FURTHER RESEARCHES ON THE CLOSURE OF THE CORONARY ARTERIES

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The purpose of this communication is to examine the chief phenomena which follow closure of the coronary arteries, and to inquire into the cause of these phenomena, in the hope of clearing up, if possible, a confusing and not altogether necessary controversy.

I. The Frequency with which Arrest of the Heart follows Closure of the Coronary Arteries.

The closure of the coronary arteries was accomplished in my experiments by stopping the mouth of the artery in the sinus of Valsalva, or by plugging the branches with emboli composed of lycopodium spores, or by ligation of the arteries on the surface of the heart.

The first two methods were employed in twenty dogs. In each case the heart was promptly arrested.

Closure by ligation was done in sixty-seven dogs. The frequency with which the heart was arrested is shown in the following table:

Artery ligated.	Series I.		Series II.		Series III.		Series IV.	
	Arrest.	No arrest.	Arrest.	No arrest.	Arrest.	No arrest.	Arrest.	No arrest.
Ramus circumflexus	4	1	0	2	0	1	3	0
Ramus descendens	4	4	0	7	2	16	5	1
Ramus septi	0	2	0	3				
Coronaria dextra	2	9	0	3				

The reason for the division of the experiments into series will be stated after the consideration of the ligations as a whole.

The summary of the four series of experiments discloses two facts of great interest. The first is that *the frequency of arrest is in proportion to the size of the artery ligated.* The smallest artery of the four is the arteria septi, the ligation of which has not caused

arrest; the next in size is the coronaria dextra, fourteen per cent of its ligations having been followed by arrest; then comes the still larger descendens, with twenty-eight per cent; and finally the circumflexus, the largest artery of all, with sixty-four per cent.

Summary of Ligations.

Artery ligated.	No. of cases.	Arrest.	No arrest.	Percentage of arrests.
Ramus circumflexus	11	7	4	64
Ramus descendens	39	11	28	28
Ramus septi	5	0	5	0
Coronaria dextra	14	2	12	14

The second fact of interest is that *arrest is least frequent after the ligation of the arteries the preparation of which most injures the cardiac tissues.* In my experience, the preparation of the circumflex is made with less injury to the heart than the preparation of any other artery. It is done without loss of blood, without touching the cardiac muscle, and without any necessary injury of the ventricular nerves, excepting those in the artery itself, presumably of vasomotor nature.* The descendens is less easy to prepare, although this artery, like the circumflex, can usually be laid bare by merely incising the visceral pericardium and connective tissue. The position of the coronaria dextra, lying in a mass of fat which is richly provided with blood vessels and traversed by nerves, makes its isolation much less easy. The ligation of the arteria septi is really a difficult operation. This artery is never seen on the surface of the heart. It is the only artery of the four the preparation of which inevitably lacerates the cardiac muscle. Yet the ligation of this artery never stopped the heart, while the ligation of the circumflex, least difficult of all to prepare without injuring the heart, caused arrest eleven times in eighteen cases. †

Equally interesting facts are revealed by a further analysis of these statistics. It will be noticed that the ligations are presented

* Heymanns and Demoor. Étude de l'innervation du cœur des vertébrés à l'aide de la méthode de Golgi. *Arch. biol.*, 1895, xiii, pp. 619–676. W. T. Porter. The Vasomotor Nerves of the Heart. *The Boston Med. and Surg. Journal*, 1896, p. 39.

† The difficulty of reconciling these facts with the idea that the arrest of the heart after ligation of a coronary artery is due to mechanical injury of the heart will be insisted upon in the discussion of the cause of standstill.

in four series. The first series was made in Berlin,* the dogs being given curare and, in four cases, morphine; the second was made in St. Louis,† ether alone being used; the third and fourth were done in Boston. In the third, one dog was anæsthetized with morphine and ether throughout the operation, the remainder being etherized until the destruction of the bulb at its junction with the spinal cord made further etherization superfluous. In the fourth series the treatment was as follows:

Date.	Treatment.	Artery ligated.	Result of ligation.
1895.			
Jan. 17	Bulb cut; peptone. ‡	Descendens.	No arrest.
" 31	Morphine; curare; peptone.	"	Arrest.
Feb. 4	" " "	"	"
" 6	" " "	"	"
" 7	" "	"	"
" 12	" " peptone.	"	No arrest.
" 26	" bulb cut; "	Circumflex.	Arrest.
" 28	" " "	"	"
Mar. 1	" " "	"	"

The four series may therefore be divided into two groups. In the first group, comprising Series I and IV, morphine or curare or both were employed; in the second group, comprising Series II and III, neither of these agents was used, with the exception of a single case in Series III, the animals being narcotized with ether or the brain cut off by section of the bulb. The condition of the heart evidently can not have been the same in the two groups, for morphine and curare do not affect the heart as ether or bulbar section do. Compare now the results of ligation in the two groups. It will be seen that the results are not alike.

The number of ligations of the circumflex, arteria septi, and right coronary arteries in Group II is so small that I will not use them for comparison with those of Group III further than to point out that they make it probable that the condition of the heart is a factor of im-

* On the Results of Ligation of the Coronary Arteries. *The Journal of Physiology*, 1894, xv, pp. 121–138.

† See Ueber die Frage eines Coordinations-centrums im Herzventrikel. *Arch. f. d. ges. Physiol.*, 1894, lv, pp. 366–371.

‡ The peptone was employed to prevent the coagulation of the blood during the measurement of the blood discharged from the left ventricle before and after the ligation of a coronary artery.

portance in the results of ligation. This probability is made a certainty by the comparison of the arrests from ligation of the descendens, the arrests being sixty-four per cent where morphine and curare are used, and only eight per cent where they are not used. The *frequency of arrest is greatly increased by morphine and curare.*

Group I, *Comprising Series I and IV.*					Group II, *Comprising Series II and III.*				
Morphine, curare, or both ; sometimes peptone.					Ether or section of bulb.				
Artery.	No. of cases.	Arrest.	No arrest.	Per cent arrested.	Artery.	No. of cases.	Arrest.	No arrest.	Per cent arrested.
Circumflex.....	8	7	1	88	Circumflex.....	3	0	3	0
Descendens....	14	9	5	64	Descendens....	25	2	23	8
Septi.....	2	0	2	0	Septi.....	3	0	3	0
Coronaria dextra	11	2	9	14	Coronaria dextra	3	0	3	0

II. The Effect of Closure of the Coronary Arteries on the Blood Pressure and on the Force and Frequency of the Heart Beat.

In my paper On the Results of Ligation of the Coronary Arteries the conclusions were reached that "a gradual and continuous decrease in the height of the intraventricular upstroke appears almost immediately after ligation. When ligation does not cause standstill this lowering of the upstroke is absent or transient. When standstill follows ligation the diastolic intraventricular pressure is invariably increased."

Further experience has supported these statements.

The diastolic rise of pressure is particularly important. The normal mean pressure in the auricles and in the pulmonary veins is known to be very low.* It is probable, therefore, that the pressure in the coronary veins near their mouths is also low. A rise of a few millimetres in the auricular pressure would in that case interrupt the entire coronary circulation, unless overcome by a compensatory rise of pressure in the coronary arteries. This rise in the auricular pressure is certainly present after the ligations which are followed by arrest, for the rise of diastolic pressure which has been shown to

* W. T. Porter. *The Journal of Physiology*, 1892, xiii, pp. 513–553.

take place in the ventricle must be accompanied by a similar rise in the auricle, owing to the free communication between the two chambers during the greater part of diastole. The rise in auricular pressure after ligation is, moreover, not compensated by increased pressure in the coronary arteries. On the contrary, the pressure in the arteries is falling while that in the auricles is rising.

It must be acknowledged, then, that a rising auricular pressure after ligation may at length put a stop to the whole blood supply of the cardiac muscle, and, as this rise is often occasioned by the closure of a single vessel, it is plain that the entire coronary circulation can in fact be interrupted by the ligation of one coronary artery.

This possibly explains the fact that both ventricles, if arrested at all, usually stop at the same instant, no matter which ventricle the ligated artery supplied. But in our present ignorance of the nature of the cardiac co-ordinating mechanism it would be hazardous to insist on this explanation.

The frequency of the ventricular beat is seldom changed when ligation is not followed by standstill. When, however, ligation is followed by standstill, the frequency is usually sooner or later altered. But some hearts beat with unchanged rhythm to the last. In hearts isolated by a modification of Ludwig's method, to be described in the next section, the frequency after ligation is less regular, the explanation of the difference doubtless being that the hearts thus isolated are placed under very unusual conditions.

III. The Effect of Closure of the Coronary Arteries on the Quantity of Blood discharged by the Left Ventricle.

The method employed to measure the outflow from the heart was in the main that used by Pawlow * in Ludwig's laboratory. The differences were the exposure of the heart, in order to reach the coronary arteries; the closure of the aorta by ligation above the root of the left lung instead of closure by distending a bag introduced into the aorta through the subclavian artery; and the omission of the floats in the measuring cylinders, the change of current which

* *Archiv für Physiologie*, 1887, pp. 452–468.

they would have produced by making a contact at the top of the cylinders being secured in my experiments by turning a double key (*Wippe*) when the blood rose to a certain mark on the cylinder. This method of turning the current into first one and then the other of the magnets which control the inflow and outflow from the measuring cylinders was found to be sufficiently exact for the business in hand. The turns of the double key were recorded electrically on the smoked paper. The quantity of blood thrown out by the left ventricle was not essentially changed by ligations that were not followed by arrest. On the other hand, *the quantity of blood thrown out by the left ventricle steadily diminished after the ligations that were followed by arrest.* (Fig. 1.) The details of the experiments are shown in the tabular view on page 7.

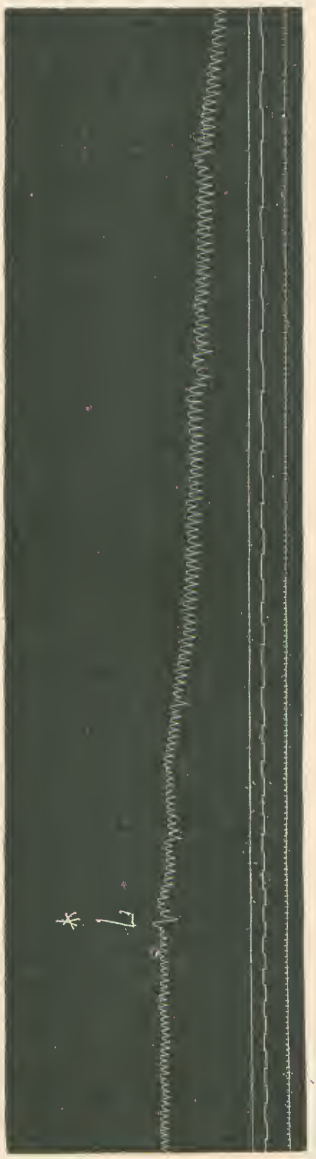

Fig. 1.—Showing fall in arterial pressure and diminished output of left ventricle in consequence of the ligation of the circumflex artery. The curve reads from left to right. It is one half the original size. The upper curve is the pressure in the carotid artery. The unbroken line is atmospheric pressure. The next curve is the measurement of the outflow from the left ventricle, each rise and each fall indicating the passage of 50 c. c. of blood into the aorta. The lower line is a time curve in seconds. At * the circumflex artery was ligated.

The anæsthetics and peptone employed in the experiments are given on page 3, in the account of the fourth series of ligations.

The results of these experiments are in accord with the measurements of intracardiac pressure already mentioned. The fall of pressure in systole and the rise in diastole are accompanied by a

The Number of Cubic Centimetres of Blood thrown out by the Left Ventricle per Fifty Seconds before and after the Ligation of a Coronary Artery.

Date.	Jan. 17.	Feb. 12.		Jan. 31.	Feb. 6.		Feb. 26.		Feb. 28.		March 1.	
Seconds.	C. cm.	C. cm.	Pulse.	C. cm.	C. cm.	Pulse.	C. cm.	Pulse.	C. cm.	Pulse.	C. cm.	Pulse.
1– 50....	387	482	87	392	405	93	720	130	725	43	315	83
51–100....	387	477	87	333	468	97	675	105	702	47	293	80
101–150....	342	432	..	293	446	98	720	93	743	45	315	81
151–200....	333	392	87	293	423	96	765	96	720	45	315	82
											Ligation of circumflex.	
201–250....	342	378	87	329	455	93	765	94	720	46	297	76
	Ligat. des'n.	Ligation of descendens.		Ligat. des'n.			Ligation of circumflex.		Ligation of circumflex.			
251–300....	351	482	87	446	441	95	648	126	608	37	270	78
301–350....	324	468	82	243	441	96	558	123	486	36	234	75
							Arrest 7 sec. later.					
351–400....	320	441	84	180	423	94	...	...	419	36	221	76
				Ar- rest.	Ligation of descendens.				Arrest 20 sec. later.#			
401–450....	329	405	..	...	482	99	...	...	...	...	167	67
											Arrest 35 sec. later.‖	
451–500....	315	482†	83	...	405	94						
501–550....	324*			...	387	91						
					Arrest 30 sec. later.‡							

diminished outflow from the left ventricle, while the frequency of beat is usually little changed. These changes in the heart beat, together with the slowing of the systole demonstrated in my first paper, are the fundamental alterations in the activity of the heart which usher in the loss of co-ordinating power and final arrest of the heart after the ligation of the coronary arteries.

We must now inquire the cause of these phenomena. Two explanations have been offered. The changes in the heart beat are produced either by the sudden arrest of the nutrition of a sufficiently large part of the heart or by the mechanical injury done the heart in the operation of ligation. I shall show that the closure of a coronary artery puts an end to the nutrition of the area which it sup-

* The experiment of January 17th continued 2,190 seconds longer. Ligation was not followed by arrest.

† The record of outflow continued until the fourteen hundredth second. No important change could be perceived. The heart beat, in all, 2,900 seconds, and was then stopped by the clotting of the blood in the measuring cylinders.

‡ During these 30 seconds 225 cubic centimetres were thrown out.

During these 20 seconds 135 cubic centimetres were thrown out.

‖ During these 35 seconds 113 cubic centimetres were thrown out.

plied and that the phenomena which follow the ligation of the coronary arteries are not due to the mechanical injury of the heart.

IV. The Ligation of a Coronary Artery puts an End to the Nutrition of the Area which it supplied.

That the closure of a coronary artery puts an end to the nutrition of the area which it supplied is an accepted truth in pathology, so well established by observation and direct experiment that it would be unnecessary to mention it here had not some recent writers neglected the obvious bearing of this fact on the correctness of their own hypotheses. The present state of pathological opinion regarding this matter is assuredly fairly expressed in such works as Ziegler's *Allgemeine Pathologie*, eighth edition, 1895. I find there the following statements: "Anæmic infarcts occur principally in the spleen, heart, kidneys, and retina" (page 175). "Anæmic infarcts are formed when the vascular area closed possesses no communications through which blood can be received; the area then remains bloodless and dies" (page 173). These words certainly represent the general beliefof pathologists regarding the anæmic infarcts of the heart.

Hæmorrhagic infarcts are also sometimes, though very rarely, present in the heart. The infarcted area is then infiltrated with blood. Investigators differ as to the source of this blood, some believing it to be derived from neighbouring capillaries, others through back flow from the veins. But investigators are agreed that in no case is the circulation re-established. On this point there is no dispute. The blood which slowly works in from neighbouring vessels "stagnates" * and can not preserve the life of the part.

The present unanimity of opinion as to the entire interruption of the circulation in the area of infarction rests, it must be remembered, not merely on post-mortem observations, but also on the consequences of the experimental closure of terminal arteries in the living animal. So also is the speedy death of the infarcted area a matter of direct observation. The experimental closure of terminal arteries in the living animal for the purpose of studying the infarcts

* Ziegler, *loc. cit.*, p. 145.

formed has until very recently been done on organs other than the heart—the kidney, for example. The experimental production of infarcts in the heart has been attempted, so far as I am aware, only by Kolster and myself, in each case with complete success.

Kolster * tied a small branch of the ramus descendens in the dog and kept the animal alive from one day to seventeen months. The microscopical examination of the hearts of dogs killed twenty-four hours after ligation showed a "typical coagulation necrosis in the area of the artery ligated." Kolster remarks that "nothing else could have been expected, for Weigert (Virchow's *Archiv*, Bd. lxxix) took these very cardiac infarcts as a type of coagulation necrosis. All the alterations which Weigert gives as characteristic of the necrosis established by him as the consequence of cutting off the blood supply are to be found here" (page 24). In dogs kept longer alive the progressive alterations were traced from day to day and from month to month.

My own experiments † were made on the main coronary trunks, the descendens, circumflex, or arteria septi, and in some cases more than one of these arteries, being ligated close to their origin, and the animals allowed to live. Two dogs in which the descendens was ligated a few millimetres from its origin lived respectively four days and fourteen days and a half. Characteristic anæmic infarcts were found occupying the anterior part of the septum and that part of the anterior wall of the left ventricle which adjoins the interventricular furrow. The infarcted areas were examined macroscopically, thin sections being made with a sharp knife.‡ The area infarcted was completely degenerated, except close to its borders. These experiments show (1) that the arteries ligated are terminal arteries;# (2) that the rapid closure of a coronary artery is followed

* *Skand. Arch. f. Physiol.*, 1893, iv, pp. 1–45.

† *Arch. f. d. ges. Physiol.*, 1894, lv, p. 366–371.

‡ The well-known descriptions of the microscopic appearance of infarcts in the human heart and the very minute description of infarcts in the dog's heart, published by Kolster a few months before my work, seemed to make a microscopical examination superfluous.

I do not speak here of the immediate object of the experiments published in the *Archiv f. d. ges. Physiologie*—namely, the demonstration of the absence in the infarcted area of any nerve centre essential to the co-ordination of the contraction of the heart.

by the death of the part which it supplies; and (3) that each part of the heart wall receives its blood supply essentially from one main artery; for example, the branches of the circumflex do not contribute any supply of importance to the area embraced by the branches of the descendens. This last fact is in accord with Cohnheim's statement that each coronary artery in the dog's heart keeps to its own boundaries, and does not, as a rule, pass into the field of another artery. Kolster's observation that the infarcted area contained spots of normal heart tissue depends probably on his having tied a small branch and not a main trunk.

The attempts made by Michaelis* and others to overthrow the great mass of pathological observations and the unequivocal testimony of infarcts experimentally produced will hardly commend themselves. Michaelis concludes that the coronary arteries are not terminal arteries, because a skilful injector (Wickersheimer) has succeeded in making an injection liquid pass from one artery, through communicating branches, to another. No one, so far as I know, has ever denied that one coronary artery could be injected from another. Cohnheim himself makes special mention of the passage of liquids through the communicating branches under pressure.† Every one agrees that the coronary arteries anastomose. It is not the absence, but the character of the anastomosis that is the basis of the present pathological teaching. The incontestable fact is that the anastomosis is too slight to permit a collateral circulation sufficient to keep a vascular area alive after the closure of the artery which supplies it.

The argument of those who rely on injections to prove the absence of terminal arteries appears to premise that one artery can be injected from another only when arterial communications exist, and that terminal arteries do not have arterial communications. The first premise is incorrect. Thin injections can be forced through any blood vessels. The second premise is inexact. Terminal arteries may possess arterial anastomoses, provided the resistance in the communicating vessels is high. The idea of terminal arteries is physio-

* *Zeitschrift für klinische Medicin*, 1894, xxiv, pp. 270–294.

† Virchow's *Archiv*, 1881, lxxxv, p. 509.

logical, not anatomical. Terminal arteries differ from other arteries in that the peripheral resistance in the anastomosing vessels is too high to be overcome by the normal blood pressure in any of the arteries of which the communicating vessels are branches. Hence the rapid closure of any terminal artery cuts off the nutrition of its own capillary area because sufficient blood for the life of the area can not be sent through the communicating vessels on account of the high resistance in them. The resistance in the communicating vessels, and not their size, is the factor of first importance. The circumstance on which Michaelis lays so much stress—namely, that one coronary artery can be injected from another—has long been known, and has no force against the pathological and experimental evidence of the terminal nature of coronary arteries.

I conclude, then, that the rapid closure of a coronary artery puts an end to the nutrition of the area which it supplied.

If now it can be proved that the changes in the heart beat produced by the ligation of a coronary artery are not the result of the mechanical injuries of the operation, it will follow that these changes are the consequence of a sudden interruption of the nutrition of the heart.

I shall determine, first, the consequences of extensive mechanical injuries of the tissues surrounding the coronary arteries; second, the effects of the mechanical injury done the heart in preparing a coronary artery for ligation; and last, the results which follow the closure of the coronary arteries without mechanical injury.

V. The Consequences of Extensive Mechanical Injuries of the Tissues surrounding the Coronary Arteries.

The experiments * about to be described were made on dogs poisoned with curare. I have already shown that curare increases the frequency of arrest after ligation (page 4). Notwithstanding the unfavourable influence of curare, arrest took place but once in ten cases of sudden and violent crushing of the periarterial tissues. The method of operating will be seen in the following example:

* These experiments were done in the University of Berlin in 1892.

Experiment July 7, 1892.—Dog; 8,100 grammes; curare; artificial respiration. The descendens was quickly and carefully freed from its bed at a point thirteen millimetres from the aortic origin of the left coronary artery. Only the visceral pericardium and the connective tissue over the artery were injured. A strongly curved, threaded needle was now passed into the cardiac muscle, entering on one side of the interventricular furrow opposite the place where the artery lay bare and emerging on the opposite side. The distance between the point of entry and of exit was about twelve millimetres. The needle, thanks to its curve, passed through the cardiac muscle three millimetres beneath the artery. The thread was now brought back underneath the artery. Thus the periarterial tissues were included in the ligature, but the artery was not included. This ligature was drawn tight, crushing the tissues embraced in it and dragging, doubtless, on many ventricular nerves. The intraventricular pulse, recorded by a Gad-Cowl manometer, was counted during four hundred and sixty-five seconds. Before the ligation, the frequency per ten seconds was twenty-three; after the ligation, the frequency varied from twenty-one to twenty per ten seconds. There was no arrest.

The number of experiments after this method was ten. In five the tissues about the descendens alone were crushed, in three those about the circumflex alone, and in two those about both arteries. In nine of the ten animals the heart continued to beat; slight irregularity is noted in three, and in one an increase both in force and frequency. The following case of double crushing is especially noteworthy:

Experiment July 27, 1892.—Prepared periarterial tissues around the circumflexus about six millimetres from the aortic origin of the left coronary artery and about the descendens on a line with the anterior edge of the pulmonary artery. Drew both ligatures tight. No great irregularity.

In the case in which arrest followed the crushing, the periarterial tissues about both circumflex and descendens were prepared. As in all experiments, the tissues were included for at least ten millimetres, the thread at its deepest point being about three millimetres below the surface. On drawing the circumflex periarterial ligature tight, the heart fell into fibrillary contractions.

The result of this series of deliberate, extensive injuries to the cardiac muscle and nerves lying about the coronary arteries is most instructive. It shows clearly that too much has been made of the supposed effects of such injuries on the heart, and that they by no means explain the consequences of ligation of the coronary arteries. This conclusion will become more and more probable as we proceed.

VI. Mechanical Injury of the Heart in preparing the Artery for Ligation.

The mechanical injuries said to be the cause of the phenomena which often follow the closure of a coronary artery are produced by the preparation of the artery for ligation. They can hardly be produced by the injury to the artery itself in the act of ligation, for not even the most ardent advocate of mechanical injury would, I presume, venture to claim that the crushing of the arterial wall alone seriously affects the heart beat. The extent of the injuries produced by the preparation of the artery have surely been greatly exaggerated. The coronary arteries, excepting the arteria septi, can be prepared without the injury of a single muscle fibre, or even in many cases the loss of a single drop of blood. The superficial nerves which are sometimes pulled upon or torn during the operation are, so far as is known, centripetal nerves, the section and direct stimulation of which does not cause the effects the explanation of which we seek.*

The statistics that are available do not show that the preparation of the artery has any serious consequence whatever. It will be remembered that Fenoglio and Drogoul † clamped or ligated a coronary artery in fifty dogs without once seeing the phenomena that precede arrest. The notes of nearly one hundred ligations made by me show that the only effect of the preparation of an artery is the occasional dropping of a beat. The changes in intracardiac pressure and the engorgement of the heart which form the unvarying introduction to the arrest that often follows ligation have never been observed. Several operations were made during the continuous recording of the blood pressure in the carotid artery by a Hürthle manometer. The number of dropped beats and the state of the blood pressure were thus accurately determined. One of the curves is here reproduced. (Fig. 2.) The records thus secured confirmed the observations with the unaided eye. An example of these experiments will be given.

* Wooldridge, L, *Archiv für Physiol.*, 1883, pp. 522–541. McWilliams, *Journal of Physiology*, 1887, viii, p. 298.

† *Archives italiennes de biologie*, 1888, ix, p. 49.

Experiment September 20, 1895.—Dog; ether; tracheotomy; division of bulb near spinal cord; artificial respiration; continuous curve of carotid pulse and pressure. Prepared descendens for ligation thirteen millimetres from the aortic origin of the left coronary artery. Occasionally a dropped beat during the preparation; nothing more. After seventy-three seconds the ligature was drawn tight. Speedy arrest of the heart with tumultuous fibrillary contractions and strong auricular pumping.

In addition to the facts just mentioned, the reader will remember those demonstrated in the first section of this paper—namely, that the frequency of arrest is in proportion to the size of the artery ligated, and is least frequent after the ligation of arteries the preparation of which most injures the cardiac tissues. These observations can not be reconciled with the mechanical-injury explanation.

I am therefore able to conclude that the necessary mechanical injury of the heart in the preparation of an artery for ligation may

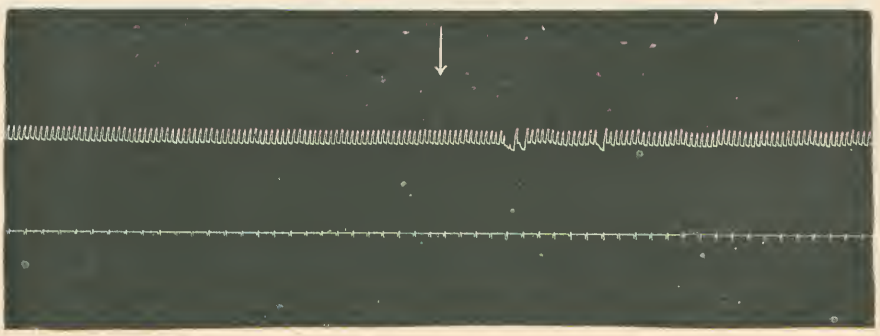

Fig. 2.—Showing the character of the irregularity sometimes occurring during the preparation of a coronary artery for ligation. The curve reads from left to right. Upper line is carotid pressure and pulse curve. Lower line is atmospheric pressure and time in seconds. At ↓ the preparation of the descendens for ligation was begun.

cause a slight irregularity in the ventricular stroke, but that this irregularity is almost invariably transient and unimportant.

VII. The Closure of the Coronary Arteries without Mechanical Injury.*

It has now been shown that extensive sudden injuries of the tissues lying about the coronary arteries rarely arrest the heart, or do

* The first mention of my method for this purpose was made in the *Centralblatt f. Physiol.*, 1895, No. 16, p. 481. See also the reply to R. Tigerstedt in a later number of the same year.

more than cause a passing irregularity. It has been shown also that in nearly one hundred consecutive ligations of the coronary arteries not one case was found in which the preparation of the artery for ligation materially affected the beat of the heart. The methods thus far employed can not, however, wholly exclude the influence of mechanical injury, because ligation can not be accomplished without such injury. It is possible, nevertheless, to close a coronary artery without the slightest injury either of the artery itself or of the surrounding tissues. This is done by passing a glass rod through the aorta into the aortic opening of the coronary artery, or by plugging the branches of the coronary arteries by means of emboli composed of lycopodium spores. The first method is carried out as follows:

The dog is etherized and tracheotomized, the bulb destroyed near its junction with the spinal cord, and artificial respiration begun. The left first rib is exposed near the sternum, and a small opening made into the chest in the angle formed by the rib and the sterno-cleido-mastoid muscle. Through this opening, the left internal mammary artery is easily secured. The first five ribs on the right side and the first three on the left side are now exposed by a straight incision along the margins of the sternum. Stout ligatures are passed with a large bent aneurism hook around the eight exposed ribs some distance from the sternum, and around the left fourth and fifth and the right first, second, and third ribs near the sternum. Another strong ligature is tied around the sternum between the third and fourth pairs of ribs. The ligated ribs and the upper part of the sternum may now be removed. It is best to begin with the fifth rib on the left side, cutting along the outer line of ligatures, raising the ribs as soon as possible, and securing the right internal mammary artery by reaching underneath the sternum. The pericardium should be slit a little to the right of the left phrenic nerve, and sewed to the margins of the chest opening with three or four stitches. The innominate artery is found beneath the inner border of the innominate vein, ligated as near the neck as possible, a rubber band placed under it near the cardiac side of the ligature, a compression forceps applied about fifteen millimetres below the

ligature, and the previously oiled glass rod introduced into the artery through as small a hole as possible. The artery should now be compressed about the rod by tying the rubber band, which should press tightly enough to prevent bleeding along the rod, but not so tightly as to hinder the operator in moving the rod. The rod is passed down toward the left anterior sinus of Valsalva. As soon as the resistance of the aortic valve is felt, the rod is withdrawn a little and its head made to traverse the aortic wall near the bottom of the sinus. The opening of the left coronary artery will presently be found. Into this the rod is passed and fastened in place by tying a ligature around the innominate artery, including the rod. A finger of the left hand placed very gently over the left coronary artery will readily determine whether the rod is in the right place. The rod is 210 millimetres long, the head and neck being of the size and shape represented in the accompanying figure. (Fig. 3.) The position of the rod was always carefully examined post mortem by the method to be described in the account of the following experiment of September 20, 1895.

Fig. 3.—Lower portion of glass rod (actual size) used to plug the left coronary artery.

Plugging the left coronary artery during life is not a very difficult operation. I have attempted it in nineteen dogs, each time with complete success. The closure of the artery was always promptly followed by arrest. Fibrillary contractions were present in every case but one.

It seems hardly possible that the gentle introduction of the glass rod into the artery could in any way injure the artery, and, in view of the facts presented in former sections of this paper, it is wholly improbable that any slight injury which might be thus inflicted would stop the heart. Nevertheless, even this remote possibility can be excluded.

Testimony against injury by the rod is furnished by the experiment of September 20:

Experiment September 20, 1895.—Dog; 9,500 grammes; ether; tracheotomy; artificial respiration; section of bulb at its junction with the spinal cord.

The heart being exposed, the glass rod was passed through the innominate artery into the supposed trunk of the left coronary artery. The head of the rod was distinctly felt by a finger placed over the circumflex artery. The handle of the rod was now tied in place. The expected standstill did not follow, nor could any irregularity in the heart beat be detected. After waiting some time for any sign of heart failure, and perceiving none, the descendens was laid bare. The descendens pulsated. It was now ligated thirteen millimetres from the aorta. Speedy standstill followed, with tumultuous fibrillary contractions and strong auricular pumping. The heart was greatly distended.

Autopsy: Find head of rod in the circumflex artery, nine millimetres from the aorta. Open circumflex just beyond the head of the rod. No blood escapes. Raise the pressure in the aorta. Still no blood escapes; closure perfect. Open descendens on cardiac side of ligature. Blood immediately runs out in a stream. Outflow hastened by raising the pressure in the aorta. Descendens not closed by rod. Find that each artery has a separate origin, the circumflex opening being situated between the middle and left end of the sinus of Valsalva, the descendens near the right end. The circumflex was tightly plugged, the descendens not at all.

In this experiment, then, the plugging of the circumflex artery caused no disturbance of the heart beat. The operation of plugging was precisely the same in this case as in others in which closure was followed by arrest with fibrillary contractions. The constant arrest after complete closure and the nearly constant fibrillary contractions can not therefore be explained by the mechanical injury done by the rod.

The next experiment is even more instructive.

Experiment September 23, 1895.—Dog ; 11,000 grammes; ether; tracheotomy; section of bulb near spinal cord; artificial respiration. The search for the opening of the left coronary artery lasted forty-four seconds. Not a heart beat fell out. Immediately after closure of the artery, the crural blood pressure began to sink, the individual heart beats grew weaker and weaker, and the heart began to swell. At the sixty-fifth second after closure, the blood pressure had fallen from 60 millimetres, Hg., to 25 millimetres. The rod was now drawn back into the aorta. The pressure continued to fall a few millimetres during twenty-two seconds, then rose gradually, reached its former height in fifty-five seconds, and then rose farther to 85 millimetres, after which a slight fall occurred. As the blood pressure rose, the individual beats increased in strength and the heart returned to its normal size. (Fig. 4.)

Fig. 4.—Illustrating experiment of September 23d. The curve reads from left to right. It is one half the original size. The upper line is the pressure in the crural artery. The lower line marks atmospheric pressure and time in seconds. At * the left coronary artery was plugged. At † the plug was withdrawn.

The artery was now closed again. The result was quite as before. The blood pressure sank, the heart swelled, and the beats were small. After forty-six seconds, the rod was once more withdrawn. All the threatening symptoms disappeared. In fifty-six seconds the heart was working as well as before.

A third and a fourth time was this repeated. The fourth time the artery remained closed fifty seconds. The heart swelled enormously. Its beats were scarcely perceptible in the curve. During 127 seconds, it went from bad to worse. Finally, it remained seven seconds without a beat. Strong massage was then employed, the heart being compressed six times in seven seconds. The beat returned. The massage was twice repeated, each time with good results. Finally, the heart beat again strongly and regularly.

Once more the artery was closed and the entire series of these interesting phenomena called back. The artery was shut for fifty seconds. This time, however, the heart beat did not return after the withdrawal of the plug. Massage helped some, but the highly swollen heart could be made to contract but a few times.

If the introduction of the rod had caused the arrest in this experiment through mechanical injury, the arrest would have been permanent. The injury done by the introduction of the rod would not have been undone by its withdrawal.

The observations now to be described appear to be conclusive:

Experiment October 14, 1895.—Dog; 11,500 grammes; ether; tracheotomy; section of bulb near spinal cord. A glass tube, slightly conical at the end, with a diameter of 2·75 millimetres at the outlet, was connected with a bottle of warmed defibrinated ox blood, diluted one half with normal saline solution (0·6 per cent). The bottle was 150 centimetres above the heart. The blood was warmed nearly to the body temperature, and kept thoroughly oxygenated by a constant stream of oxygen. The glass tube was now in-

troduced into the aortic opening of the left coronary artery. As usual, it entered the circumflex, closing the mouth of the descendens. The blood was at once turned on and allowed to flow for eight minutes. During this time 318 cubic centimetres flowed through the circumflex. The heart continued to beat. There were no symptoms of arrest. At the end of eight minutes the blood was shut off. Arrest followed in 120 seconds. The left coronary artery was found tightly plugged by the glass tube, which extended into the circumflex, stopping the descendens with its side.

Experiment October 17, 1895.—Dog ; 9,500 grammes ; ether ; tracheotomy; section of bulb. At 11.39 A. M. the descendens was ligated about one centimetre from the aorta. No arrest. At 12.15 P. M. the glass tube used in the preceding experiment was passed through the aorta into the circumflex artery, and warm defibrinated, oxygenated, diluted ox blood was sent through the tube at a pressure of 140 centimetres (blood). The heart was at first stimulated, the blood pressure rising. The blood pressure returned then to its former level or a little less. Every alternate beat was weak. After four minutes, 114 cubic centimetres of blood mixture having run through, the oxygenated blood was suddenly replaced with carbon-monoxide blood. The heart became within four seconds very irregular. After twenty-eight seconds the carbon-monoxide blood was turned off and oxygenated blood allowed to flow again, but it was too late. Four seconds thereafter arrest with fibrillary contractions occurred.

The blood was prepared by dividing 960 cubic centimetres of defibrinated ox blood into two parts and diluting each with an equal volume of normal saline solution (0·6 per cent). Through one part carbon monoxide was passed during forty-five minutes; through the other, oxygen. Both mixtures were afterward warmed in stoppered flasks to near the body temperature. The carbon monoxide was made from oxalic and sulphuric acids, and the carbon dioxide removed by passing the gas through two flasks filled with a strong solution of sodium hydrate. The gas was then conducted through a wash flask, and finally into the blood. Passing the purified carbon dioxide through barium hydrate gave no precipitate, showing that the carbon dioxide had been wholly removed.

The experiments just cited show that the presence of the tube in the coronary artery is not the cause of the arrest with fibrillary contractions observed after closure of the artery. Were this arrest due to a mechanical injury by the tube, it could not have been prevented by circulating oxygenated blood through the tube. If the glass tube did not cause arrest though mechanical injury, the arrest that followed the introduction of the glass rod could not have been due to mechanical injury, for the tube was fully as large as the rod.

Arrest with fibrillary contractions follows the stopping of the coronary arteries with lycopodium spores. The method is illustrated by the following experiment :

Experiment December 17, 1895.—A dog was etherized, the bulb severed, and artificial respiration begun. The left carotid and left subclavian arteries were tied near their origin. Ligatures were placed around the common origin of the right subclavian and carotid arteries and about the aorta below the left subclavian artery, but were not drawn tight. The cannula of a syringe filled with the warmed, defibrinated, oxygenated blood from the same dog was tied into the left carotid artery. This blood contained a great quantity of lycopodium spores. The hitherto open ligatures around the right subclavian and carotid arteries and the aorta were now drawn tight, and at the same moment the lycopodium blood was driven through the carotid into the aorta. There was now but one outlet for the blood in the arch of the aorta—namely, the outlet through the coronary arteries. These vessels were at once distended with the blood mixed with locypodium. At this instant the ligatures were loosed again, forty-two seconds after they had been drawn tight. The circulation was free to go on as before. About twenty seconds later the heart, although beating strongly, suddenly became irregular, stopped short, and fell almost at once into violent fibrillary contractions. At the autopsy, the smaller coronary branches ramifying over the surface of both ventricles were seen to be plugged with masses of lycopodium.

In this experiment the heart was not once touched by the operator. The heart itself closed the coronary arteries. It is well known that a brief ligation of the aorta is borne by the dog's heart without apparent injury. In this dog the heart still contracted strongly after the aortic ligature was loosed. There can therefore be no thought of mechanical injury in this experiment.

The inquiries regarding the relation between mechanical injury of the heart and the results that follow the rapid closure of a coronary artery have now been answered. It has been shown (1) that sudden extensive injuries of the tissues lying about the coronary arteries rarely arrest the heart or do more than cause some irregularity; (2) that in almost one hundred consecutive ligations of the coronary arteries not one case was found in which the preparation of the artery for ligation materially affected the beat of the heart; and (3) that closure of a coronary artery without mechanical injury produces all the phenomena that have been ascribed to the mechanical injury of the heart. Hence, of the two conceivable reasons for the changes in the action of the heart after closure of the coronary arteries, one—the mechanical injury of the heart—is excluded. The phenomena brought on by closure of the coronary arteries are due, therefore, to the sudden stopping of the nutrition of a considerable part of the heart.

VIII. The Changes in the Heart Beat that follow the Opening of the Great Arteries.

The principal factor in the creation of the prevailing difference of opinion regarding the cause of the phenomena that follow closure of the arteries has been a serious misconception—namely, that the phenomena in question differ essentially from the changes produced by the sudden stopping of the supply of blood to the heart muscle, when the great arteries are opened freely. When the carotid arteries or other large branches of the aorta are opened, the co-ordinated contractions of the heart grow weaker and weaker until they finally disappear. Very different from this is the picture that Cohnheim and others have drawn of the changes following the closure of the coronary arteries. In the widely circulated paper of Cohnheim and von Schulthess-Rechberg,* it is stated that the ligation of a principal branch of the left coronary artery has no immediate influence on the action of the heart, neither the frequency nor the character of the pulse nor the blood pressure being altered during the first thirty to forty seconds, and often still longer after ligation. Only as arhythmia becomes pronounced does the blood pressure sink, and then but slightly. And this is the more surprising, for the strongly beating although irregular heart now suddenly stops and the arterial pressure falls swiftly to the abscissa (page 513).

I have already shown the incorrectness of Cohnheim's generalizations. The force of the heart beat, the height of the blood pressure, the power of the ventricle to discharge its contents, and the amount of blood thrown into the aorta, are all progressively diminished by those ligations that are followed by arrest, and this chain of alterations is seen to begin within a few seconds after the closure of a sufficiently large branch. They do not begin instantly because the capillaries are not instantly emptied, the more so for the reason that the pressure from behind is largely cut off by the tying of the artery. The heart, then, is not struck down by a single blow in the midst of full activity. On the contrary, the fatal result is

* Virchow's *Archiv*, 1881, lxxxv, pp. 503–536.

always preceded by the changes mentioned above. The irritability of some hearts, however, is so great that they are brought to a stop before the characteristic alterations have gone very far. The smallness of the alteration observed by Cohnheim is probably to be explained by the high irritability and consequent speedy arrest produced by the curare that he used, a drug which increases the sensitiveness of the heart to closure of the coronary arteries, as I have pointed out above.

The rise of diastolic pressure so constantly present after the closure of the coronary vessels is not seen when the anæmia of the heart muscle is brought about by bleeding from the great arteries. In the former case the high peripheral resistance against which the ventricle must pump prevents the enfeebled organ from emptying its contents into the aorta; in the latter the peripheral resistance is almost nothing, and even weak contractions expel the contents of the ventricle with ease. The ventricle, moreover, receives less than the usual quantity of blood through the auricle. The difference in the height of diastolic pressure can not therefore be used in support of the idea that the results of anæmia due to closure of the coronary arteries are essentially different from those due to anæmia from great hæmorrhage; and the alleged essential difference in the other symptoms that precede arrest does not exist, as I have already clearly demonstrated.

A second argument in favour of a difference between anæmia from hæmorrhage and anæmia from closure of the coronary arteries is sought in the statement of Cohnheim and von Schulthess-Rechberg that "no sort of stimulus will make the dog's heart give even a single contraction after standstill has occurred" (page 516). The impossibility of restoring the heart beat after standstill has once occurred, the authors insist, shows most conclusively that the arrest can not be due to anæmia. According to them, the ligature about the coronary artery can be loosed as soon as standstill has occurred and blood forced through the coronary arteries by massage of the ventricles, but the heart does not beat again (pages 521–525). This argument has no longer any force, for it has been shown by Arnaud,*

* *Arch. de physiol.*, 1891, pp. 396–400.

Hédon and Gilis,* Langendorff,† and myself ‡ that the heart brought to a standstill by bleeding from the great vessels can be made to beat again for long periods by forcing blood through the coronary arteries, and I have proved in the preceding section of this paper that a heart arrested by plugging the coronary arteries can recover its power of co-ordinated contraction when the plug is withdrawn and the heart is massaged. There is then no essential difference here.

It is charged, especially by Langendorff,# that fibrillary contractions are absent when anæmia of the heart muscle is produced by opening the great vessels.

Fibrillary contractions are simply inco-ordinated, irregular contractions of individual cardiac muscle cells or groups of cells. When a dog is bled from the carotid arteries, the contractions of the heart, as has been already said, grow feebler and feebler, until they finally disappear. Immediately or very soon thereafter three kinds of contractions can be seen in the heart—first, contractions in various parts of the ventricles, very often not co-ordinated with each other, and of small area; second, small, sharply marked, narrowly circumscribed twitchings here and there on the surface of the heart. These two kinds of movements are apparently the last traces of the action of a co-ordinating mechanism that is no longer master of the whole heart. Third, slight fibrillary contractions, commonly very faintly, sometimes almost or altogether unrecognizable, at other times quite unmistakable.

There is, I believe, no fundamental difference between these various contractions and the pronounced fibrillary contractions heretofore considered in this paper. They are identical in that they are all circumscribed contractions of a part of the heart wall appearing after a temporary or permanent loss of the power of general co-ordination. They are further alike in that they can be made to give place to co-ordinated contractions. The restoration of the co-ordinated beat is easy in all mammals yet investigated, except the dog. Tigerstedt, Michaelis, and others declare that fibrillary contractions of the dog's heart are invariably fatal. In taking this position, they

* *Comptes Rendus Soc. de biol.*, 1892, pp. 760, 761.
† *Arch. f. d. ges. Physiol.*, 1895, lxi, pp. 291–332.
‡ *The Boston Med. and Surg. Journal*, 1896, p. 39. # *Loc. cit.*

assume a fundamental difference between the heart of the dog and the hearts of nearly related mammals. They oppose, moreover, their negative results to the positive observations of McWilliam,* who more than once has seen fibrillary contractions in the dog's heart give place to regular co-ordinated beats; and they do this in the face of the fact that no one, so far as I am aware, has attempted to restore the dog's heart, after fibrillary contractions have begun, by the systematic employment of an artificial circulation through the coronary arteries. It is evident that without this, recoveries will be rare indeed.

It can not be admitted, then, that fibrillary contractions differ in kind from the irregular, inco-ordinated contractions that appear after standstill brought on by opening the great vessels.

The difference in degree is certainly great. The cause of this difference lies probably in the fact that after closure of the coronary arteries the heart continues to work against a high peripheral resistance. The co-ordinating mechanism of the strongly working anæmic heart soon gives way, while the less highly specialized contractility of the muscle fibres is still considerable. Pronounced fibrillary contractions are then possible. The heart made anæmic by opening the arteries, on the contrary, contracts against almost no peripheral resistance. It does little or no work. The co-ordinating mechanism is only gradually borne down. The contractility of the cardiac muscle cell sinks with it, and when arrest has finally come the contractility remaining is not sufficient for outspoken fibrillary contractions.

An example of this is seen in the single case in which my closure of the left coronary artery with the glass rod produced arrest without the ordinary tumultuous fibrillary contractions. The heart of this dog was brought slowly to standstill, and the contractility, or, perhaps one should say, the irritability, of the muscle fibres was probably so much reduced thereby that decided fibrillary contractions were no longer possible. The changes in the heart beat that follow the opening of the great arteries are therefore, in my opinion, not fundamentally different from those produced by the sudden closure of the coronary arteries.

* *Loc. cit.*, p. 299.