On the Pathology of the Dropsy produced by Obstruction of the Superior and Inferior Venæ Cavæ and the Portal Vein.—Preliminary Communication.

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(From the Pathological Laboratory, University College.)

In August, 1903, I published a paper in the 'Journal of Pathology' (1), in which I demonstrated a method of experimentally producing uncompensated heart disease in an animal, which was compatible with life. This method consisted in diminishing the size of the pericardial sac by stitches, so that the diastolic filling of the heart was impeded. The main symptoms of this condition were dropsy and diminution in the amount of urine excreted.

As the immediate result of this interference with the action of the heart, there occurred a rise of pressure throughout the whole systemic venous system extending as far back as the capillaries, and a fall of the mean arterial blood-pressure. Further, I found that the pressure in all the veins fell to the normal limit again within the space of about one hour, and that subsequently, when dropsy was being produced, the venous pressure in all parts of the body was normal, and the arterial pressure had almost recovered itself.

I wish to draw special attention to the fact that the venous pressure was at first raised not only in the great veins near the heart, but also in the head, limbs, and intestines, that it very rapidly reached the normal limit again, and that the dropsy was produced whilst the venous pressure was normal, the arterial pressure very little if at all lowered, and the capillary pressure therefore not raised.

My reason for so doing is because Starling's (2) theory of hydræmic plethora is founded upon the assumption that the venous pressure primarily falls below the normal in the limbs and intestines, although it rises in the great veins near the heart. The low venous pressure in the limbs and intestines, according to Starling, initiates the absorption of lymph, which continues until the capillary pressure in the limbs as well as in the trunk is raised above normal by the hydræmic plethora so produced. Dropsy is then brought about by the *raised capillary pressure*. He also considers that there must be an alteration in the capillary wall, and he lays great stress upon this point.

In order to examine the immediate effects upon the circulation of the blood, Starling produced his uncompensated condition of the circulation by introducing oil into the pericardium, which brings about precisely the same immediate results as any other condition interfering with the diastolic filling of the heart. He, however, registered the venous pressure in the limb by means of a plethysmograph instead of by the direct introduction of a cannula into a vein of the foot. The result was that he obtained a contraction of the limb, which he interpreted as indicating a fall of venous pressure. I have already pointed out in my paper that this contraction was an indication of the vaso-motor constriction, which occurs as the result of asphyxia of the vaso-motor centre. If the venous pressure be taken by means of a cannula inserted into a vein of the foot, it is quite easy to demonstrate at once a rise of venous pressure in that part, whether the pericardium be filled with oil (see Ref. 1, experiment) or constricted by means of stitches (Ref. 1), or whether the inferior vena cava be obstructed (see Ref. 1, experiment). I, moreover, showed that it was impossible to keep up the high venous pressure by the injection of salt solution so as to produce hydræmic plethora. This is owing to the ready distensibility of the veins and the increased activity of the excretory glands.

The results of my experiments were, therefore, antagonistic to Starling's theory of hydræmic plethora, and I maintained that passive œdema was primarily due to *malnutrition of the capillary wall*, raised capillary pressure playing no actual part in its production.

The present investigation was undertaken from three points of view:—(1) To confirm my previous results by employing a different method. (2) To discover a more easy method of obstructing the venous flow into the heart, and one which admitted of different degrees of obstruction, which could be accurately measured. (3) To bring the results of general venous obstruction into line with those of local venous obstruction, in order to discover the common principle underlying both.

The subject will be treated of under the following headings:—

1. Method.

2. Effects of obstruction of the superior vena cava:—

   (*a*) Upon the production of dropsy.
   (*b*) Upon the circulation of the blood.

3. Effects of obstruction of the inferior vena cava:—

   (*a*) Upon the production of dropsy.
   (*b*) Upon the circulation of the blood.

4. Effects of obstruction of the portal vein :—
   (*a*) Upon the production of dropsy.
   (*b*) Upon the circulation of the blood.
5. Effects of obstruction of the superior, together with the inferior, vena cava :—
   (*a*) Upon the production of dropsy.
   (*b*) Upon the circulation of the blood.
6. Production of hydræmic plethora after obstruction of the inferior vena cava.
7. Conclusions.

1. Method.

The animals used were cats. The anæsthetic in all cases was ether, and morphia was administered in addition in those experiments relating to the effects upon the blood-pressures.

In order to obtain access to the superior and inferior venæ cavæ, the chest was opened by an incision an inch or more long and parallel to the ribs in the third right intercostal space in the case of the superior, and in the seventh right space in the case of the inferior vena cava. The ribs were drawn apart by weighted retractors and the lung held aside by a small copper spatula.

If the vein were to be completely obstructed, it was ligatured with silk ; if incompletely obstructed, a piece of Jacques' rubber catheter of the appropriate diameter and about $\frac{1}{4}$ inch in length was placed round the vein and tied on.

In those experiments, which were done in order to determine, by a gradually increasing constriction, at what point the venous or arterial pressure was first altered, a fine wire was passed round the vein and the free ends of this wire pushed through a piece of glass tubing so as to form a snare. The loop so formed was gradually tightened until an effect was observed upon the blood-pressure ; the vein was then cut through and the wire loop removed and its diameter measured.

In all cases during the operation, artificial respiration was maintained through a tracheotomy tube if the animal were to be killed at the end of the experiment ; but if it were to be allowed to live, a piece of glass tubing was introduced into the larynx through the mouth and artificial respiration maintained in this way, the air being blown through a bottle containing ether. Strict antiseptic precautions were observed and a *post-mortem* bacteriological examination made in most of the cases.

No difficulty with regard to pneumothorax was experienced after the chest was stitched up, and the animals began to breathe naturally at once.

The arterial blood-pressure was registered by means of a mercurial manometer, the cannula being placed in either the carotid or femoral artery, and a float, which traced the pressure curve on a kymograph.

The venous pressures were taken in the inferior vena cava, the cannula being introduced into the external iliac vein; at the lower end of the femoral vein where it divides into two branches at the ankle, the cannula being inserted into one of the branches and pushed on until its point was flush with the opening into the femoral vein; in the portal vein, the cannula being introduced into a branch of the splenic vein, the spleen being then placed back in the abdomen; at the upper end of the external jugular vein, the cannula being inserted into the posterior auricular vein and pushed down until its point was flush with the opening into the jugular vein. The venous pressure was registered on the kymograph by means of an air tambour connected with the top of the venous manometer by means of rubber tubing. This simply demonstrates whether a rise or fall of venous pressure occurs: it is no indication of the exact amount of such rise or fall. The diameter of the inferior vena cava is 5 mm., that of the superior vena cava practically the same or a trifle smaller, and that of the portal vein 4 mm.

2. Effects of Obstruction of the Superior Vena Cava.

(a) *Upon the Production of Dropsy.*

The vein was obstructed both above and below the entrance of the azygos vein (*i.e.*, between the entrances of the internal mammary and azygos veins, and between the azygos vein and the right auricle).

Obstruction below the Azygos Vein.

Complete Occlusion.—In each case death resulted either on the day following the operation or five or six days later. The *post-mortem* findings were the same in all cases. There was marked œdema of the mediastinum, extending up into the neck and down along the inferior vena cava to the diaphragm, the whole of the cellular tissue being distended with clear serous fluid. A slight amount of clear fluid was found in the pericardium, and bilateral hydrothorax was present. In one case 25 c.c. serous fluid was found in each pleural cavity; sometimes this fluid is blood stained. The œdema of the mediastinum may extend through the diaphragm, and out as far as the axillæ. There is no free fluid in the abdomen. Œdema at the seat of the wound occurs in the subcutaneous and muscular tissues, but this is not continuous with the mediastinal œdema and is dependent upon mechanical laceration of

the tissues. The urine is diminished in amount, the animal refuses food, and wastes.

Obstruction above the Azygos Vein.

Complete Occlusion.—I have been able to show that an animal may completely survive this operation. The animal lived for three months, and at the *post-mortem* examination the vein was absolutely occluded and not a trace of œdema to be seen. The anastomoses were established by the comes nervi phrenici, the internal mammary, and the azygos veins chiefly; the veins of the diaphragm were also distended.

Before these anastomoses are established, however, œdema is regularly produced, and apparently may directly lead to the death of the animal, or absolutely disappear as in the above case. This can be proved by killing the animal on the day after the operation or at a later date. Œdema of the mediastinum, slight hydropericardium, and bilateral hydrothorax are found. It seems to be the exception for all the fluid to be absorbed. One animal died 18 days after the operation in an attack of dyspnœa, and 145 c.c. slightly blood-stained fluid was found in the right pleural cavity and 125 c.c. in the left; œdema of the mediastinum was also present. I have never found any free fluid in the peritoneal cavity. The urine is diminished in amount.

Incomplete Occlusion. Diameter of Tube, $1\frac{1}{2}$ *mm.*—The result of constriction to this size is absolutely the same as that of complete ligature. As a fact, the tube practically obliterates the vein, since water cannot be made to flow through it *post mortem.* At any rate, if not absolutely obliterated, thrombosis no doubt completes the obstruction.

Diameter of Tube, 2 *mm.* Œdema of the mediastinum and hydrothorax are produced in this case also. Fluid flows slowly through the constriction *post mortem.*

Diameter of Tube, 3 *mm.*—Œdema of the mediastinum is produced with this constriction also, but only the merest trace of fluid in the pleural cavity is found. Fluid flows quite easily through the constriction *post mortem.*

Diameter of Tube, 4 *mm.* No œdema is produced by this amount of constriction of the superior vena cava. There is slight hæmorrhage and œdema in the subcutaneous tissues at the seat of the wound, but this, as in all the other cases, is the direct result of the injury to the tissues.

The wall of the vein is so very thin that its diameter is practically the same as that of the enclosing tube in the case of 3- and 4-mm. constrictions. The general statement may therefore be made that when the diameter of the superior vena cava is constricted to three-fifths of its normal size, œdema of the mediastinum and hydrothorax begin to appear, and that

it is possible, but not usual, for an animal to absorb the fluid and completely recover when the superior vena cava is absolutely obliterated. This statement applies to constrictions which are suddenly produced.

(b) *Upon the Circulation of the Blood.*

Arterial Pressure.

Complete ligature of the superior vena cava produces only a very slight effect upon the arterial blood-pressure curve. The output of the heart is slightly diminished, and there may be a very trifling fall in the pressure, but usually there is none. On the following day, *when the animal has developed dropsy, the blood-pressure is of precisely the same height as it was in the normal animal.* The fact that there is no immediate fall in the blood-pressure on complete ligature of the superior vena cava was, of course, well known in the days of Cohnheim (3).

Constriction of the superior vena cava similarly brings about no alteration in the height of the blood-pressure tracing.

Venous Pressure.

External Jugular Vein.—A *gradually increasing constriction* of the superior vena cava produces no change whatever upon the pressure at the upper end of the external jugular vein, until the former vein is narrowed to a diameter of 3 or $2\frac{1}{2}$ mm. At this point the pressure in the jugular vein rises to a height varying from 20 to 40 mm. $MgSO_4$ solution above what it was before the constriction was commenced.

Complete ligature causes a rise of pressure at the upper end of the external jugular vein of about 130 mm. $MgSO_4$ solution above the normal. This high pressure is not maintained, for, whether the superior vena cava has been completely ligatured or merely constricted, the pressure in the jugular vein gradually falls, and *within the space of about an hour has reached the normal limit once more.* On the following day, *when the animal has developed dropsy, the venous pressure in the external jugular vein is still normal.*

The following experiment shows the effects of obstruction of the superior vena cava upon the pressure at the upper end of the external jugular vein:—

Oct. 10, 1906. Cat; weight, 2280 grammes. Morphia, $\frac{1}{7}$ grain. Ether and artificial respiration.

Pressures.	Femoral artery.	External jugular vein.
Before obstruction	60 mm. Hg	100 mm. $HgSO_4$ solution
Obstruction to 2 mm.	60 „	111 „ „
1 minute later	—	112 „ „
1 „ „	—	112 „ „
1 „ „	66 mm. Hg	113 „ „
Complete obstruction	54 „	205 „ „
5 minutes later	—	221 „ „
5 „ „	—	206 „ „
5 „ „	—	185 „ „
5 „ „	—	174 „ „
5 „ „	—	170 „ „
5 „ „	60 mm. Hg	130 „ „
5 „ „	—	110 „ „
5 „ „	—	105 „ „

Inferior Vena Cava.—On complete ligature of the superior vena cava there is a very trifling and temporary fall of about 10 or 15 mm. $MgSO_4$ solution in the pressure in the inferior vena cava.

Portal Vein.—Complete occlusion of the superior vena cava or constriction of its diameter to 2 mm. causes a very transitory fall of pressure of about 5 mm. $MgSO_4$ solution in the portal vein.

The only significance of this slight fall of pressure in the portal vein and inferior vena cava is that it indicates the abstraction of blood from these venous territories and its retention in that of the superior vena cava.

It is quite apparent, therefore, that the smallest degree of constriction of the superior vena cava, which is necessary to produce any effect upon the venous pressure, will give rise to dropsy.

3. Effects of Obstruction of the Inferior Vena Cava.

(a) *Upon the Production of Dropsy.*

In all cases the vein was obstructed just below the heart, between it and the diaphragm.

Complete Occlusion.—Complete ligature of the inferior vena cava above the diaphragm leads to death in a few hours. There is regularly found 15 c.c. or more blood-stained fluid in the peritoneal cavity. No œdema is found anywhere else. This is exactly the result obtained by Richard Lower (4), more than 200 years ago, by ligature of the inferior vena cava in the chest, although it is usually misquoted in the text books, which state that he obtained œdema of the hind legs. Antiseptics were not recognised in his day and, so far as I am aware, he left the lung collapsed. In fact, it was

precisely this collapse of the lung which induced Ranvier (5) to ligature the vein in the abdomen, thinking that if dropsy were to be produced by venous obstruction he should obtain it by this means; however, in this case the anastomoses are too readily established, and Ranvier fell into error in thinking he had disproved Lower's results.

Incomplete Occlusion. Diameter of Tube, $1\frac{1}{2}$ *mm.*—This practically amounts to total occlusion of the vein, and death results with about 20 c.c. fluid in the peritoneal cavity.

Diameter of Tubes, 2 *and* $2\frac{1}{2}$ *mm.*—Constrictions to both these diameters may lead to death in a few hours, with 15 to 20 c.c. blood-stained fluid in the peritoneal cavity; on the other hand, the animal may survive the operation and develop ascites, but for how long I have not determined.

Diameter of Tube, 3 *mm.*—The animal survives, but if killed 24 hours after the operation, 25 to 35 c.c. clear straw-coloured fluid will be found in the peritoneal cavity, and possibly a few drops of fluid in the pleuræ. One animal lived four months, and at the autopsy showed no dropsy at all. Anastomoses were well established in the abdominal wall, carrying the blood to the superior vena cava. I have found ascites present 13 days after the operation in one case.

The fluid, therefore, is absorbed when the anastomoses are established. The urine is diminished in amount when dropsy is being produced.

Diameter of Tube, 4 *mm.*—A constriction to this amount does not lead to ascites.

The same general statement which was made with regard to constriction of the superior vena cava may be made in the case of the inferior vena cava. When the diameter of this vein is constricted to three-fifths of its normal size, ascites appears, and when the anastomoses are completely established this fluid disappears. If the vein is constricted below two-fifths of its diameter, or if it is completely ligatured, death will result in a few hours, and some ascitic fluid will be found in the peritoneal cavity.

This statement, of course, applies to suddenly produced constrictions.

(b) *Upon the Circulation of the Blood.*

Arterial Pressure.

A gradually increasing constriction of the inferior vena cava in the chest is perfectly compensated for until a diameter of 3 mm. is reached, when the arterial blood-pressure falls about 20 mm. Hg. Constrictions greater than this produce proportionately greater depressions in the blood-pressure curve, and *complete ligature* of the inferior vena cava causes the arterial pressure to fall to 30 or 40 mm. Hg above zero.

It has for many years been known that ligature of either the inferior vena cava or the portal vein causes a great fall in the arterial pressure owing to accumulation of blood in the splanchnic area (3).

On the following day, when ascites is present, the arterial blood-pressure is usually below what it was before the operation, if the animal survives.

Venous Pressure.

Inferior Cava.—A gradually increasing constriction of the inferior vena cava in the chest produces no rise of pressure at the lower end of that vein until its diameter has been reduced to 3 mm., when the pressure rises about 20 to 30 mm. $MgSO_4$ solution.

Constriction to a diameter of 2 mm. produces a rise of about 50 mm. $MgSO_4$ solution, and complete ligature a rise of 100 mm. or more. Whatever be the degree of constriction, however, *the pressure in the inferior vena cava gradually falls* and after an hour or longer has reached the normal.

Moreover, on the following day, *when the animal has developed ascites, the pressure in the inferior vena cava still remains normal.*

The following experiment shows the relative effects of constriction of the inferior vena cava in the chest to a diameter of $2\frac{1}{2}$ mm., and of complete ligature. The arterial pressure was taken in the carotid artery and the venous pressure in the external iliac vein.

Sept. 22, 1906. Cat; weight, 2600 grammes. Morphia, $\frac{1}{7}$ grain. Ether and artificial respiration.

Pressures.	Carotid artery.	External iliac vein.
Before obstruction	90 mm. Hg	95 mm. $MgSO_4$ solution
Obstruction to $2\frac{1}{2}$ mm.	66 ,,	115 ,, ,,
8 minutes later	82 ,,	130 ,, ,,
Vein completely occluded	30 ,,	210 ,, ,,
2 minutes later	30 ,,	215 ,, ,,

Veins of Foot.—Complete ligature of the inferior vena cava in the chest produces a rise of pressure in the veins of the foot of 60 mm. $MgSO_4$ solution or more. Constriction to a diameter of 2 mm. may cause a rise of 50 mm. $MgSO_4$ solution in the veins of the foot. This is a more gradual rise than that in the inferior vena cava, because it is produced in veins farther removed from the seat of obstruction.

The pressure in these veins falls to the normal limit again in about one hour after the occlusion has been produced.

The following experiment shows the effects of obstruction of the inferior vena cava in the chest upon the venous pressure in the foot.

Oct. 24, 1906. Cat; weight, 3200 grammes. Morphia, $\frac{1}{6}$ grain. Ether and artificial respiration.

Pressures.	Carotid artery.	Vein of foot.
Before obstruction	110 mm. Hg	142 mm. $MgSO_4$ solution
After complete obstruction	46 „	204 „ „
Obstruction removed	104 „	120 „ „
2 minutes later	110 „	135 „ „
Obstruction to 2 mm.	64 „	160 „ „
5 minutes later	—	195 „ „
5 „ „	96 mm. Hg	191 „ „
5 „ „	—	193 „ „
5 „ „	—	183 „ „
5 „ „	—	184 „ „
5 „ „	—	183 „ „
5 „ „	—	185 „ „
5 „ „	—	172 „ „
5 „ „	70 mm. Hg	165 „ „
5 „ „	—	164 „ „
5 „ „	56 mm. Hg	158 „ „
5 „ „	—	152 „ „
5 „ „	—	143 „ „
Obstruction removed	74 mm. Hg	123 „ „
3 minutes later	80 „	120 „ „

The following experiment demonstrates the fact that the pressure in the veins of the foot rises when the pressure in the pericardium is increased by the introduction of oil into that sac.

Nov. 24, 1906. Cat; weight, 3050 grammes. Morphia, $\frac{1}{5}$ grain. Ether and artificial respiration.

Pressures.	Carotid artery.	Vein of foot.
Before introduction of oil	84 mm. Hg	120 mm. $MgSo_4$ solution
During injection, $\frac{1}{2}$ minute intervals	—	135 „ „ 142 „ „ 145 „ „ 148 „ „
Injection stopped	48 mm. Hg	152 „ „
Oil allowed to run out	—	148 „ „
Pressures at $\frac{1}{2}$ minute intervals	—	141 „ „ 135 „ „ 135 „ „
	90 mm. Hg	132 „ „ 132 „ „
	84 „	130 „ „
Oil introduced 2nd time	—	135 „ „
Pressures at $\frac{1}{2}$-minute intervals	—	143 „ „ 148 „ „
	32 mm. Hg	150 „ „
Oil allowed to run out	—	138 „ „
Pressures at $\frac{1}{2}$-minute intervals	—	135 „ „ 130 „ „ 126 „ „ 124 „ „
	90 mm. Hg	115 „ „

Portal Vein.—Whether the inferior vena cava be completely occluded or constricted to 2 mm. in diameter, the pressure in the portal vein rises, in the former case about 90 mm., in the latter 50 to 60 mm. $MgSO_4$ solution. The pressure falls to the normal limit again in about the same time as it does in the case of the inferior vena cava. On the following day, *when ascites is present, the pressure in the portal vein is still normal.*

The following experiment shows the effects of obstruction of the inferior vena cava in the chest upon the pressure in the splenic vein.

Oct. 1, 1906. Cat; weight, 2535 grammes. Morphia, $\frac{1}{7}$ grain. Ether and artificial respiration.

Pressures.	Carotid artery.	Splenic vein.
Before obstruction	120 mm. Hg	113 mm. $MgSO_4$ solution
After complete obstruction	60 „	200 „ „
2 minutes later	44 „	175 „ „
2 „ „	—	133 „ „
1 „ „	—	115 „ „
Obstruction removed	80 mm. Hg	77 „ „
1 minute later	—	90 „ „
1 „ „	—	114 „ „
$\frac{1}{2}$ „ „	90 mm. Hg	113 „ „
Complete obstruction, 2nd time	42 „	170 „ „
2 minutes later	—	177 „ „
2 „ „	—	135 „ „
1 „ „	—	115 „ „
Obstruction removed	88 mm. Hg	85 „ „
2 minutes later	86 „	120 „ „
1 „ „	—	113 „ „

External Jugular Vein.—When the inferior vena cava is obstructed to 2 mm., the pressure at the upper end of the external jugular vein falls to the trifling extent of about 10 or 15 mm. $MgSO_4$ solution. This fall indicates an abstraction of blood from the territory of the superior vena cava, on account of the accumulation of blood in the portal area.

The following experiment shows that on obstructing the inferior vena cava in the chest the pressure in the external jugular vein falls :—

Oct. 18, 1906. Cat; weight, 2750 grammes. Morphia, $\frac{1}{7}$ grain. Ether and artificial respiration.

Pressures.	Carotid artery.	External jugular vein.
Before obstruction	74 mm. Hg	56 mm. $MgSO_4$ solution
Directly after complete obstruction	32 „	25 „ „
Obstruction removed	70 „	56 „ „

The smallest constriction, therefore, of the inferior vena cava, which is necessary to produce any effect upon the blood-pressures, will give rise to ascites.

4. Effects of Obstruction of the Portal Vein.

(a) *Upon the Production of Dropsy.*

Complete Occlusion.—Ligature of the portal vein at the spot where it enters the liver brings about death in a variable number of hours. There is regularly found about 6 or 10 c.c. slightly blood-stained fluid in the peritoneal cavity and small hæmorrhages in the mesentery may be seen. Since ligature of the superior mesenteric vein causes hæmorrhagic infarction of the intestine, whilst ligature of the portal vein does not, the latter fact is to be explained by the circumstance that the veins from the stomach and spleen are included in the ligature, and, therefore, a certain amount of venous anastomosis can become established and the spleen itself can act as a reservoir, but the anastomoses are not sufficient to prevent the occurrence of dropsy or the great fall of arterial blood-pressure which brings about the death of the animal.

Incomplete Occlusion. Diameter of Tube, $1\frac{1}{2}$ *mm.*—Constriction of the portal vein down to $1\frac{1}{2}$ mm. diameter may or may not cause the death of the animal.

If the animal dies, about the same amount of free ascitic fluid is found in the peritoneal cavity as when the portal vein is completely ligatured. If the animal lives and is killed on the following day, 20 c.c. fluid, free from blood, may be found in the peritoneal cavity.

This is precisely what would be expected, since the animal lives longer than when the vein is completely occluded, the obstruction not being so great.

Diameter of Tube, 3 *mm.*—Constriction to a diameter of 3 mm. likewise produces ascites in small amount, about 10 c.c. perfectly clear fluid being found in the peritoneum on the day after the operation. This fluid, however, may be absorbed, because in an animal whose portal vein had been constricted to this diameter seven weeks previously no ascites was found. The fluid may also be absorbed when the portal vein is constricted to 2 mm. in diameter.

Diameter of Tube, 4 *mm.*—In most large animals the diameter of the portal vein is just over 4 mm. in size, and a slight but definite constriction is produced by a tube of 4 mm. in diameter. Ascites, however, is not produced by such a procedure, the abdominal cavity being perfectly normal.

Speaking broadly, therefore, constriction of the portal vein to about three-fourths of its normal diameter will give rise to dropsy of the

peritoneum. Complete ligature will only produce a small amount of dropsy of the peritoneum and small hæmorrhages into the mesentery.

It is probable that constriction of the inferior vena cava must be carried to a rather greater relative extent than that of the portal vein to produce dropsy, because the anastomoses are more readily established in the case of the former than in that of the latter.

(b) *Upon the Circulation of the Blood.*

The effects of obstruction of the portal vein, as is well known, are a marked fall of arterial blood-pressure (3) and a rise of venous pressure in the splanchnic territory.

After complete ligature of the portal vein I have found that the venous pressure in the territory of this vein, although it rises enormously behind the ligature, *falls to the normal limit again*, as in the case of the inferior and superior venæ cavæ, and the small amount of free fluid found in the peritoneum is formed whilst the portal pressure is normal. Small hæmorrhages may be produced whilst the portal pressure is raised, but the dropsy is produced after the venous pressure has reached its normal limit.

After constriction of the portal vein to 2 mm. diameter, dropsy of the peritoneum is produced within 24 hours, but this may subsequently disappear and complete compensation be established, the arterial and venous pressures being normal.

5. Effects of Obstruction of the Superior, together with the Inferior, Vena Cava.

(a) *Upon the Production of Dropsy.*

The superior vena cava was constricted, and after an interval of 14 or 20 days the inferior cava was constricted, or, *vice versâ*, the superior vena cava was constricted in an animal whose inferior vena cava had been constricted 14 or 20 days previously. In some cases the azygos vein was ligatured at the same time as the superior vena cava was constricted.

The *post-mortem* findings, both the superior and inferior cavæ being constricted, are exactly the same as I described in my former paper as resulting from constriction of the pericardium, in other words, the condition is exactly comparable to that resulting from an uncompensated heart lesion.

Dropsical fluid is found in each pleural cavity, in the peritoneal cavity, and in the mediastinum.

If the inferior cava be constricted to a diameter of 4 mm., the superior to that of 3 mm., and the azygos vein be ligatured, the animal may survive, and a month later no fluid whatever be found *post mortem*.

Dropsy of the pleuræ and peritoneum is regularly found if the inferior cava be constricted to a diameter of 3 mm., the superior to that of 3 mm., and the azygos vein be ligatured.

This is a more easy method of producing uncompensated heart disease in an animal than is constriction of the pericardium, because the exact amount of constriction is known at the time of operation, and it does not depend upon the judgment of the operator, so that there is less fear of the animal dying or of the operation being unsuccessful.

(b) *Upon the Circulation of the Blood.*

In these experiments the inferior vena cava was constricted to a diameter of 3 mm., and the superior vena cava was completely ligatured.

The same results are obtained whether the azygos be ligatured or not.

The effects upon the arterial and venous pressures are exactly the same as those produced when the pericardium is constricted, with the exception that the rise of venous pressure is most marked in the external jugular vein, because the superior vena cava is completely obstructed.

The arterial pressure falls considerably, and the venous pressure in all parts of the body rises. The venous pressure falls to the normal level again in about the same time as it does when either vein is constricted separately, and *dropsy is produced whilst the venous pressure is normal.*

The effects of obstruction of both superior and inferior venæ cavæ are, therefore, precisely the same as those produced by an uncompensated heart lesion.

6. Production of Hydræmic Plethora after Obstruction of the Inferior Vena Cava.

If the inferior vena cava be constricted, and if, after the pressure in the external iliac vein has fallen to its normal level subsequently, salt solution be very slowly injected into the external jugular vein in quantities of 5 c.c. at a time, a large amount may be introduced without raising the venous pressure behind the constriction or the arterial pressure. If during the injection the venous pressure rises 10 mm. $MgSO_4$ solution (less than a pressure of 1 mm. Hg), it quickly falls again after the injection. In this way, during one and a-half hours I have injected 130 c.c., and still the pressures, arterial and venous, remained normal. Absorption of lymph occurs much more slowly than this, and the composition of lymph is different from that of salt solution. It is therefore inconceivable to me how an animal by absorption can raise its capillary pressure by the production of hydræmic plethora. In the case in point 10 c.c. ascitic fluid was found in the peritoneal cavity at the

end of the injections, and this fluid was produced with a normal capillary pressure.

If such a procedure be carried out in the case of a normal animal, no ascites is found after intravenous injection of 130 c.c. fluid.

7. Conclusions.

Of whatever nature the impediment be which opposes the free flow of blood into the heart and diminishes thereby the diastolic blood quantum, it will bring about precisely the same effects upon the circulation of the blood. There will be a general rise of systemic pressure affecting all the veins of the body and extending back as far as the capillaries, and a fall of the mean arterial blood-pressure. This effect is due to accumulation of blood in the veins. The venous pressure, however, soon falls to its normal level again, if the animal lives, and the arterial pressure is raised more or less completely to its former level owing to vaso-motor constriction. Dropsy is produced after several hours, whilst the capillary pressure is normal or even below normal.

The reason why the venous pressure returns to the normal level is because the veins passively distend and likewise the capillaries, which normally are not completely filled. The veins which distend are those of the thorax and abdomen, because the superior and inferior cavæ can be seen distended and the liver enlarged; the venæ cavæ are less supported than those in other parts of the body, they are situated within the suction action of the thorax, the bed of the blood stream is here smaller than in the more peripheral parts of the body, and muscular tension empties the veins in the latter situation towards the heart. In the erect posture, when gravity is of the greatest importance, the blood will tend to collect in the most dependent parts.

The dropsy is produced in this situation where the veins and capillaries are distended and where the blood flows with a diminished velocity, and it probably *depends entirely upon an altered condition of the vessel wall*, and not upon an altered condition of the nutrition of the tissues themselves, as maintained by Lazarus-Barlow (6), although, of course, these experiments do not disprove Barlow's theory.

This alteration is probably of a pathological nature and not such as would lead to an increase of the normal function of the capillary endothelium (7). *Raised capillary pressure plays no part in the production of this œdema, and the arterial pressure may be normal or less than normal, it matters not which.*

It might be argued that during the first hour the raised pressure which occurs would damage the vessel wall, but in those animals which recover

and develop dropsy, and in which the constriction is not very complete, the raised pressure is relatively insignificant and not to be compared with that occurring during muscular movement. The earliest dropsy, therefore, in uncompensated heart disease is strictly local in origin, and the capillaries of the district affected become, practically speaking, an excretory organ. In the remaining parts of the body absorption must occur *pari passu* with this increased output of fluid, in order to keep up the normal amount of blood in the body, but in the part affected absorption by the veins must be retarded.

As the disease becomes more extensive the area of production of the dropsy must extend.

When the superior or inferior vena cava is obstructed alone, the same initial rise of pressure occurs behind the obstruction as far back as the capillaries, and it soon falls to the normal level again, owing to distension of the particular veins in question and also, to some extent, on account of the anastomotic channels, which after many days may effect complete compensation if the constriction is not too complete. The dropsy is produced in exactly the same way as described above, when *all* the venous channels opening into the heart are obstructed, and it disappears in those cases in which complete compensation is subsequently effected by the anastomoses.

Absolutely the same remarks apply to obstruction of the portal vein.

Are there any conditions in which the dropsy of venous stagnation is produced when the capillary pressure is high?

In answer to this question it may be said that the necessary conditions are: *Firstly*, that the venous territory in which the obstruction is situated be not too large in proportion to the rest of the vascular territories of the body, so that sufficient blood can be spared to maintain a high venous pressure, and, *secondly*, that the anastomoses be not too free. Under these circumstances the dropsy of venous stagnation will occur with a high capillary pressure, but the actual cause of the œdema is, however, an alteration in the capillary wall, the high pressure being merely a concomitant circumstance, or at the most a contributing factor. A parallel instance is seen in the case of hæmorrhagic infarction. The escape of blood from the vessels in hæmorrhagic infarction may occur when the capillary pressure is high, as in venous obstruction, but it may also occur when the capillary pressure is low, as in arterial obstruction.

The dropsy of *local* venous stagnation is, therefore, produced in exactly the same manner as that resulting from *general* venous stagnation, the common factor underlying both being an altered condition of the vessel wall.

In the former case the capillary pressure may be high, but not so in the latter case. To maintain the volume of the blood normal in both these conditions, absorption must occur in the unaffected portions of the vascula system, but this absorption is not so great as it would be if the excretion of urine were not diminished. The dropsy of general venous stagnation is essentially local in origin, and the locality increases in extent as the disease advances.

Experiments are now being undertaken to estimate the lymph flow in the various pathological conditions considered above.

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