ON THE RESULTS OF LIGATION OF THE CORONARY ARTERIES. By W. TOWNSEND PORTER. (Pl. II.)

I. LITERATURE.*

THE experimental study of the influence of an interruption of the coronary circulation on the action of the heart may be said to have begun with Erichsen[6]. It is true that Chirac[4] had tied a coronary artery in a dog nearly one hundred and fifty years before, and had seen the heart soon after cease to beat, yet this isolated observation appears to have borne no fruit. Perhaps Chirac would have gone further had the physicians of his day taken much interest in the coronary arteries, but the frequency and serious consequences of the disease of these vessels were then and for many years thereafter quite unknown.

Chirac had long been dead when Morgagni[14], Thebesius[14] and Crell[14] observed calcification of the coronary arteries. It was near the end of the eighteenth century, before Jenner[11] and Parry[16] associated Angina pectoris, the new disease which Rougnon[18] and Heberden[9] had shortly established, with this calcification, and Jenner made his celebrated diagnosis of John Hunter's malady. The death of Hunter[10] in 1793 in a paroxysm of angina, and the discovery that his coronary arteries were indeed calcareous, as Jenner had predicted, was a great stimulus to the clinical and pathological study of these vessels. This interest, with some fluctuations, has continued to the present time and has been especially strong in the past ten years.

Erichsen, as we have said, was the first to make an experimental study of this theme. His research appears to have been incited by the opinion of Marshall Hall[8] that an interruption of the coronary circulation was a frequent cause of sudden death. His first experiment was as follows: "A moderately large dog, about two years of age, was pithed; artificial respiration was then set up by an assistant, the thorax opened, and the heart exposed as rapidly as possible. It was acting forcibly and

* The numbers after authors' names refer to list of cited works, p. 135 et seq.

pretty regularly from 90 to 100 beats per minute. Fine silk ligatures were then introduced under the coronary arteries, as close as possible to their origins, by means of one of Liston's small nævus needles (a curved needle with an eye near the point fixed in a handle), as it was found impracticable to tie the vessels in the usual way, whilst the heart was acting strongly. The ligatures were then tied, about six minutes after the death of the animal, the heart covered up by means of a portion of the walls of the thorax that had been removed, and artificial respiration continued. At 12 minutes after the ligature of the vessels (18 after the death of the animal) the heart was beating from 36 to 40 per minute. At 17 minutes it had fallen to 28—30. At 21 minutes the action of the ventricles had ceased, with the exception of a slight tremulous motion. The auricles still acted, and continued to do so for some time longer" (p. 561). In a second dog, the ventricles ceased beating in three minutes after the vessels were tied. These experiments were repeated on five rabbits of from eight to ten weeks of age. Ventricular standstill occurred in 24, 22, 21, 31 and 22 minutes respectively.

Twenty years after this work of Erichsen's, Panum[15] filled the coronary arteries and the aorta of a young dog by injecting from the truncus anonymus a mixture of tallow, wax, oil and lamp-black. He observed very exactly the action of the heart before, during and after the injection. Before the injection the cardiac movements were pretty regular, 80—90 in the minute. During the injection they were altered only in so far that the rhythm (on account of the high temperature of the injection mass) became quicker, and that the contractions of the left side of the heart, which was strongly distended with blood, diminished in extent. This latter phenomenon, he says, can be attributed with probability to the circumstance that the blood which flowed continuously to the left heart was not able to flow away. The left ventricle continued to beat 75 minutes, the right ventricle 90 minutes after the injection. Panum concluded that the lack of oxygenated blood does not bring the heart to an immediate standstill.

The Würzburg laboratory published in 1867 two researches on the coronary circulation. The clamping of the rabbit's coronaria magna (the left coronary artery) near its origin caused no immediate alteration of the pulse rate in the majority of the experiments. When an alteration was observed it was more frequently a diminution than an increase of the rate. The usual course was that the heart beat with unchanged rhythm for 10—20 seconds, and then began to beat more slowly. This

slower rhythm regularly showed itself first in the left ventricle, the remaining parts making often two contractions to one of this chamber. The period of irregular rhythm was closed by fibrillar contractions of the left ventricle ; the right ventricle and the auricles as a rule continuing to pulsate. This fibrillar contraction is described in unmistakable terms in 9 of 20 animals. In 7 of these, regular pulsations returned when the clamp was taken from the coronary artery. The usual procedure was to remove the clamp when irregularity began, but even when the clamp was left on until complete standstill regular contractions usually came back after its removal. The longer the chest was open before clamping, the longer the interval between the latter and fibrillar contractions. The higher the aortic pressure after closure of the coronary artery, the quicker the pulsations of the left ventricle became irregular. With high intracardiac pressures standstill may suddenly replace normal heart beats. Hearts brought to standstill may be recovered by the use of electric shocks, by artificial contractions (massage), and by stimulation of the vagus. v. Bezold[2] concludes that on closure of the coronary arteries the contractile power of the heart quickly sinks even when the regularity of the contractions is preserved. He regards the cause of fibrillar contractions " als eine sehr schnell ohne merkliche Zwischenräume getrennte Reizabgleichung vom Centralorgan zum Herzmuskel, die in benachbarten Abtheilungen des Herzens nicht mehr gleichmässig geschieht " (p. 284).

The second[3] of the two Würzburg papers concerned alterations of the heart beat following closure of the coronary veins. It was shown that in the rabbit closure of all the coronary veins produces fibrillar contractions after 15—20 minutes have passed.

The value of the experiments of v. Bezold and v. Bezold and Breymann is diminished, at least in so far as the purposes of the present research are concerned, by the fact that the spinal cord or the vagus had been cut or the brain removed before ligation. v. Bezold's estimate of intracardiac pressure was based on carotid curves recorded with a mercurial manometer.

In the *Comptes rendus*, Jan. 10, 1881, appeared a notice of the work of G. Sée, Bochefontaine and Roussy[20], on the sudden arrest of the rhythmical contractions of the ventricles of the heart after closure of the coronary arteries. These observers operated on curarized dogs narcotized with morphine, chloral or a mixture of the two. Some received daturine. Ligation of both coronary arteries near their aortic origin was followed in one or two minutes by sudden standstill of the

ventricles, their regular contractions giving place to an irregular trembling of the muscular faisceaux, more intense in the right ventricle. The same result followed ligation of the anterior (left) coronary or of two of its principal trunks. In one case, arrest followed ligation of the posterior (right) coronary alone. In another case, the ligation of this artery produced no appreciable effect during five minutes; the anterior coronary was then tied and convulsive movements appeared. The conclusion is drawn that closure of the right coronary artery causes the arrest of the heart less rapidly than closure of the left coronary. Standstill appeared almost immediately after the injection into the coronaries of about 2 c.c. of water charged with lycopodium spores, a fact which leads the authors to exclude the injury of perivascular nerves as a cause of the fibrillar contractions. The opinion was advanced that the fibrillar contractions produced by the ligation of the coronary vessels is analogous to that caused by faradization of the ventricle.

In this same year, 1881, B. Samuelson[19] compressed the left coronary artery after v. Bezold's method in five lightly curarized rabbits. The contractions of a frog's gastrocnemius, the nerve of which rested upon the ventricle, was used to show the changes in the intensity of the ventricular contractions. Samuelson sums up as follows: (1) With weak animals, speedy standstill of the heart. (2) With stronger animals, a weakening of the left ventricle, shared by the right ventricle in only slight degree. (3) In the majority of the latter cases, a simultaneous diminution of the frequency of the rhythmic contractions of the heart. (4) As a consequence of the diminished contractile force of the left ventricle, a congestion (Stauung), overfilling, and finally standstill of the left auricle. (5) *Restitutio in integrum* followed several times after a closure of two minutes' duration, once indeed after closure of four minutes; the consequence of closure for a longer period was standstill of the heart and death (p. 31).

Samuelson's contribution was followed by the important work of Cohnheim and v. Schulthess-Rechberg[5]. These observers operated for the most part on curarized dogs; morphium was used in two cases only. The average result of their experiments is thus described (p. 513). The closure of one of the large coronary branches has no immediate influence on the action of the heart. Towards the end of the first minute single beats begin to drop out. The number of intermittent beats increases. The action of both ventricles becomes plainly arythmic; regular pulses of the former quickness being followed by pauses in diastole, which are in turn followed by contractions in slower or quicker

succession. A clearly perceptible slowing in the rate of beat appears together with or shortly after the first irregularities. Meanwhile arterial pressure remains of the same mean height. During the arythmia a slight sinking of the arterial pressure shows itself for the first time. Suddenly the strongly beating, although somewhat irregular ventricles cease to beat, and the arterial pressure sinks to the abscissa. This standstill appears on the average 105 seconds after ligation, and is absolutely irreparable. Both ventricles stop in diastole, while the auricles continue to beat regularly and strongly, but somewhat less frequently. Ten or twenty seconds pass thus, then both ventricular muscles fall into exceedingly rapid, fluttering movements, somewhat like peristalsis.

The irregularity in force, in Cohnheim and Rechberg's experiments, was much more prominent than the change in frequency. Sometimes, with simultaneous writing of carotid and pulmonary curves, the diminution in frequency appeared earlier in the left ventricle than in the right. In rare cases the heart beat regularly up to the very last beat. With respect to the onset of arythmia, it made no difference whether the circumflexa, or the descendens, or both were ligated. In 75—77 secs., on an average, arythmia began. But after ligation of the small coronaria dextra, irregularities did not appear before the end of the third minute, and at least five minutes elapsed before standstill. When irregularities were well established, the two ventricles showed a frequent asynchronism, but so long as the irregularity consisted merely in the dropping of single beats, no difference between the two was apparent. The blood pressure was unchanged, or showed only an unimportant alteration until the rapid fall at standstill. Standstill was sudden, simultaneous in both ventricles and uniformly fatal.

Fenoglio and Drogoul[7] clamped or ligated a coronary artery in fifty dogs. Their conclusions are quite opposed to those of Cohnheim and v. Schulthess-Rechberg. The irregularities in the arterial pressure, on which Cohnheim lays much stress, were according to these observers merely the result of the traumatic lesions of the operation. They do not admit that the arrest of the circulation in a part of the myocardium has any influence on the arrest of the whole heart.

Some of Cohnheim's statements were contradicted also by McWilliam[13] in his paper on fibrillar contraction of the heart. McWilliam declares that the dog's ventricle may recover its normal co-ordinated rhythm even after fibrillar contractions have lasted a considerable time (p. 299).

While the experiments, described in the following pages were making, a paper by K. Bettelheim[1] was published in the• *Zeitschrift für klinische Medicin.* This observer finds that soon after ligature of the coronary artery the rate of beat is somewhat slower, and this slowing becomes marked immediately before cardiac standstill. The pressure in the carotid artery falls while that in the left auricle rises; hence the fall in arterial pressure is not due to dilatation of the blood vessels but to a loss of contractile power in the left ventricle. This weakening in contractile power does not extend to the right ventricle, for the pressure in the jugular vein, in one experiment, and in the pulmonary artery, in a second experiment, did not show any alteration of importance until just before heart death, at a time therefore when the pressure in the left auricle was already high; then the pressure in the pulmonary artery rose slightly.

Bettelheim's paper concludes the list of experimental investigations in this field*. Seldom have the results of physiological studies been more at variance. The attentive reader finds no statement that is not denied, no fact not in dispute. These controversies would alone compel a new examination of the interesting phenomena in question, and the necessity of further research is increased by the knowledge that changes in intracardiac pressure following closure of the coronary arteries have been inferred rather than determined, and have never been studied with the improved methods of the present day.

II. ANATOMICAL.

The arteria coronaria sinistra divides a few millimeters from the aorta into the ramus descendens and the ramus circumflexus.

The ramus descendens passes downwards in the intraventricular groove, giving off two sets of branches, the one running to the left into the wall of the left ventricle, the other running backwards into the ventricular septum through the interstices in the musculature. In addition to these branches, the descendens gives off, very close to its origin, the ramus septi, which immediately plunges deeply into the intraventricular septum and is not seen on the surface of the ventricle.

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* I'have not included Lukjanow, because he gives only a preliminary notice of his work and does not say by what methods his observations were recorded or whether they are true of dogs or rabbits, or of both these animals. I have not been fortunate enough to find any papers by him on this subject other than those cited in note 12.

The ramus circumflexus passes around the left side of the heart in the furrow between the auricle and the ventricle.

The arteria coronaria dextra runs a course analogous to that of the r. circumflexus.

Thus the intraventricular septum receives its blood supply from the arteria septi and the other septal branches of the descendens; the rest of the left ventricle is supplied by the remaining branches of the descendens and by the circumflexa; and the right ventricle by the arteria coronaria dextra.

Many authors believe that the coronary arteries in man anastomose only by means of the capillaries and the minute branches nearest them in size, and Cohnheim (*l.c.*, p. 508) makes a similar statement regarding the dog's coronary arteries. Porter[17] has recently shown that in the dog the coronaria dextra and the r. descendens, circumflexus and septi are truly terminal arteries (Endarterien), and that their closure is followed by sudden anæmia and subsequent infarction of the capillary areas which they supply.

III. METHODS.

Dogs were used in my experiments. The 2nd, 3rd, 4th and 5th dog of the series of 32 recorded here were given a small quantity of morphia. Voluntary movements were prevented by curare, from 7 to 12 c.c. (in one case, 15 c.c.) of a solution made by allowing 1 gr. to stand in 100 c.c. of water, being injected under the skin of the trunk.

The heart was reached by a nearly bloodless resection of part of the six upper ribs on the left side. The edges of the pericardium were stitched to the edges of the thoracic opening. The length of the operation was noted in several instances, as a factor of importance in determining the reaction of the ventricle to ligation of its arteries. In Exp. X., the pericardium was opened 18 minutes after the first tracheotomy incision. In the next operation, Exp. XI., 40 minutes elapsed between the first tracheotomy incision and ligature of the ramus septi. In Exp. IX., the pressure in the left ventricle, and the contractions of the right ventricle were recorded, and the coronaria dextra, septi and circumflexa successively tied, the entire experiment occupying 100 minutes.

The arteries ligated were the coronaria dextra, the descendens, the circumflexa and the septi. The coronaria dextra was tied about 1 cm. from the aorta, and the various branches of the arteria coronaria sinistra very near their origin. The arteries were freed from their beds for one

or two millimeters, great care being taken to operate with the least possible injury to the peri-arterial tissues.   In each case a careful dissection post-mortem put the efficiency of the ligature beyond doubt. The coronaria dextra, the descendens and the circumflexa may be prepared without the loss of a drop of blood and without injury to the surrounding parts, except the adipose tissue in which the arteries are imbedded.   The preparation of the ramus septi is difficult, and involves necessarily a slight laceration of the ventricular tissues.

In the course of the investigation fifty arteries were prepared for ligation.   In no case did the operation *per se* produce a serious disturbance of the heart's action.   As a rule, no disturbance referable to the operative procedure could be noticed.   Exceptionally, a slight irregularity in the force or the frequency of the ventricular stroke was observed, but this alteration was almost invariably transient and to all appearances unimportant.   My results are therefore opposed to the conclusions of Fenoglio and Drogoul, who declare that the alterations in the action of the ventricles following ligation of the coronary arteries are due to the mechanical insults of the operation.

IV. THE FREQUENCY OF STANDSTILL, THE INTERVAL BETWEEN LIGATION AND HEART FAILURE AND THE EFFECT OF LIGATION UPON THE RATE OF BEAT AND THE SYNCHRONISM OF THE VENTRICLES.

Standstill followed ligation of a single artery 10 times in 26 cases. The ligation of the septal branch was wholly unsuccessful, and the

Frequency of standstill after ligation of a single artery.

Artery ligated	Number of ligations	Standstill followed	No standstill followed
Cor. dextra	11	2	9
Descendens	8	4	4
Circumflexa	5	4	1
Septi	2	0	2

coronaria dextra scarcely more effective, while in striking contrast is an almost uniform standstill following ligation of the circumflexa.

In 14 dogs a second artery was tied, the closure of the first not having caused standstill.   Of these double ligations, 9 were successful and 5 unsuccessful.

Frequency of standstill after ligation of two arteries.

First artery tied	Second artery tied	Standstill	No standstill
Cor. dextra	Circumflexa	3	1
Cor. dextra	Descendens		2
Cor. dextra	Septi		1
Septi	Cor. dextra	1	1
Circumflexa	Descendens	1	
Descendens	Circumflexa	4	

Three ligations were made in 5 animals. Standstill followed without exception.

In considering these results, we cannot lose sight of the fact that standstill might after all have occurred in some of the cases in which no standstill is recorded, provided the time of observation had been sufficiently prolonged. I sought to exclude such mistakes by waiting for ten to thirty minutes after ligation. If the heart then showed no signs of approaching standstill, if the ventricles had never lost or had regained an apparently normal stroke, it was considered that this particular ligation was not sufficient to stop the ventricles. The impression gained by observation of the heart was that this conclusion caused but little error.

The number of seconds during which the heart continued to beat after ligation varied with the artery occluded. The coronaria dextra furnishes three cases, 1002, 1008, 343 seconds. With the descendens, the average duration of activity in 8 cases was 233 seconds, the limits being 334 and 135 seconds. The time required for standstill was much less when the circumflexa was tied, the average in 11 cases being 119 seconds, the extremes 26 and 204 seconds. In a 12th case, the beat continued about 10 minutes. It might be supposed that ligation of a second artery, the first not having stopped the ventricle, would cause speedy standstill. This idea is not borne out by the facts. The accompanying Table shows the effect of successive ligations.

Seconds required for standstill after ligation of one or more arteries.

Artery	No. of cases	When first artery ligated	No. of cases	When second artery ligated	No. of cases	When third artery ligated
Descendens	4	206 secs.	3	155 secs.	2	245 secs.
Circumflexa	3	125 „	5	106 „	2	142 „

A pause was made after each ligation, as explained in the preceding paragraph.

The frequency of the heart was estimated by counting the upstrokes in curves of intraventricular pressure recorded with the aid of a cannula inserted through the auricular appendix and coupled to a Gad manometer. Seconds were marked by a Baltzer clock and Pfeil chronograph. In 12 animals the intraventricular record was controlled by a myogram from the surface of one of the ventricles. It will be convenient to first consider the frequency in the cases in which ligation was not followed by standstill. In the 14 experiments in which no standstill followed ligation, the frequency was unchanged in 12 and diminished in 2. In one of these latter, the diminution was only temporary. The remaining cases, ligation with standstill, were 22 in number: in six, the frequency was unchanged; in one, the rate remained unaltered to the last six seconds; in another, the rate rose one beat in ten seconds, sixty seconds before standstill; and in a fourth, the frequency was unvaried throughout the observation, but the last ten seconds were not recorded; in 4 animals, ligation sooner or later increased, and in 9 diminished frequency.

Do both ventricles cease to beat at the same instant?

Exp.	Arteries ligated	Yes	No	Method of observation
II	Descendens	yes		
III	Descendens	yes		Pressure-curves, both ventricles
V	Descendens and circumflexa	yes		„ „
VII	Cor. dextra and circumflexa	yes		Eye
X	Cor. dextra	yes		Eye
XI	Septi and cor. dextra	yes		Eye
XIII	Cor. dextra, septi and descendens	yes		Pressure-curve, left ventricle, and myogram, right ventricle
XVI	Branch of cor. dextra and circumflexa	yes		Pressure-curve, left ventricle, and myogram, right ventricle
XIX	Cor. dextra, branch of descendens and circumflexa	yes		Pressure-curve, left ventricle, and myogram, right ventricle
XXI	Descendens and circumflexa		no	Myograms, both ventricles
XXII	Descendens and circumflexa		no	Eye

Both ventricles cease to beat as a rule at the same moment. Such was the fact in 9 cases of 11 observed. In 7 of these, a graphic registration was employed. In one of the two exceptions, the graphic record showed that the right ventricle beat one second longer than the left. In the other, the right ventricle beat 93 seconds after the left had ceased. It is particularly interesting that this synchronism in standstill was the same no matter which ventricle the ligated arteries supplied.

The moment when fibrillary contractions began was observed in 10 instances. In 6, they followed standstill instantly. In 4, they are noted as appearing respectively 2 and 3 seconds, "within a few seconds," and " very promptly " after the standstill.

The standstill was always permanent. When fibrillary contractions had once set in, the ventricles could not be made to beat again.

The conclusions reached in this section are briefly :

1. Ventricular standstill was never observed after ligation of the arteria septi alone, rarely observed (18 p.c.) with the arteria coronaria dextra, frequently (50 p.c.) with the descendens, and almost uniformly (80 p.c.) with the arteria circumflexa.

2. Ligation of two of the above-named arteries failed to stop the ventricles in 5 out of 14 cases. In each of the 5, the coronaria dextra was one of the arteries tied.

3. Ligation of three arteries caused standstill always.

4. The number of seconds during which the ventricles continued to beat after ligation varied with the artery occluded, and was shortest with the circumflexa.

5. Standstill did not occur more quickly after ligation of a second or a third artery than after ligation of a single artery.

6. When standstill did not follow ligation, the frequency of the ventricular beat was seldom changed (84 p.c.).

7. When standstill followed ligation, frequency was sooner or later usually altered. But some hearts (27 p.c.) beat with unchanged rhythm to the last.

8. As a rule both ventricles stopped at the same moment (82 p.c.), no matter which ventricle the ligated arteries supplied.

9. Fibrillary contractions followed standstill instantly (60 p.c.), or within a very few seconds.

10. Standstill was always permanent.

V. The effect of ligation on the intraventricular pressure.

The effect of ligation on the intraventricular pressure was noted in 27 ligations made in 18 dogs. In 21, the height of ventricular upstroke was diminished by the ligation. The other ligations were none of them followed by standstill. The diminution in the height of the upstroke was gradual and began almost without exception a very few seconds after closure of the artery. Accompanying this gradual fall in the maximum height of intraventricular pressure was a retardation of both the upstroke and the downstroke in the intraventricular curve, indicating an increasing slowness in contraction and relaxation. Fifteen hearts were investigated with reference to this matter, and the retardation was visible in all the curves. In one animal, many beats were slowed while others were exceedingly quick, and one heart gave occasional apparently normal beats until the final failure. The diastolic pressure is raised when standstill follows ligation. The curves* from 13 animals were used to determine this question, and the diastolic pressure was found increased in every instance.

Irregularities in the force of the ventricular contractions did not always appear. Of 10 sets of intraventricular curves in which no standstill followed ligation, no irregularity in the force of the contractions

Interval between ligation and onset of irregularity and standstill.

Experiment	Artery ligated*	Irregularities		Standstill
III	Descendens[1]	85 secs.	132	169
IV	Descendens[2]	65	115	135
V	Circumflexa[2]	145		158
XI	Cor. dextra[2]	60	110	343
XIII	Descendens[2]	82	95	171
XVIII	Cor. dextra[1]	77	80	108
XXII	Circumflexa[1]	22		26
XXV	Circumflexa[1]	42		600
XXVI	Descendens[1]	144		264
XXVIII	Circumflexa[1]	48		145

* The number placed after the artery indicates whether it was the 1st, 2nd, or 3rd artery tied.

could be observed in 7, and in one of the remainder, the irregularity in force was only temporary. Of 11 standstill cases, irregularities sooner

* Previous to each experiment, it was proved by the usual methods that the writing-lever of the manometer returned accurately to the zero-abscissa when the manometer chamber was put at atmospheric pressure.

or later appeared in 10; in one of these, but a single beat was dropped. These irregularities never began within a few seconds of ligation, as does the fall in the maximum height of intraventricular pressure, but were separated by a much longer interval from the moment of closure. This interval is shown in the accompanying table. Where two figures are given, the second indicates the point at which irregularity may be said to be fairly established.

Summary of the changes in intraventricular pressure.

1. A gradual and continuous decrease in the height of the intraventricular upstroke appeared almost immediately after ligation. When ligation did not cause standstill, this lowering of the upstroke was absent (22 p.c.) or transient.

2. Ligation was uniformly followed by a slowing of the upstroke and downstroke of the intraventricular curve. In a few instances, beats of normal or increased quickness were mingled with the retarded beats.

3. When standstill followed ligation, the diastolic intraventricular pressure was invariably increased.

4. Irregularities in the force of the intraventricular beat were seldom absent when the moment of standstill drew near; but when ligation did not cause standstill, irregularities were commonly absent (70 p.c.) or temporary.

VI. THE INFLUENCE OF ANÆMIA OF ONE VENTRICLE ON THE CONTRACTION OF THE OTHER VENTRICLE.

K. Bettelheim[1] believes that ligation of the coronaria sinistra does not affect the contractile power of the right ventricle. He found that closure of this artery was followed by a rise of pressure in the left auricle and a fall in the aorta, and inferred that the contractile force of the left ventricle was weakened. Two experiments were made by him to determine whether this weakening extended to the right ventricle. A simultaneous registration of the pressure in the carotid artery and jugular vein showed that during the fall in arterial pressure after ligation the venous pressure rather sank than rose. In another experiment, the pressure was measured simultaneously in the carotid and pulmonary arteries. The pressure in the latter rose a little shortly before cardiac standstill. Bettelheim concludes that closure of the coronaria sinistra makes only the left ventricle insufficient.

My experiments lead in part to similar results. Twice the pressure

in the pulmonary and the carotid artery was compared (Exp. XXIX. XXX). In neither case was any alteration in the pulmonary curve observed until just before standstill, when the curve rose very slightly. A little further investigation, however, shows that these data are too few to establish Bettelheim's conclusion. In Exp. II. the pressure in both ventricles was recorded simultaneously. Ligation of the ramus descendens was followed by irregularities in force which appeared in both ventricles, were almost perfectly synchronous, especially towards the last, and were terminated by synchronous standstill. Experiment III. was very similar. Again cannulas were placed in both ventricles and the ramus descendens ligated. At 132 seconds, irregularities in force appeared in both ventricles. Progressive diminution in the height of the upstroke and the slowing of both upstroke and down-stroke were evident in the right ventricle as early as in the left. The ventricle stopped beating at 169 seconds. These experiments show that the intraventricular pressure and the character of the contraction and relaxation in one ventricle may be speedily affected by ligation of a coronary artery supplying the other ventricle.

Other observations strengthen this statement. In Exp. XVIII. ligature of the coronaria dextra was followed by marked irregularities in the pressure in the left ventricle. With still another heart, Exp. XI. the left intraventricular pressure-curve was recorded together with a myogram of the right ventricle. Sixty seconds after the ligation of the coronaria dextra, the pressure in the left ventricle showed a slight and transient irregularity; at 110 seconds, pronounced irregularity set in, but it was not until 206 seconds that the myogram of the right ventricle began to be irregular, and standstill did not follow until 344 seconds. In Exp. XVIII. the diastolic pressure in the left ventricle increased after ligature of the coronaria dextra, a fact difficult to reconcile with a diminution of contractile power in the right ventricle alone.

The observations detailed above permit the statement that the character of the contraction and relaxation of one ventricle may be speedily affected by ligation of an artery supplying a part of the walls of the other ventricle.

VII. An unsuccessful attempt to connect fibrillary contraction with fragmentation of the heart.

The recent work on fragmentation of the heart suggests the thought that fibrillar contractions may be due to an alteration in the cement

substance leading to an interruption of the contraction-wave. The contraction-wave would be thus prevented from running its usual course, and the normal coordinated action of the ventricular cells would give place to the confusion conspicuous in fibrillary contractions.

I have made a search for fragmentation within and beyond the area supplied by the artery ligated. The method was similar to that by which Alessandro Tedeschi[21] demonstrated the existence of fragmentation in the human heart. Pieces about 1 c.c. in volume were placed for eight days in a large quantity of Müller's fluid diluted with an equal quantity of water; the fluid was changed every day. They were then placed for eight days in Müller's fluid of full strength, the solution being frequently renewed, washed in water 24 hours, carried through 30 and 70 per cent. alcohol, one day each, and hardened in 90 per cent. alcohol. Finally, the tissue passed through absolute alcohol, xylol, xylol-paraffin and pure paraffin. The paraffin sections were fastened to the object-glass with a mixture of glycerine and egg-albumin, and stained on the slide with hæmatoxylin and eosine in the customary way.

Specimens from six hearts were examined. The nuclei took the stain well, the striation of the fibres was distinct, and no difference could be made out between the cement substance in the anæmic area, and that in sections from a normal ventricle.

Thus no proof of a break in the cement substance was secured. Without this proof, it would be hazardous to offer fragmentation as the cause of standstill with fibrillary contractions. Yet it should be noted that the plausibility of such an explanation would not be destroyed by a failure to find anatomical evidence of such a break. For a change sufficient to block the passage of the contraction wave might not be recognizable with the present histological methods.

The vivisections which form the basis of this paper were made in 1892 in the Physiological Institute of the University in Berlin. I am much indebted to Prof. Gad for his unstinted support and for the liberality with which the resources of the Vivisectorium were put at my disposal.

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(5)   Cohnheim, J. und A. v. Schulthess-Rechberg. "Ueber die Folgen der Kranz-Arterien-Verschliessung für das Herz." *Virchow's Archiv*, 1881, Bd. 85, S. 503—537.

(6)   Erichsen, John E. "On the influence of the coronary circulation on the action of the heart." *The London Medical Gazette*, 1842, Vol. II. pp. 561—564.

(7)   Fenoglio, J. et G. Drogoul. "Observations sur l'occlusion des coronaires cardiaques." *Archives italiennes de biologie*, IX. pp. 49—50.

(8)   Hall, Marshall. "On the mutual relations between Anatomy, Physiology, Pathology, and Therapeutics." *Gulstonian Lectures*, read at the British Association for the Advancement of Science, June 24, 1842. Cited by Erichsen.

(9)   Heberden. *Commentaries on the History and Cure of Disease*, 4th Edition, London, 1816, Chapter 70 and page 303.

(10)   Hunter, John. *A treatise on the blood, inflammation and gunshot-wounds*, to which is prefixed a short account of the author's life, by Everard Home, London, 1794, p. LXIII.

(11)   Jenner. See Parry(16).

(12)   Lukjanow, S. M. "Zur Lehre von den Functionsstörungen einzelner Herzhöhlen. Vorläufige Mitteilung." *Centralblatt für die medicinischen Wissenschaften*, 1881, Nr. 49, S. 881—883, und 1882, Nr. 18, S. 321—323.

(13)   McWilliam, J. A. "Fibrillar Contraction of the Heart." *The Journal of Physiology*, 1887, VIII. p. 296—310.

(14)   Morgagni, Jo. Baptista. *De sedibus et causis morborum, per anatomen indagatis*, Venetiis 1761, Lib. II. XXIV. 16, p. 252. An emaciated old man was examined by Morgagni in December, 1743. "Cordis exteriorem faciem examinanti arteria se obtulit coronaria sinistra in canalem osseum ab ipsa origine ad tractum plurium digitorum mutata, qua basis magnam partem amplectitur. Sed et rami illius praelongi, quem per anteriorem cordis faciem demittit, pars erat ossea jam facta ad tantum spatium, quantum digiti transversi tres operirent."

     In the next paragraph, XXIV. 17, p. 253, reference is made to the observations of Thebesius and Cl. Crellius.

(15) Panum, P. L. "Experimentelle Beiträge zur Lehre von der Embolie.'
      Virchow's Archiv, 1862, Bd. 25, S. 312.

(16) Parry, Caleb Hillier. *An inquiry into the symptoms and causes of
      the syncope anginosa, commonly called Angina Pectoris.* London,
      1799.

> On pages 3, 4 and 5, of the introduction to this Essay, Parry
> prints a most interesting letter from Jenner, in which the latter
> relates how he first got the idea that Angina Pectoris was due to
> ossification, or some similar disease of the coronary arteries. "At
> this very time," Jenner continues, "my valued friend, Mr John
> Hunter, began to have the symptoms of Angina Pectoris too
> strongly marked upon him; and this circumstance prevented any
> publication of my ideas on the subject, as it must have brought on
> an unpleasant conference between Mr Hunter and me. I men-
> tioned both to Mr Cline and Mr Home, my notions of the matter,
> at one of Mr Hunter's Sunday night meetings; but they did not
> seem to think much of them. When, however, Mr Hunter died,
> Mr Home very candidly wrote to me, immediately after the dissec-
> tion, to tell me I was right."

(17) Porter, W. Townsend. "Ueber die Frage eines Coordinations-
      Centrum im Herz-Ventrikel. (*Pflüger's*) *Archiv für die gesammte
      Physiologie*, 1893.

(18) Rougnon, N. F. *Pathologisch-semiotische Betrachtungen aller Ver-
      richtungen des menschlichen Körpers.* Translated from the Latin by
      K. G. Kühn. Halle & Leipzig, 1801, Bd. i. S. 202.

(19) Samuelson, B. "Ueber den Einfluss der Coronar-Arterien-Ver-
      schliessung auf die Herzaction." *Zeitschrift für klinische Medicin*,
      Bd. ii. S. 12—33.

(20) Sée, G., Bochefontaine et Roussy. " Arrêt rapide des contractions
      rythmiques des ventricules cardiaques sous l'influence de l'occlusion
      des artères coronaires." *Comptes rendus*, Jan. 10, 1881, pp. 86—89.

(21) Tedeschi, Alessandro. "Ueber die Fragmentation des Myocardium."
      Virchow's Archiv, 1892, Bd. 128, S. 185—204.

A DESCRIPTION OF THE FIGURES IN PLATE.

The curves were taken with Gad's manometer, which was connected
by a wide glass tube with a large cannula inserted in the left ventricle
through the auricular appendix. In fig. 1, the time-curve records two
seconds intervals; in the other figures, second intervals. All curves
read from left to right.

Fig. 1, Exp. XXII. An arrow shows the moment at which the

arteria circumflexa was ligated. Standstill with fibrillary contractions followed in 26 seconds. The fall in the height of the upstroke and the rise in diastolic pressure subsequent to ligation are evident.

Fig. 2, Exp. V. The break in the curve indicates an interval of 25 seconds, during which the circumflexa was tied. The change in the character of the curve cannot escape notice.

Fig. 3. The last beats in the same curve from which fig. 2 was cut. Irregularities first appeared at 145 seconds, standstill taking place at 158 seconds.

Figs. 4, 5, 6, 7 and 8 are parts of one curve, Exp. IV. fig. 4; was written before ligation; the circumflexa was then ligated, but the only result was to lengthen the contraction and relaxation, as shown in fig. 5. In fig. 6, 91 seconds after closure, the effect of the operation has become very noticeable, and in fig. 7, 135 seconds after ligation, the slowing of upstroke and downstroke and the rise of diastolic pressure are so great as to plainly indicate a swiftly approaching failure. At 135 seconds the ventricles stop; the last three beats appear in fig. 8.

145 Sec.

Fig. 3.

158

Fig. 2.

Fig. 1.

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.