg (in a few minutes falling to 90 mm., where it remained till the animal was killed); inferior vena cava (right external iliac), 85 mm. MgSO_4 solution.

Post-mortem.—About 5 c.c. of blood-stained fluid in each pleural cavity, and a little œdema round pericardium and superior vena cava. No signs of inflammation anywhere; wound free from sepsis; a little œdema round it.

EXPERIMENT B.—*January 28, 1903.*—Cat. Weight, 3750 grms. Anæsthetised with ether. Cannulæ in left femoral artery and left external iliac vein.

Normal Pressures.—Femoral artery, 160 mm. Hg; inferior vena cava, about 70 mm. MgSO_4 solution.

Intubation and artificial respiration, when the pressure became—artery, 120 mm. Hg; vein, 75 mm. MgSO_4 solution (approx.).

The left side of the chest was opened, and the apex of the pericardium was seized in forceps and stitched, the pressures at once becoming—artery, 60 mm. Hg; vein, 117 mm. MgSO_4 solution.

The chest was stitched up, and when breathing naturally, an hour after the

operation, the pressures were—artery, 75 to 80 mm. Hg; inferior vena cava, 80 mm. MgSO_4 solution.

29th.—Passed 56 c.c. of urine; respirations, 32; looks ill; has taken only 50 c.c. of milk. 30th.—64 c.c. of urine; respirations, 36; has taken 40 c.c. of milk. 31st.—55 c.c. of urine; respiration, about 30. Anæsthetised with ether, and, when breathing naturally, the pressures were—right femoral artery, 100 to 120 mm. Hg; inferior vena cava, 75 mm. MgSO_4 solution; portal vein, 85 mm. MgSO_4 solution. The animal was now killed.

Post-mortem.—The wound was quite free from sepsis; there was a little œdema around it. Each pleural cavity contained from 5 to 6 c.c. of blood-stained fluid.

There was œdema of the mediastinum around the superior vena cava and the inferior vena cava, and also round the base of the heart, and in the fat outside the pericardium. The œdema extended along the superior vena cava, and the right and left axillary vessels into the axillæ, and to the lower ends of the jugular veins. No fluid in the abdomen. There were no signs of inflammation or sepsis anywhere.

These experiments show that the fall of arterial pressure which occurs during the constriction of the pericardium is, to a large extent, recovered from, but that when œdema occurs, the arterial pressure has a lower range than normal. The venous pressure, which has been previously shown to rise during the constriction of the pericardium and subsequently to fall to normal again, still remains at its normal level.

CONCLUDING SECTION.

The chief object of this investigation has been to introduce a condition more comparable with uncompensated heart disease than in Cohnheim's oil experiment, and one also which is compatible with life.

Cohnheim's experiment is more nearly allied to hæmorrhage into the pericardium than to any other pathological condition, and in this accident death soon occurs from a rapid rise of intra-pericardial pressure.

It is also closely allied to pericardial effusion, but in the latter the fluid is poured out slowly, and the pericardium very readily stretches as a result of the inflammatory process, and will hold a large amount of fluid without its tension being appreciably raised; it is also probable that when a tension of any high degree is attained, the patient will die unless paracentesis is performed. The implication of the cardiac muscle, as Cohnheim himself pointed out, also contributes to the production of many of the symptoms of pericarditis. Moreover, neither the symptoms of hæmorrhage into the pericardium, nor those of pericarditis are comparable to those occurring during the course of an uncompensated heart lesion.

On the other hand, the method of constriction employed in this investigation is almost exactly parallel with those cases of adherent pericardium, in which the adhesions are dense and prevent the heart from dilating (although the usual effect of pericardial adhesions, at

any rate eventually, is dilatation of the heart). The clinical picture of adherent pericardium, whether the heart is dilated or not, is (speaking broadly) identical with that of uncompensated valvular disease of the heart.

The only possible conclusion to which Cohnheim could have come from his experiment was that the venous pressure was high and maintained its height, and this conclusion is wrong only because his method of experiment is not strictly comparable to uncompensated heart disease. By a more exact imitation of this pathological condition, as suggested by adherent pericardium and its general symptomatology, the present investigation shows that the high venous pressure is only temporary, and that very soon it is followed by a normal venous pressure, and a low capillary pressure. It is, however, a fact that when tricuspid regurgitation occurs there must be waves of increased pressure in the veins. The venous pressure must also be raised in cases of temporary embarrassment of the right side of the heart when it becomes distended, and in these cases, if relief is not obtained by bleeding or cardiac stimulation, death results.

Granted the existence of a low capillary pressure and a diminished velocity of the blood stream, it seems, to the writer, more probable that passive œdema is primarily due to impairment or other alteration in the capillary wall, especially as some distension of the veins occurs, than that it is due to excessive secretion of the capillary endothelial cells, or to the needs of the tissues primarily; further investigation is, however, required before a final conclusion on this point can be arrived at.

In the main, therefore, the writer agrees with Starling in the final result of his investigation, although he differs materially from him in several of the important details whereby he has arrived at his conclusions.

It is the pleasant duty of the writer to thank Dr. Sidney Martin, F.R.S., Professor of Pathology at University College, for granting him the privilege of working in his laboratory, and Dr. J. M. Coutts, Assistant in Bacteriology at University College, for his very kind assistance in some of the later experiments.

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