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28.

"On the Effect of Electrical Stimulation of the Frog's Heart, and its Modification by Heat, Cold, and the Action of Drugs."

By T. LAUDER BRUNTON, M.D., F.R.S., and THEODORE CASH, M.D. Received May 16, 1881. Read June 16, 1881. Revised June 13, 1883.

In the following research we have examined the effect of electrical stimuli applied to the different cavities of a frog's heart, and the modifications of their effect by heat, cold, and the action of strychnia. The effect of electrical stimuli upon the ventricle, and the alterations occasioned in it by the application of heat, have already been studied by Professor Marey. The time relations of excitation in the frog's heart have also been very exactly determined by Dr. Burdon Sanderson and Mr. Page. But it seemed desirable to extend the scope of the research, and instead of confining ourselves like previous observers to the effect of stimulation applied to the ventricle alone, to observe also the effect of stimulation of the ventricle, auricle, and venous sinus, both on the ventricular and the auricular contractions. This we did with the hope that from such series of observations we might be able to arrive at some conclusions regarding the transmission of stimuli from one part of the heart to the other in the ordinary course of the circulation. Professor Marey found that when an electrical stimulus was applied to the ventricle of a pulsating frog's heart the effect differed according to the condition of contraction or relaxation in which the ventricle was at the time the stimulus was applied. During the first part of the contraction of the ventricle, from the commencement of the contraction until nearly its maximum, stimulation had no apparent effect at all, and this period Marey terms the "refractory period." Following this phase is a second one, to which we have given in the following paper the term of the "sensitive phase," lasting from the maximum of systole to its end. The refractory period varies in duration according to the intensity of the stimulus, and the conditions under which the heart is operated upon. The feebler the stimulus, the longer is the refractory period. When the stimulus is very slight the refractory period may persist during the whole ventricular systole; as the stimulus is increased, the refractory period becomes shorter, and finally, when it is very strong, disappears altogether.

Heat applied to the heart shortens the refractory period or abolishes it altogether. Cold has an opposite effect, and lengthens the refractory period. The contractions caused by artificial stimulation do not much alter the cardiac rhythm, for the accelerated beat is followed

by a longer pause than usual, which compensates for the diminished interval between the two first beats. Sometimes no ventricular contraction is induced, and then instead of acceleration there is apparent inhibition, the application of the stimulus being followed simply by a longer diastolic pause than usual.

Marey's observations were confined entirely to the movements of the ventricle, but we have extended ours to the movement of the auricle as well. We employed two levers: one resting upon the ventricle, and the other upon the auricle, which recorded movements upon a revolving cylinder covered with smoked paper.

It is unnecessary to enter here into a fuller description of the apparatus, which is given elsewhere.*

By the method employed we are able to study the effects of maximal and minimal stimulation applied to the ventricle, auricle, and venous sinus upon the movements both of auricle and ventricle.

By minimal stimulation we understand the smallest shock that produces any visible effect that in any way modifies the course of contraction or the rhythm of the organ; and by maximal stimulation we mean the electrical irritation of such a strength that its intensification produces no visible increase in its effect.

The apparatus for stimulation consisted of a bichromate battery with two zinc ($3\frac{1}{2}$ inches by 2 inches) and three carbon plates, the size of these being 8 inches by 2 inches. This was connected with a coil, and a key was interposed by which the primary circuit could be made and broken at pleasure. The moments of opening and closing the circuit were registered upon the same revolving cylinder as that upon which the cardiac pulsations were noted, by means of an electro-magnet, the marker of which was placed immediately under the pens of the cardiac levers. In all the tracings the upper curved line shows the ventricular contractions, the lower curved line the auricular contractions, and the broken straight line the moment of excitation. The descent of the line indicates the opening, the ascent the closing of the current.

In the secondary circuit were placed the electrodes for stimulating the various parts of the frog's heart, and this circuit also could be broken or changed at pleasure by means of an interposed double key.

The heart was stimulated by a single induction shock. In minimal stimulation only the breaking shock was effective, in maximal stimulation both making and breaking shocks. The apparatus, which is described in a separate note, admitted of the venous sinus, auricle, or ventricle being stimulated at will.

When recording the effects of stimulation of the venous sinus we speak only of changes in rhythm of auricle and ventricle.

We shall examine *seriatim* the results of irritation of each of these.

* Cash. "Journal of Physiology," vol. iv, No. 2.

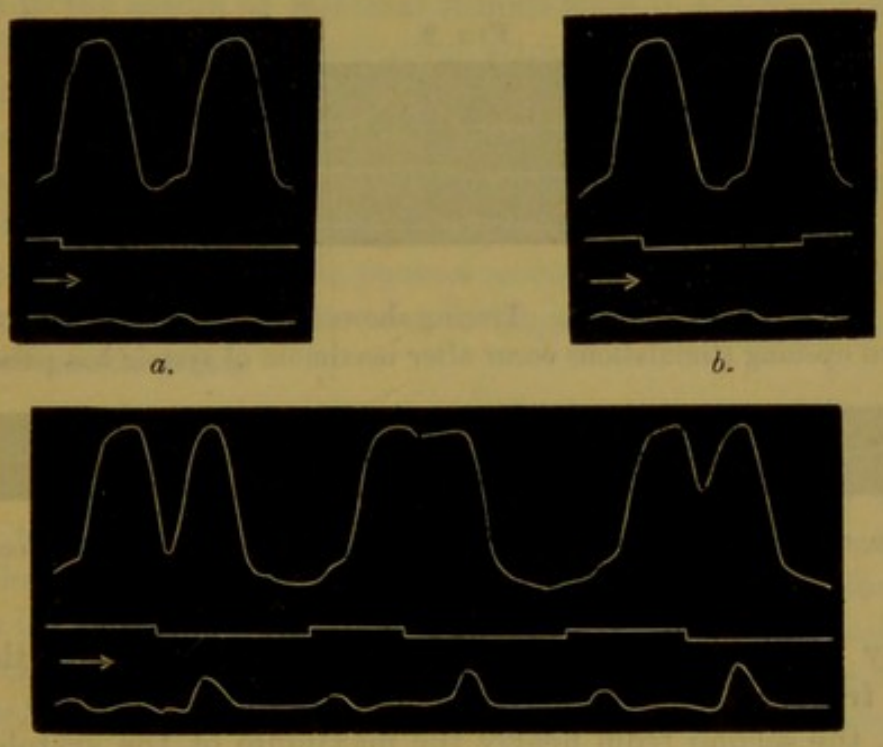
The temperature of the room in which the experiments were conducted was 67° to 70° F. The frog employed was, on all occasions, the *Rana temporaria*.

Stimulation of the Ventricle—Minimal.

On stimulating the ventricle with a single induction shock of minimal potency we find—

(1.) That between the commencement of the ventricular systole up to or nearly up to its maximum there is a refractory period (fig. 1,

FIG. 1.



Stimulation of Ventricle (minimal).

a and *b*, stimulation in different phases of refractory period.
c, stimulation after refractory period has passed, showing different forms of reduplication.

a and *b*) during which stimulation applied to the ventricle has no effect whatever on that beat of the heart, or the one succeeding it, nor is the auricle in anywise affected.

(2.) That after the refractory period has elapsed stimulation causes a reduplication of the beat (fig. 1, *c*).

(3.) The latency of this reduplicated beat becomes distinctly shorter as the systole passes into the diastole. Thus supposing the value of a single cardiac systole to be 1″·3, stimulation falling just at the maximum of a beat will cause a reduplicated beat with a latency of ·33. When the stimulation occurs half way down the curve of relaxation, the latency is ·18 or ·2, and when applied at the instant before the abscissæ would have been reached the latency is only ·13.

(4.) Where acceleration or reduplication occurs, the subsequent diastolic pause is prolonged, so that the time occupied by the two beats, the interval between them longer or shorter, and the subsequent pause, is nearly equal to the time which would be occupied by two normal beats with their associated diastolic pauses (fig. 1, *c*).

(5.) The ventricular reduplication is often associated with a reduplication of the auricular beat, but in no case has the latter its commencement before the former. It is usually, in fact, distinctly later (fig. 2, *a*).

It is to be noted that, *minimal stimulation* applied to the *ventricle* during its refractory period produces *no* effect on the *auricle*.

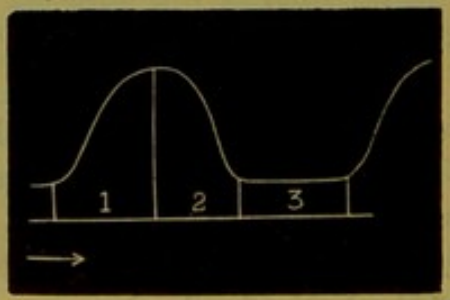
Fig. 2.

a.

Stimulation of Ventricle (minimal). Tracing shows long pause after reduplication. The two opening stimulations occur after maximum of systole has passed.

Time-Writer, marking seconds. Applicable to all tracings in the paper, except those in the Appendices.

We may divide each ventricular cycle into three parts, the first reaching from the commencement of systole nearly up to its maximum, the second from nearly the maximum of the systole to its end, and the third embracing the whole diastolic period from the end of one systole to the beginning of another (*vide* diagram A) except



A.

Diagram A shows the division of the ventricular cycle into three parts.—
1. Refractory period. 2. Sensitive period. 3. Accelerative period.

when the stimulation falls immediately after the end of the refractory period. In all these points our results agree with those already obtained by Marey.*

* *Op. citat.*, p. 72.

Stimulation applied to the ventricle during the first period has no effect whatever either in accelerating the occurrence of the second beat, or altering the length of the subsequent pauses. This constitutes the refractory period.

Stimulation applied during the second period causes reduplication of the systole, the next systole succeeding with a constantly diminishing latency up to the end of the period. When the stimulation is applied in this period, the two systoles being more or less united, there is no distinct pause between them, but the diastolic pause succeeding the second occupies very nearly the interval of time corresponding to two normal diastolic pauses. In this second period the heart is more sensitive to the action of minimal stimuli than in the first period. In the third period, that of acceleration, stimulus applied to the ventricle hastens the advent of the succeeding systole, and the latent period is very short, being nearly equal throughout its whole extent to the latency at the end of the second period. The sensibility of the heart to stimuli is scarcely so great in this period as in the second.

The length of the diastolic pause succeeding the accelerated systole is longer than normal, the increase in length being nearly equal to the amount of acceleration.

Stimulation of the Ventricle—Maximal.

When stimuli of maximal potency are applied to the ventricle between the maximum auricular systole and the commencement of ventricular systole, the ventricular systole immediately following the stimulus is rarely slightly higher than normal, and the diastolic pause succeeding it is excessively long—so long, indeed, as to be nearly, if not quite, equal to the time which would, as a rule, be occupied by two diastoles, so that the time occupied by the systole and diastole after stimulation applied at this period of the heart's cycle, is equal to the time usually occupied by one systole and two diastolic pauses.

In most cases this systole was apparently no higher than normal, and consequently we cannot with plausibility regard it as a case of superposition of two systoles.

In some cases the time within which this pause may be produced is strictly limited to the point indicated; in others, however, it may extend some little distance towards the maximum of systole, though it never reaches this. In other words, it may encroach upon the refractory period which we have mentioned when speaking of minimal stimuli, although it never extends through the whole of it.

This phase may occasionally, though rarely, be absent. Its place is then taken by reduplication, or very rarely by insensibility to stimulation, as in the refractory period.

Reduplication with maximal stimuli occurs during all times of the cycle, except at the very commencement of the systole.

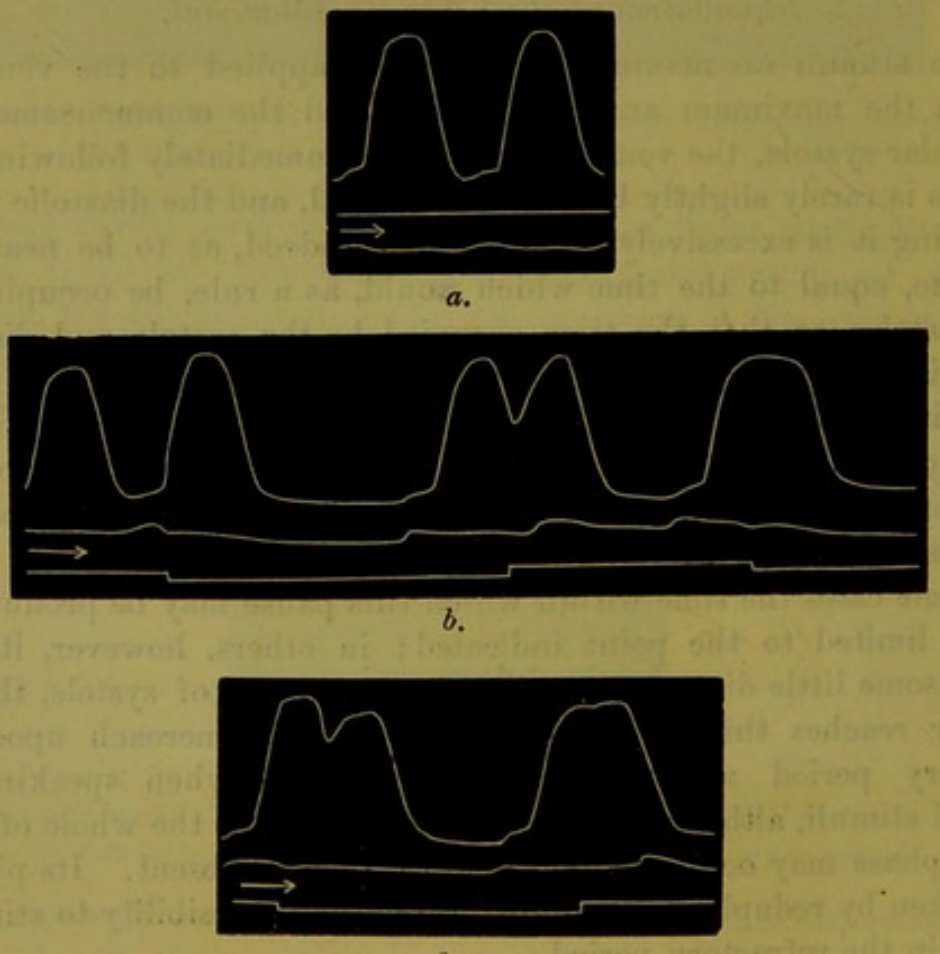
A very considerable latency is to be observed in cases where stimulation falls early in the systole. The latency, when this is the position of the shock, is usually ·5′ or even more, and occasionally where stimulation is coincident with the earliest possible attempt at systole, nearly the whole beat may lapse before reduplication.

The latency is greatest when the stimulus is applied at the commencement of the ventricular systole (with the exception of its very beginning), and it gradually decreases towards the end of systole, at which time it is at a minimum. During the diastole the latency seems to remain constantly the same as at the end of systole. The later in the phase of ventricular activity the reduplicated systole commences the more perfect is it.

In all the points already mentioned our results agree with those of Marey.

Stimulation of the ventricle falling before or at the maximum of ventricular systole, *i.e.*, during the refractory period of a minimal stimulation, frequently causes a reduplication of the auricular systole which holds the same relation to the induced ventricular beat that the auricular contraction normally holds to the ventricular.

Fig. 3.



a.

b.

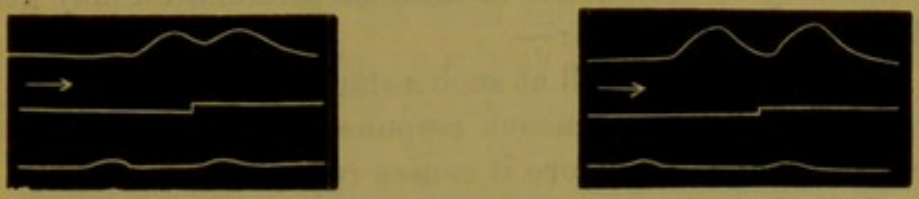
c.

Stimulation of Ventricle (maximal).

a, normal tracing; *b*, effect of maximal stimulation. In *b* inhibition is seen.

Stimulation falling after the maximum of ventricular systole may cause an induced auricular contraction, but this is nearly synchronous with, or even subsequent to, the induced ventricular contraction (fig. 4, *a* and *b*, and fig. 3, *c*).

FIG. 4.



a. *b.*

Stimulation of Ventricle (maximal).

Sometimes reduplication of the ventricular beat may occur without reduplication of the ventricular (fig. 3, *c*).

These results may be possibly due, in part at least, to direct stimulation of the auricle itself by the strong current used to stimulate the ventricle.

Stimulation of the Auricle—Minimal.

When minimal stimuli are applied to the auricle, there is occasionally a refractory period, extending from the beginning to the maximum of auricular systole. When the stimulus is applied at the maximum of auricular systole, or just after it, it sometimes produces an omission, or, as we may term it, an apparent inhibition of the next auricular and ventricular systoles (fig. 5, *b*). Stimulation falling after this point and occasionally on it, will cause a reduplication of auricular and ventricular contractions to occur which may have a latency of as much as 1·25 seconds.

FIG. 5.

a.

b.

Stimulation of Auricle (minimal).

No secondary contraction can usually be produced in the ventricle till an induced auricular contraction has occurred; and as the auricular latency is considerable, the ventricular latency is also very long. Thus, should the stimulus producing contraction fall at the commencement of ventricular systole, the auricle may have a latency of one second and the ventricle of 1·4 seconds.

The sensibility of the auricle to minimal stimulation may generally be divided into three phases:—

1stly. Stimulation may fall at such a stage of auricular activity that it does not cause an instantaneous response, but allows the auricle to pass through its diastole before it causes reduplication.

2ndly. It falls at such a time that the auricle responds instantaneously.

3rdly. About or shortly after the period of auricular maximum stimulation may cause inhibition of the auricular and the ventricular sequential beat.

Stimulation at any period during the diastole of the auricle until the abscissa is reached, causes a reduplication. The latency of this reduplicated beat is shorter the further the diastole is advanced. It is followed by an induced ventricular beat in ordinary rhythm.

Stimulation during complete auricular diastole and before systole commences causes a contraction with very short latency, succeeded by an induced ventricular contraction. But it is to be noted that occasionally stimulation at this period causes a normal auricular contraction with an appreciable latency, and followed by a ventricular contraction.

Stimulation of the Auricle—Maximal.

Maximal stimulation of the auricle almost always produces some effect both on the ventricular and auricular beat: this effect is usually one of stimulation, but it may be of apparent inhibition.

Fig. 6.

a.

b.

Stimulation of Auricle (maximal).

Maximal stimulation usually induces a ventricular beat whenever it is applied (fig. 6, *a*), excepting when it falls just after the summit of the auricular contraction.

Stimulation at this point may cause no auricular contraction, but on the contrary may induce omission of the subsequent auricular and ventricular beat (fig. 6, *b* 2).

When an auricular beat has been induced by stimulation, it is followed in the ordinary way by a beat of the ventricle, excepting when the stimulus is applied to the auricle just at the commencement of the ventricular systole. In this case an auricular beat may be induced, which instead of being followed by a corresponding ventricular one, is followed, on the contrary, by an omission of the ventricular beat (fig. 6, *a* 1).

At this point the latent period may be looked upon as indefinitely long, as stimulation produces no contraction at all.

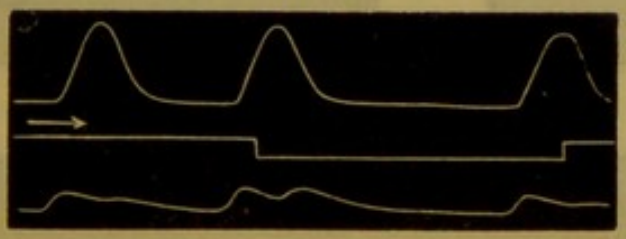
The more closely after this point stimulation is applied the longer is the ventricular latency.

Stimulation of Venous Sinus—Minimal.

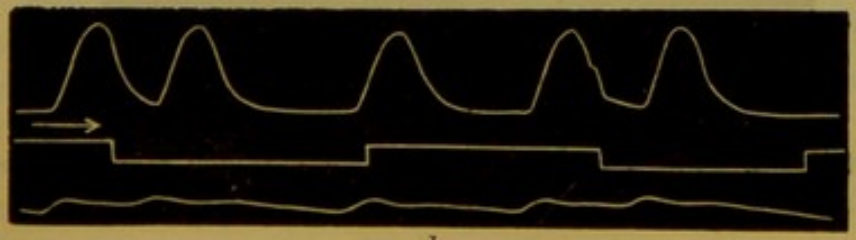
The venous sinus appears to be more sensitive to stimulation than either auricle or ventricle, so that stimuli applied to it produce an effect, although they are much slighter than the minimal stimuli of either auricle or ventricle.

Stimulation of the venous sinus by a minimal shock is usually potent to produce some effect or other at every stage of ventricular activity (fig. 7, *b*).

FIG. 7.



a.



b.

Stimulation of Venous Sinus (minimal). In neither *a* nor *b* is the closing shock effective.

Stimulation at the instant of commencement of ventricular systole

usually causes omission of the following sequential beat of both auricle and ventricle.

This period may occasionally be slightly prolonged into systole.

Stimulation of the sinus at all other periods of ventricular activity causes a reduplication of the systole. This induced ventricular systole is preceded by an induced auricular systole, and therefore has the prolonged latency before referred to.

Stimulation falling at the commencement of ventricular systole may cause auricular reduplication with ventricular omission (fig. 7, *a*).

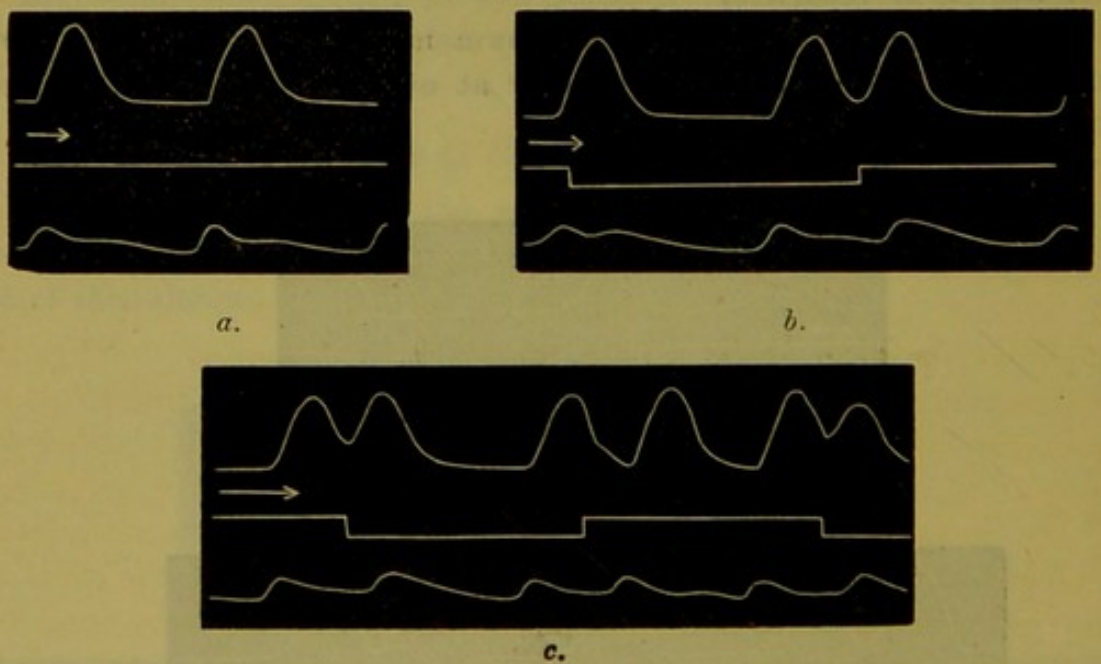
In consequence of the long latency, we find all ventricular curves separated by a distinct interval from (their) reduplications.

Stimulation of Venous Sinus—Maximal.

The period during which stimulation causes ventricular omission is well marked, and in some cases extends into the ventricular systole as it advances towards its maximum, though the effect is never produced at the maximum.

This omission of ventricular beat is most usually associated with a reduplication of the auricular beat, the second auricular contraction occurring within that ventricular systole at the commencement of which the shock was communicated (fig. 8, *b*).

FIG. 8.



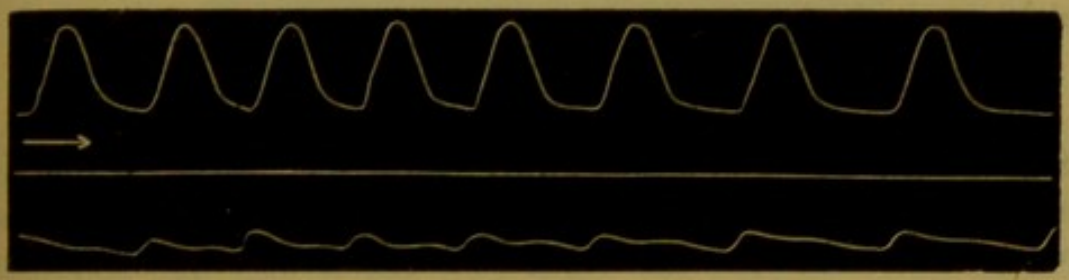
Stimulation of Venous Sinus (maximal). *a*, normal rhythm; *b* and *c*, stimulations all effective.

Reduplication occurs in all phases except at the period when stimulation causes omission. The latent period of this reduplication is usually short, as in the case of a ventricle stimulated directly, inasmuch as the induced auricular contraction does not precede the

induced ventricular, except when stimulation falls before the maximum of ventricular systole, in which case there is usually a regular sequence of auricular and ventricular contraction (fig. 8, *c*).

Usually after the maximum of ventricular systole stimulation causes a reduplicated beat with short latency, inside of which curve falls that of the induced auricular contraction; however, genuine sequential reduplication of auricle and ventricle with long latency is not uncommon. Not unfrequently, after repeated stimulation of the sinus, the heart assumes a new rhythm, which may be twice as rapid as it was originally, and though omission of the alternate beat may still be produced by stimulation at the time already indicated, the organ returns again to its accelerated pace. In time, if stimulation be withheld, the rhythm lapses again into the normal. The auricle shares in the ventricular excitement (fig. 9).

FIG. 9.



Rhythm which has been changed by repeated stimulation of Sinus returning to normal.

THE EFFECT OF COLD ON THE FROG'S HEART.

In these experiments the animal was placed upon a wire gauze grating, and covered with a small bell-jar. Underneath the grating and around the bell-jar was placed ice, so as to surround the frog, which was kept in this position for an hour or longer. When its movements had become slow and torpid it was killed, without loss of blood, and placed on the cardiograph, already described, the temperature in the vicinity being kept low by means of blocks of ice placed on the metal bars supporting the animal. The apparatus was employed in the same manner as in our observations on the effect of electrical stimuli on the normal heart, and the same order was observed in recording the results.

Effects of Electrical Stimulation of the Ventricle—Minimal Stimuli.

The contraction of the chilled frog's heart, as is well known, lasts for longer time than in the ordinary condition. When minimal stimuli are applied to the ventricle (fig. 10) it is found that there is a distinct refractory period, extending from the beginning of systole up

to the last third of the summit of the curve in the accompanying tracing, and persisting past the maximum of systole.

Fig. 10.

Stimulation of the Ventricle (minimal). Opening stimulation only effective.

It is, therefore, always longer than in the normal heart. After the refractory period has passed, stimulation causes reduplication of the ventricular beat. The later on in the diastole that the stimulus falls the shorter is the latency.

Ventricular Stimulation—Maximal.

Stimulation sometimes causes omission when applied at the very commencement of systole. All stimulation thereafter applied causes a reduplication of the ventricular systole, with a latency that becomes shorter the later the stimulation is applied. If auricular reduplication occurs it is always sequential to ventricular (fig. 11, *a*). Stimulation

Fig. 11.

a.

b.

Stimulation of the Ventricle (maximal).

at the maximum of systole may cause a blending with the reduplicated beat closely resembling one prolonged systole (fig. 11, *b*). The induced beat is most perfect when stimulation falls, just as the abscissa is

reached. Stimulation before the maximum of systole has longer latency than stimulation at the maximum.

Auricular Stimulation—Minimal.

A refractory period is obviously present, but it is not of so great length as in the case of ventricular stimulation. It may be said to extend usually through the maximum of auricular systole (fig. 12), and even up to near the maximum of ventricular systole; occasionally it exists only just at its commencement.

Fig. 12.

Stimulation of Auricle (minimal).

As regards the reduplication, we find that as in the case of the normal heart, a long latency prevails, because an induced auricular systole must occur before the ventricle contracts again. But if the stimulation fall just at the time when the abscissa is reached, or rather before this point, a ventricular contraction may exceptionally be produced with a short latency, and the auricular induced contraction succeeds it.

Auricular Stimulation—Maximal.

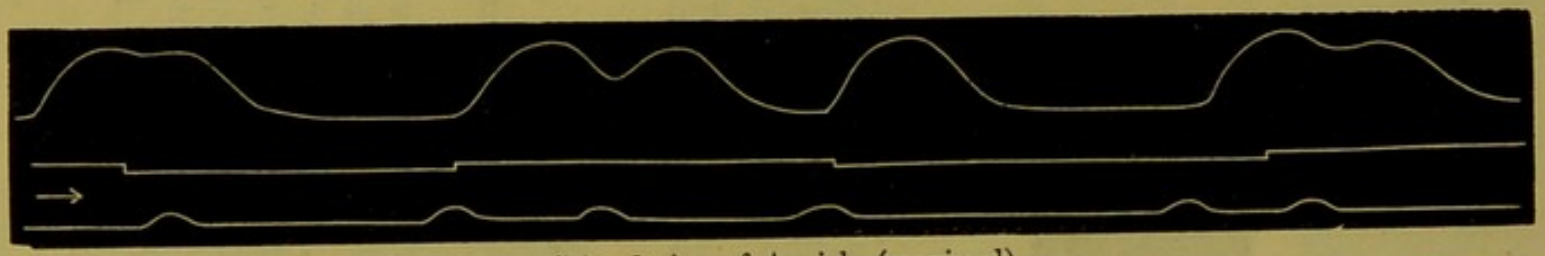
The same features are to be observed as in the last section, except that there is no refractory period (fig. 13).

Stimulation in all phases of the ventricular cycle usually causes a reduplicated auricular and ventricular beat. Should the stimulation fall before the ventricular maximum is attained, the auricular reduplication precedes the ventricular in the ordinary way, but should the stimulation fall, after the ventricular maximum, the auricular reduplication is exceptionally synchronous with, or subsequent to, the ventricular: usually, however, the induced ventricular beat precedes in ordinary rhythm the induced ventricular.

Stimulation of the Venous Sinus—Minimal.

A refractory period may be present on minimal stimulation, nearly up to the maximum of ventricular systole. Thereafter reduplication results. A strictly minimal stimulation may originate a reduplication at any period of the beat having a long latency, that is to say,

Fig. 13.

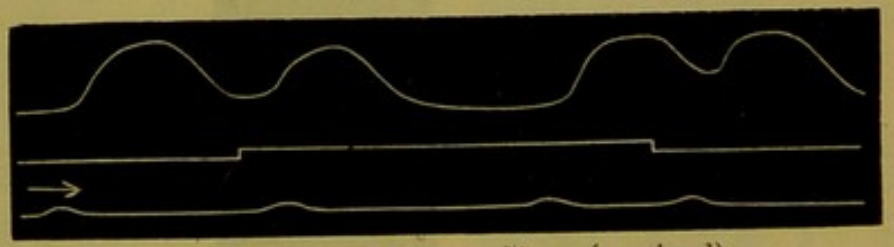


Stimulation of Auricle (maximal).

Fig. 14.

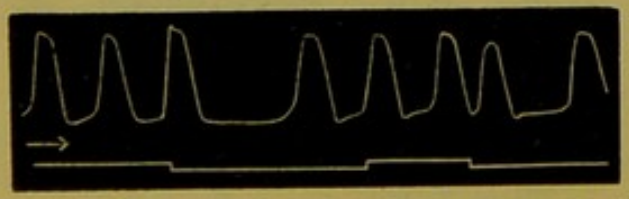
Stimulation of Venous Sinus (minimal).

Fig. 15.



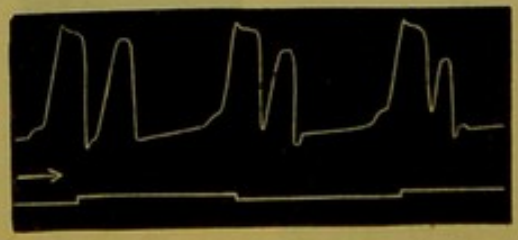
Stimulation of Venous Sinus (maximal).

Fig. 16.



Stimulation of Ventricle (minimal). Auricular tracing omitted.

Fig. 17.



Stimulation of Ventricle (maximal).

the ventricular reduplication is preceded by the auricular induced contraction (fig. 14). Thus stimulation applied just before the ventricular relaxation is completed, instead of having an instantaneous ventricular and auricular response resulting from stimulation of auricle or ventricle, has a long latency, wherein the auricle reduplicates. The further on in the systole the stimulation is applied, the shorter is the latent period, and the more perfect the reduplicated contraction.

Stimulation of the Venous Sinus—Maximal.

Omission may be caused by stimulation applied at the commencement of systole, or reduplication may occur in all phases (fig. 15).

Reduplication has the longest latency at the commencement of systole, and there is true auricular precedence up to or beyond the maximum in this phase. In the decline of systole, after the maximum is passed, and the abscissa has been nearly reached, there is occasionally reduplication with short latency, the auricular and ventricular contractions being synchronous.

Action of Heat on the Heart.

In this series of experiments the pithed frog in which the brain and spinal cord had been destroyed, was laid upon a metal plate, the temperature of which was gradually raised by means of a flame beneath it.

Ventricular Stimulation—Minimal.

The refractory phase is generally wanting in the ventricular systole, but it may be present in exceptional cases, not unfrequently in the same tracing in which stimulation most generally produces reduplication (fig. 16).

It may be noted that irregularity of response to stimulation is one of the characteristics of the heated condition. Stimulation usually causes reduplication. Should stimulation fall at the commencement of ventricular systole, no effect is produced till the whole cycle of the systole has been passed through, when reduplication by a very perfect systole occurs. Latencies diminish in proportion as the stimulation occurs later in the systole of the heart. Reduplication occurring in response to stimulation falling at the maximum is often demonstrated by a beat originating when the relaxation after systole is completed, and therefore distinct from the original beat: this is due to the fact that the curve of the heated heart is much shorter in duration, and therefore the reduplication falls outside the systole during which stimulation occurs, the latency being actually shorter, however, than in the unheated heart.

Ventricular Stimulation—Maximal stimuli.

When stimuli of maximal intensity are applied to the ventricle of the heated heart, we notice (fig. 17) :—

(1) That there is no refractory period; (2) Stimuli at the commencement of the ventricular systole may cause omission of the succeeding beat; (3) Reduplication occurs at all phases, and has the same characteristics as in minimal stimulation; (4) Latencies follow the same rule as in minimal stimulation; (5) The reduplicated beat is most perfect when stimulation falls—

I. At the very commencement of systole.
II. At its termination.

The value of any beat and its reduplication, with the time intervening and of the succeeding pause, was about equal to two normal cardiac cycles. Occasionally a double reduplication, or a series of contractions, resulted from a single stimulation.

Auricular Stimulation—Minimal Stimuli.

There is apparently no refractory period. All stimuli cause reduplication, and in all cases induced auricular systole precedes an induced ventricular systole. This occurs even in advanced auricular diastole, when occasionally in the normal heart a simultaneous auricular and ventricular systole results.

Auricular Stimulation—Maximal Stimuli.

There is no refractory period. Stimulation just after the auricular maximum has been passed frequently causes an apparent omission of the following beat.

Stimulation before the maximum of the ventricular systole causes an induced ventricular beat preceded by an auricular contraction.

After the maximum, stimulation usually has the same effect, but occasionally causes an instantaneous reduplication of both auricular and ventricular beats.

A reduplicated ventricular beat is of the character already described.

Stimulation of the Venous Sinus—Minimal Stimuli.

The venous sinus in its general absence of a refractory phase shows a resemblance to the ventricle, but it may manifest the same exception in exhibiting it.

When this occasional refractory period is present it may exist during active systole, and up to its maximum. It is exceptionally present in cases which as a rule show no refractory period.

Stimulation falling before the maximum of systole (fig. 18, a ventricular tracing alone given) causes a reduplication which is preceded by

Fig. 18.

Stimulation of Venous Sinus (minimal).

an auricular contraction, whilst stimulation falling immediately after maximum of systole causes reduplication, which may be preceded by an auricular pulsation, or may occasion an induced systole, auricle and ventricle contracting at the same time.

The most perfect reduplicated beat occurs when stimulation falls at the end of systole.

Venous Sinus—Maximal Stimulation.

Occasionally a stimulation of maximum strength falling at the commencement of the ventricular systole causes an apparent omission of the following pulsation; but this result is not so frequent as in the case of the normal heart. Usually a distinct reduplication occurs at whatever time in the cycle stimulation falls (fig. 19).

Fig. 19.

Stimulation of Venous Sinus (maximal).

The reduplication is at all times, except in the last stage of systole, preceded by an auricular contraction.

The auricular induced contraction appears to follow stimulation more rapidly than in the case of the normal heart. Therefore the induced ventricular contraction (fig. 19, ventricular tracing alone given) which follows the auricular has a shorter latency than is normally the case. The heating process having been carried so far that a rapid cardiac rhythm with imperfect systole has resulted, it is often found that there is an indifference to stimulation in the so-called refractory period, or even in all phases of the cardiac cycle alternating with the usual sensibility.

On the Effect of Strychnia upon the Frog's Heart.

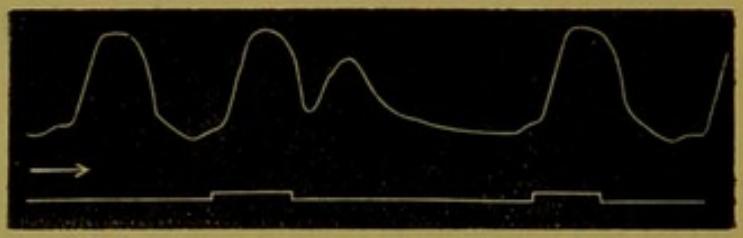
The apparatus used in this series of experiments was identical with that employed in the investigation of stimuli applied to the frog's heart. The frog was killed by the brain being destroyed, and a small

dose of strychnia was then introduced into the dorsal lymph sac. As soon as the effect of the drug upon the spinal cord was evidenced by distinct spasm, the heart was rapidly exposed, placed on the cardiograph, and stimulation applied. The same order will be observed as in the description of the experiments on the normal heart.

Stimulation of the Ventricle—Minimal.

On applying a minimal stimulus to the strychnia heart (fig. 20) we were struck, in the first instance, by the extreme length of the

Fig. 20.



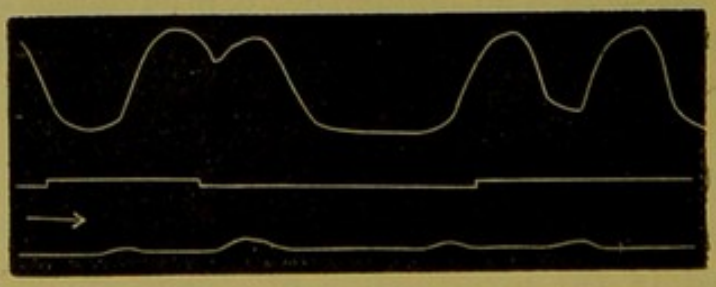
Stimulation of Ventricle (submaximal).

refractory period. Stimulation has usually no effect, not only when applied before the maximum of the systole as in the normal heart, but also in the maximum, and often far into relaxation. After the phase has passed the stage of reduplication ensues. Reduplication is very complete; its latency becomes diminished as diastole advances. The reduplicated ventricular beat is succeeded by an auricular pulsation. After the customary pause, the heart resumes its wonted rhythm. It is rarely that stimulation falling at the commencement of ventricular systole causes inhibition. If the auricle is unstimulated and its rhythm is unaltered, there is short latency for the ventricular reduplication. If the auricle is stimulated and contracts before the ventricle, there is long latency, but the latter is rarely seen when a refractory phase is present.

Ventricular Stimulation—Maximal Stimuli.

In this case no refractory period exists. An inhibitory period exists occasionally but with this exception, all stimulation produces redupli-

Fig. 21.



Stimulation of Ventricle (maximal).

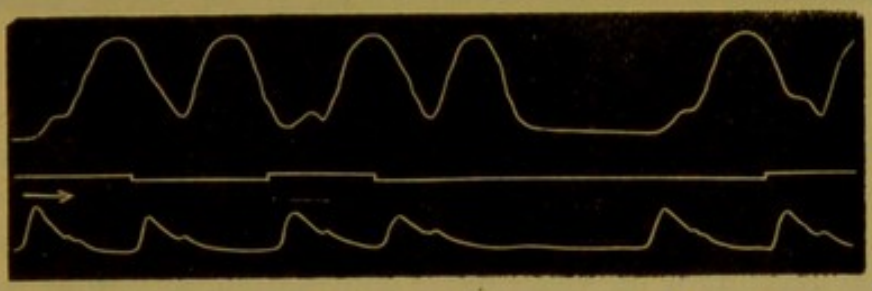
cation (fig. 21). Should stimulation fall at the commencement of systole, the latency is long, nearly equal to the length of the beat; and the reduplication is very complete.

Stimulation at the maximum of systole has a latency of about two-fifths of a second, and thereafter during the subsidence of the ventricle, the period of latency rapidly diminishes. The most perfect beat of reduplication is produced by stimulation at the commencement of systole, or after relaxation of the ventricle.

Stimulation of the Auricle—Minimal.

It is but rarely that we see a refractory period whilst applying mi nimal stimuli to the auricle. Usually, stimulation at all times causes a reduplicated beat, the auricular reduplication preceding that

Fig. 22.



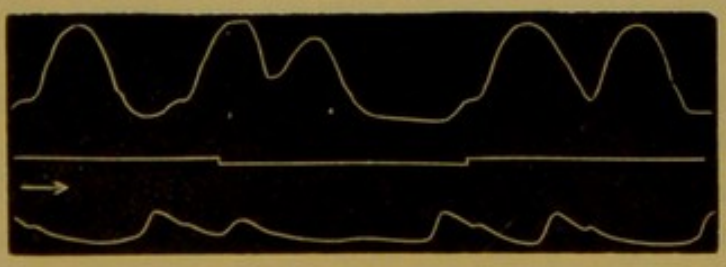
Stimulation of Auricle (minimal).

of the ventricle in the usual rhythm. On stimulation, an auricular systole is produced, and not until this movement has reached the usual point does the ventricle commence its systole (fig. 22).

Stimulation of the Auricle—Maximal.

There is no refractory period. Occasionally the stimulus falling at the very commencement of the ventricular systole will cause inhibition or coincidence of the following beat, or it may cause a reduplication with a latency of about one second (fig. 23).

Fig. 23.



Stimulation of Auricle (maximal).

The latencies are invariably long when the auricle is so stimulated that its induced beat is a normal one and precedes the induced ventricular systole in its normal rhythm.

Stimulation of the Venous Sinus—Minimal Stimuli.

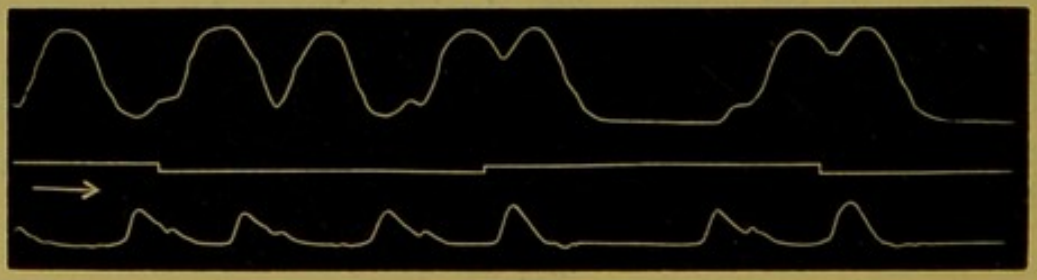
With minimal stimulation of the venous sinus there is no refractory period except occasionally for an instant at the maximum of auricular systole. Reduplication occurs at all phases of the ventricular systole. Length of latency depends upon whether the stimulation induces an auricular contraction or not. If the auricular systole follows the stimulus, then the ventricular latency must be long (fig. 24).

Fig. 24.

Stimulation of Venous Sinus (minimal).

It is longer if stimulation falls at the commencement of ventricular systole, because at that phase, until the auricle has contracted, no ventricular reduplication occurs. Occasionally, though rarely, and that after the maximum of ventricular contraction, auricular reduplication follows, or is synchronous with the ventricular systole, and then latency is invariably short. Reduplication with prolonged latency, probably from auricular reduplication, is well seen in the appended tracing (fig. 25).

Fig. 25.



Stimulation of Venous Sinus (minimal).

The stimulation at the end of relaxation in one case causes reduplication of auricle, coinciding with that of the ventricle.

The tracing illustrates the rule that when the sinus is stimulated no refractory period is observed as regards the ventricular reduplication.

Venous Sinus—Maximal Stimulation.

There is no insensitive period as far as regards the ventricle. During all phases of the systole stimulation causes a reduplication of the

ventricular beat (fig. 26). Inhibition of the ventricular systole has not been found in many of the hearts examined, though it occasionally occurs.

Fig. 26.

Stimulation of Venous Sinus (maximal).

Should the exciting shock fall at such a time as to cause an instantaneous auricular systole, we find this systole is nearly synchronous with that of the ventricle, and that the latter has a short latency, but should the shock fall so that the auricle responds by a genuine contraction, the ventricular reduplication follows with a long latency.

Inhibition of the ventricular with reduplication of the auricular beat may result occasionally from stimulation of the venous sinus.

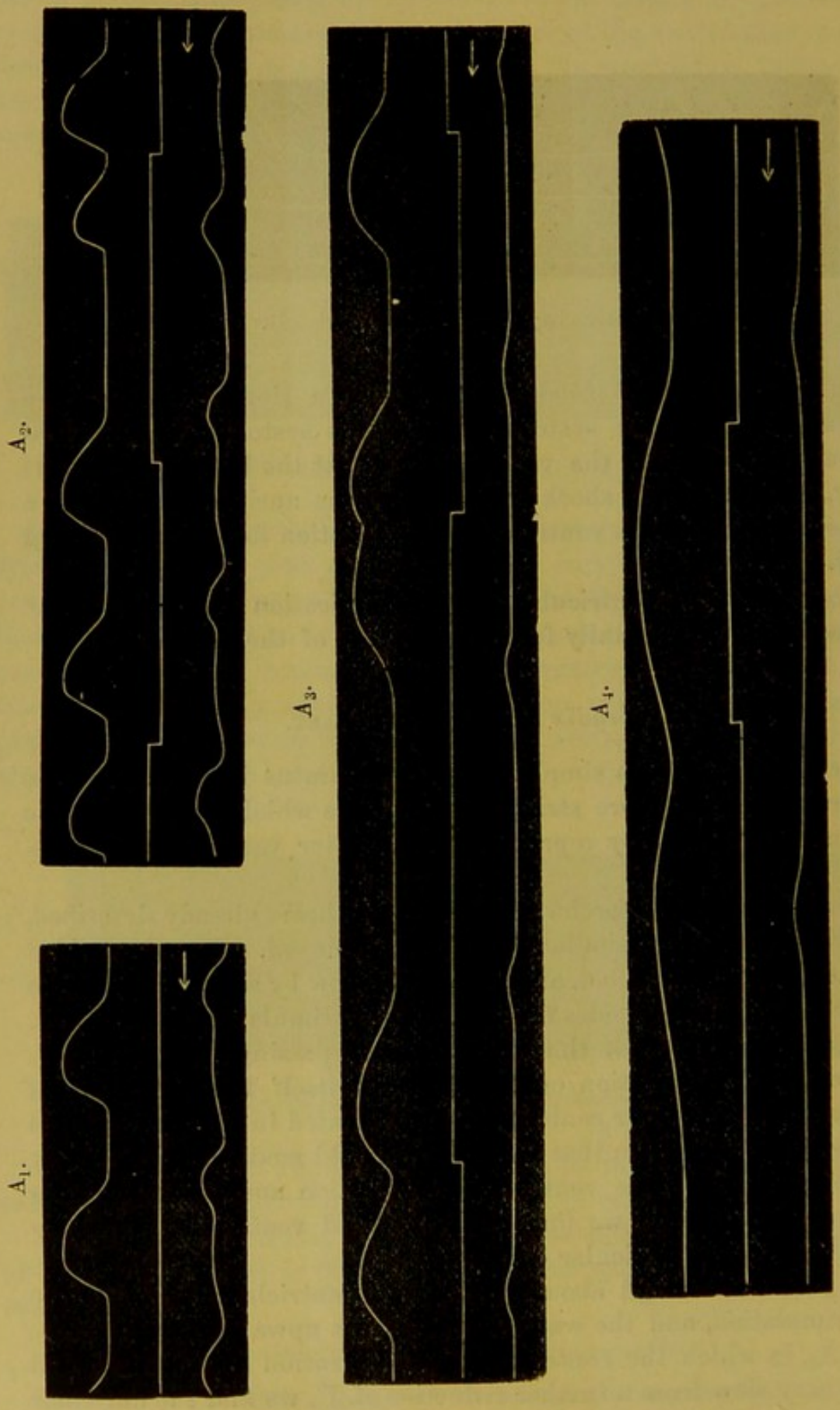
Appendix A. Cooled Heart.

The construction of a simple piece of apparatus has enabled us to obtain curves much more striking than those which appeared in the foregoing paper, as they represent a far greater variation of temperature.

Instead of the gutta-percha support for the heart already described, a hollow copper pan of similar shape was employed. It was provided with influx and efflux tubes, and insulated below by a plate of ivory in which ran also the electrodes destined for the stimulation of the sinus. This was connected with the usual support passing over the body. Upon minimal stimulation of the ventricle itself the succession of auricular and ventricular contraction is illustrated in the charts A 1–4 here inserted. It is seen that the action of cold modifies considerably the relation between the ventricular contraction and the succeeding auricular beat. In A_2 we find a reduplicated ventricular beat succeeded by a normal auricular contraction.

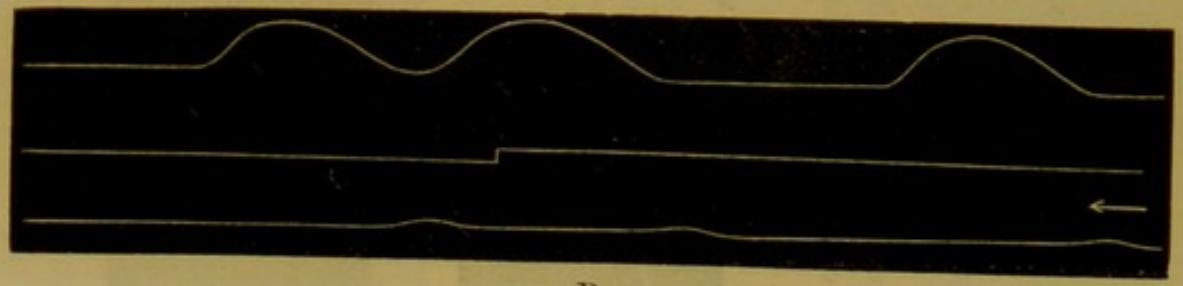
In A_3 cooled through about 2·5° C., the ventricle responds to the same stimulation, and the wave does not pass upward to the auricle; and in A_4, in which the contraction and relaxation of the heart had become very slow from a further reduction of 2°, we find the auricular rhythm is regular in spite of ventricular reduplication. There is in

A_1 and A_2 an indication of aortic expansion; it is to be noticed that after the reduplication in A_2 this is omitted.



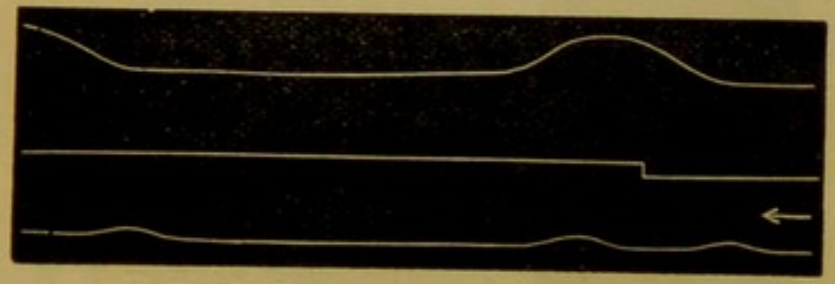
A_1. Normal Heart tracing.
A_2. Stimulation of Ventricle of the normal Heart.
A_3. Stimulation of Ventricle of Heart cooled through 2°·5 C.
A_4. Stimulation of Ventricle of Heart cooled through 4° C.

B_1.

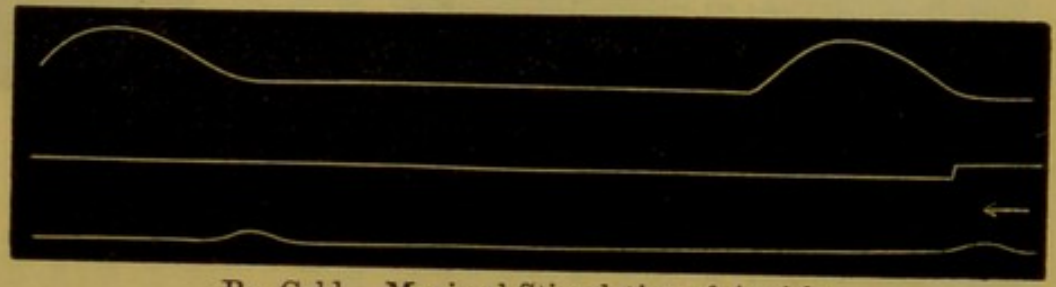


B_2.

B_3.



B_4.



B_1. Cold. Maximal Simulation of Auricle.

B_2. Considerable cold. Maximal Stimulation of Auricle.

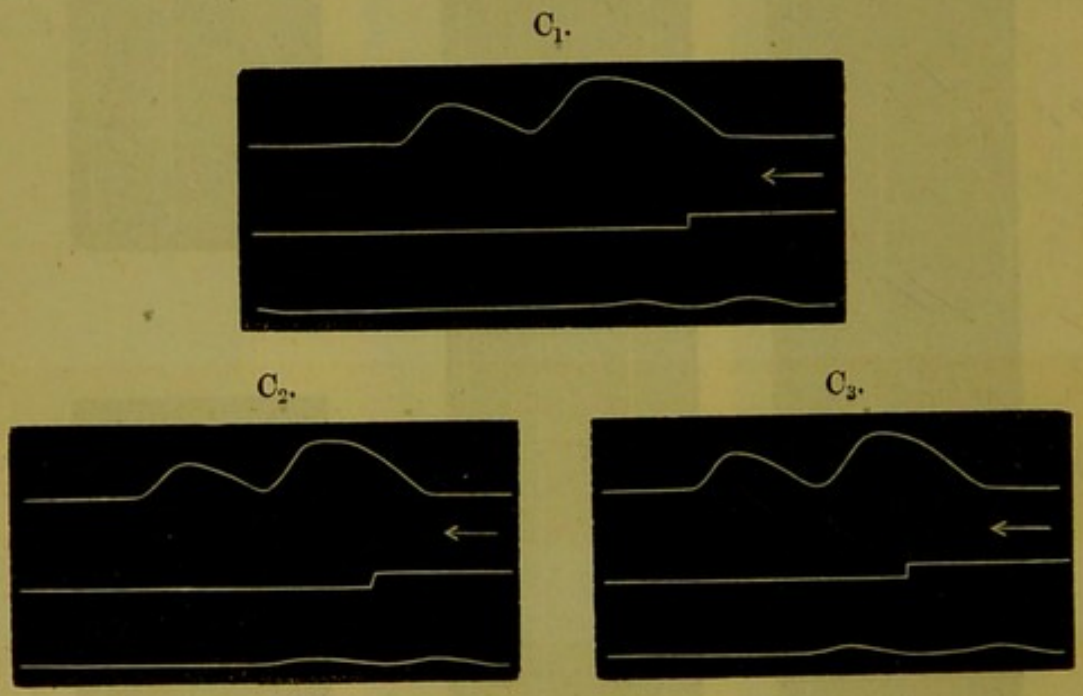
B_3. Cold. Maximal Stimulation of Auricle.

B_4. Cold. Maximal Stimulation of Auricle.

Auricular Stimulation.

Many additional experiments upon cooled hearts have tended to show that it is very rarely that stimulation of considerable strength calls forth a ventricular beat, preceding or coexistent with the auricular. Usually at all phases of stimulation which cause a reduplication of the auricular beat, the ventricular succeeds in normal relationship (B 1 and 2). There is an exception to this, however, which is frequently demonstrated; this is, that whilst the auricular beat is reduplicated the ventricular is not, but is succeeded by a long diastolic pause (B_3), after which the auricle takes up its old rhythm. Still more rarely stimulation just before commencement of ventricular systole causes omission of both succeeding auricular and ventricular beats (B_4).

The latency of reduplication varies considerably in minimal stimulation of the auricle, but this variation is not so much owing to loss of time in the auricular as in the ventricular reduplication. Thus in C_1 stimulation at the end of auricular relaxation, ventricular latency



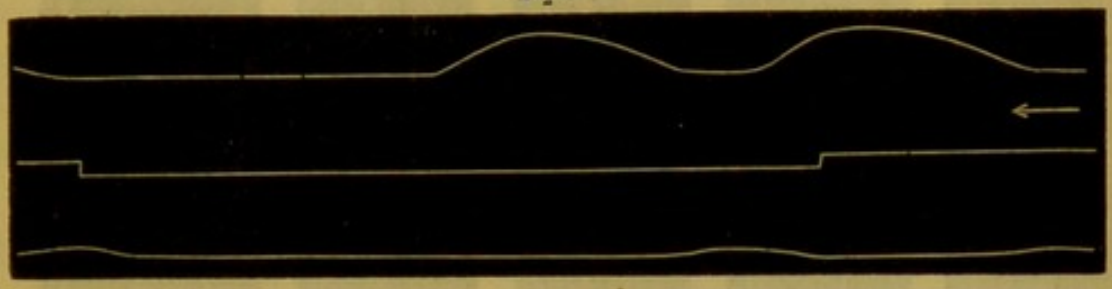
C_1 to C_3. Levers as in A. Auricular Stimulation (minimal) of Cooled Heart.

is 1″·2, in C_2 stimulation halfway to ventricular maximum latency is 1″, and in C_3, when stimulation is at ventricular maximum, the latency is for the ventricle only 6″.

On the other hand, more powerful stimulation of the auricle causes reduplications of the ventricle, which are at all times of equal or of very slightly differing values. Thus in a heart much cooled (D 1 and 2) we have towards the commencement of ventricular systole and towards the end of relaxation a latency for the induced ventricular beat of 1″·2.

D_1.

D_2.

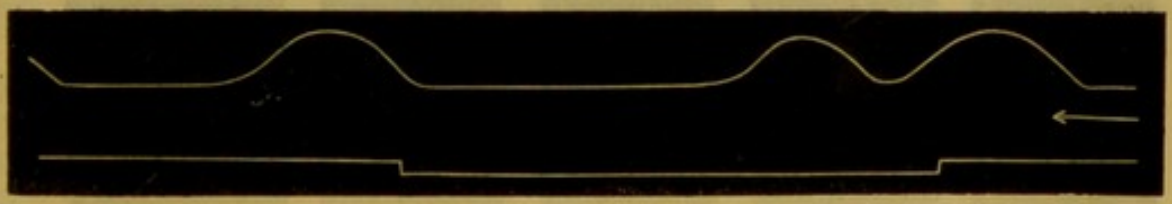


D_1 to D_2. Levers as in A. Auricular Stimulation (maximal) of Cooled Heart.

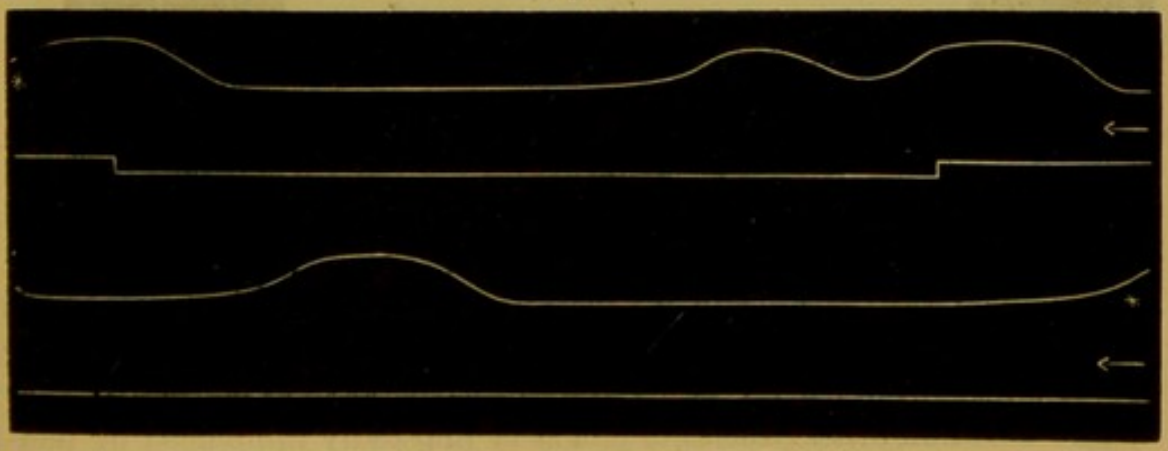
Venous Sinus.

In the heart which has been moderately or slightly cooled, 4—6° C., the occurrence of ventricular reduplication without a precedent auricular reduplication is very rare, even when strong stimulation is employed. The refractory period occasionally observed may disappear after a few stimulations have been given, or it may persist. Further-

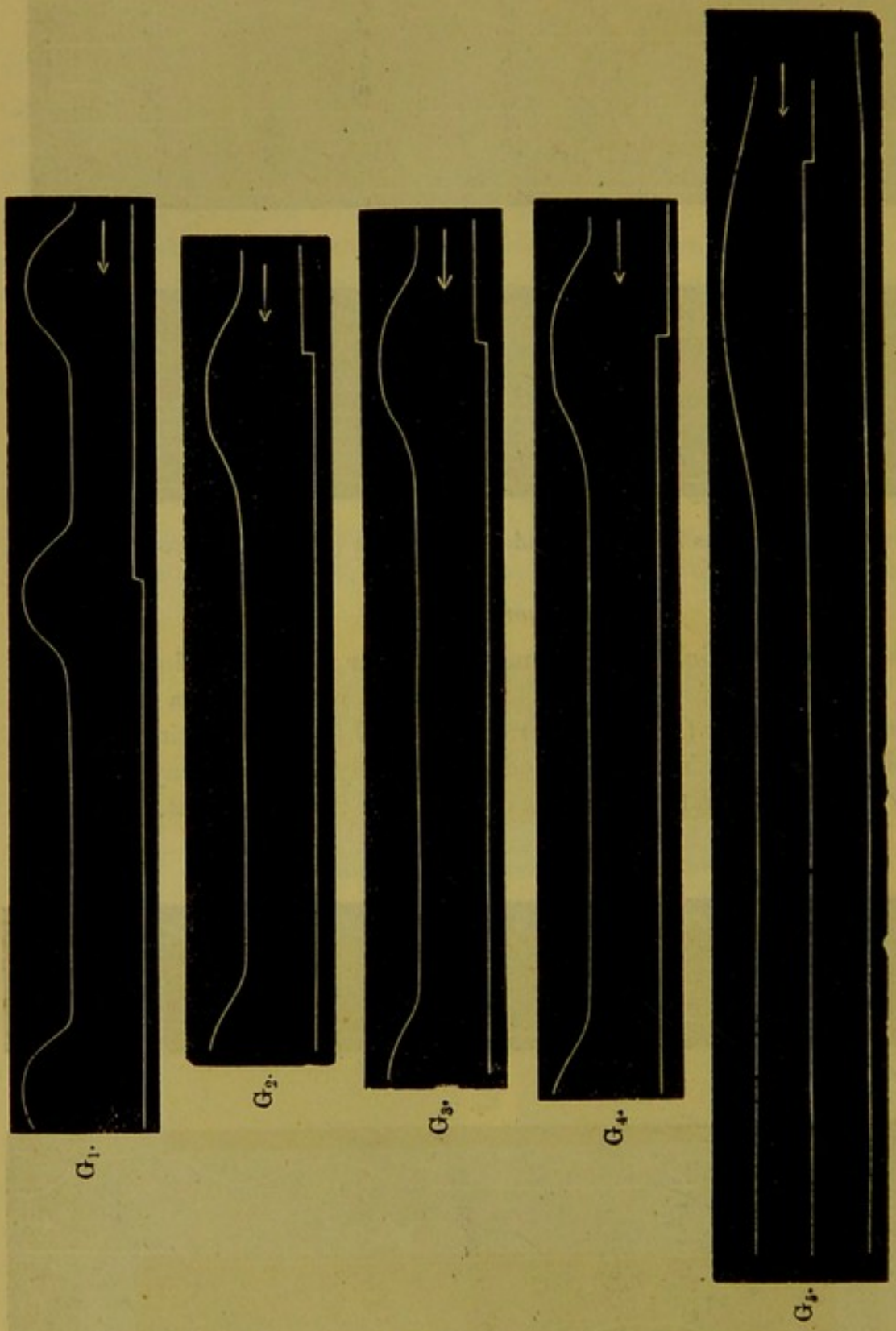
E_1.



E_2.



E_1 to E_2. Levers as in A, but no auricular tracing given. Stimulation of Venous Sinus. E_1, before cooling; E_2, after cooling.



Levers as in E. Stimulation of Venous Sinus. G_1 to G_5, gradual cooling of Heart.

more on cooling a heart which has at a certain temperature, E_1, shown a refractory period, we may find this converted into a period during which stimulation causes an omission of the following beat, E_2.

The duration of the diastolic pause is markedly influenced by temperature, whereas it appears to be but slightly affected by variation in the instant of stimulation by which it is produced.

In G_1 water of melted ice had passed through the support for two minutes.

G_2 water had passed 5′.
G_3 ,, ,, 10′.
G_4 ,, ,, 20′.

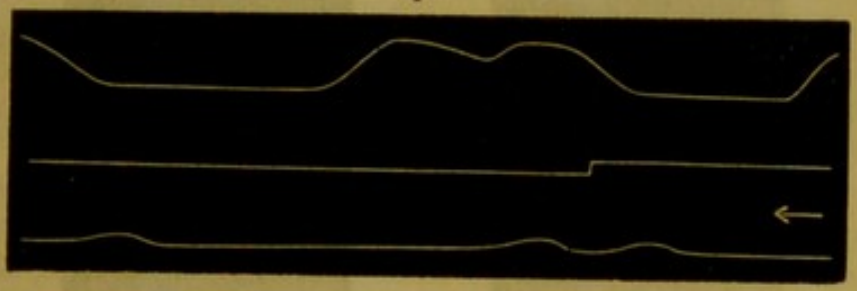
G_1	Duration of contraction		1″·4	..	Length of pause from stimulation	..	4″·2
G_2	,,	,,	1″·9	..	,,	,,	5″·6
G_3	,,	,,	2″·2	..	,,	,,	6″·0
G_4	,,	,,	2″·4	..	,,	,,	6″·2

G_5 was obtained from a heart cooled for a considerable time, and shows a remarkable prolongation of the systole and diastolic pause.

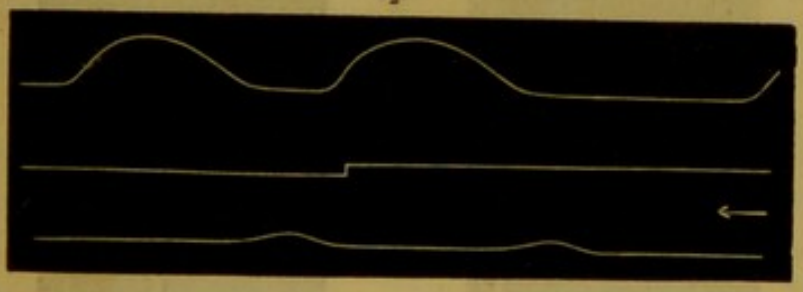
G_5	Duration of current	4″·4	..	Length of pause from stimulation. .	10″

It will be seen in all these cases that there is a certain relationship between the length of the contraction and of the pause.

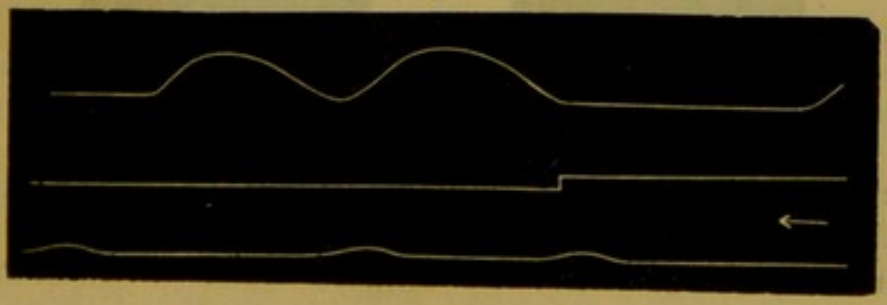
I_1.



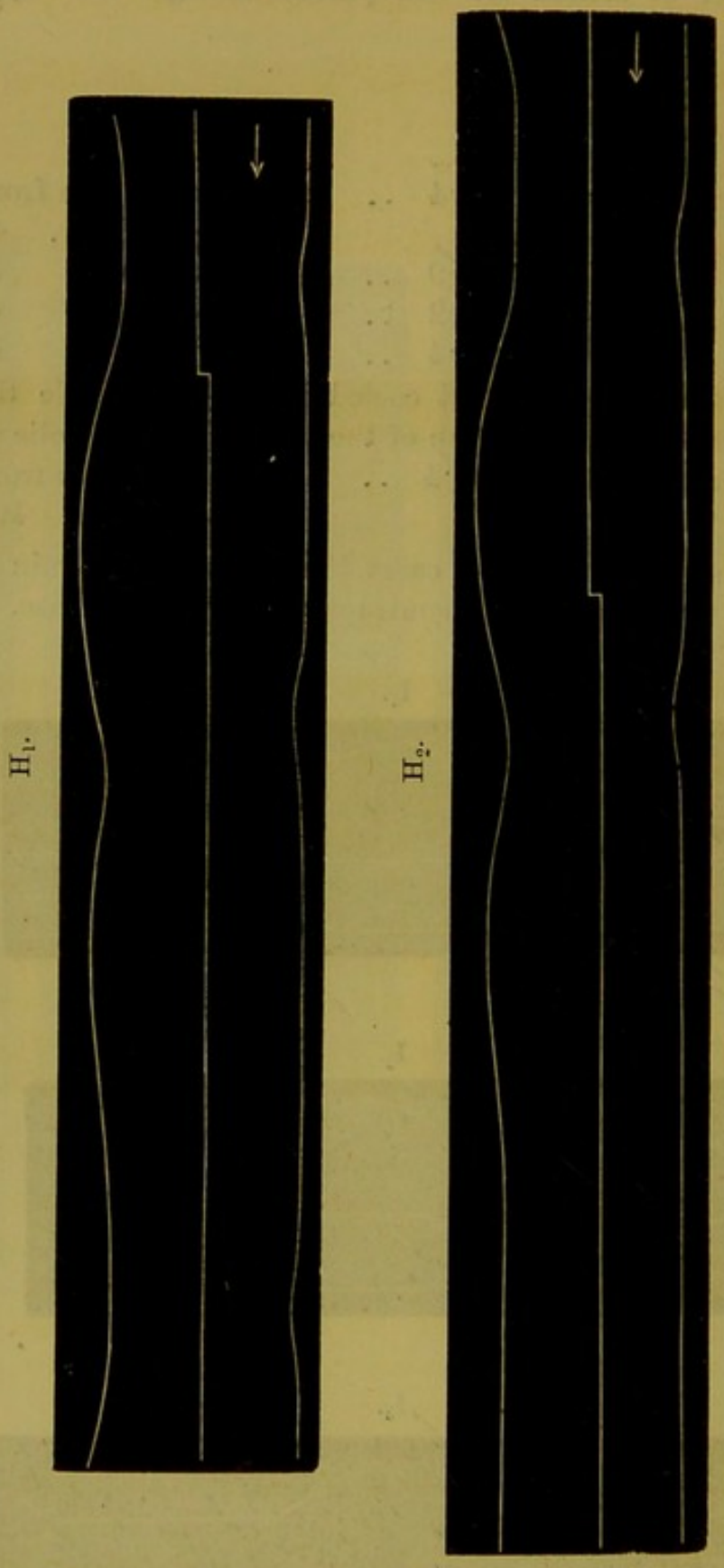
I_2.



I_3.



I_1 to I_3. Levers as in A. Stimulation of Venous Sinus (maximal).



H_1 to H_2. Levers as in A. Stimulation of Venous Sinus (minimal).

The reduplication of the ventricular beat varies in regard to the time of stimulation under minimal stimulation. Thus in H when stimulation falls near the commencement of systole, auricular reduplication occurs in 1″·8 and ventricular reduplication in 3″·2. But in the same heart a stimulation during a period of relaxation yielded an

instantaneous auricular response, the ventricular reduplication occurring 1″·3 after stimulation.

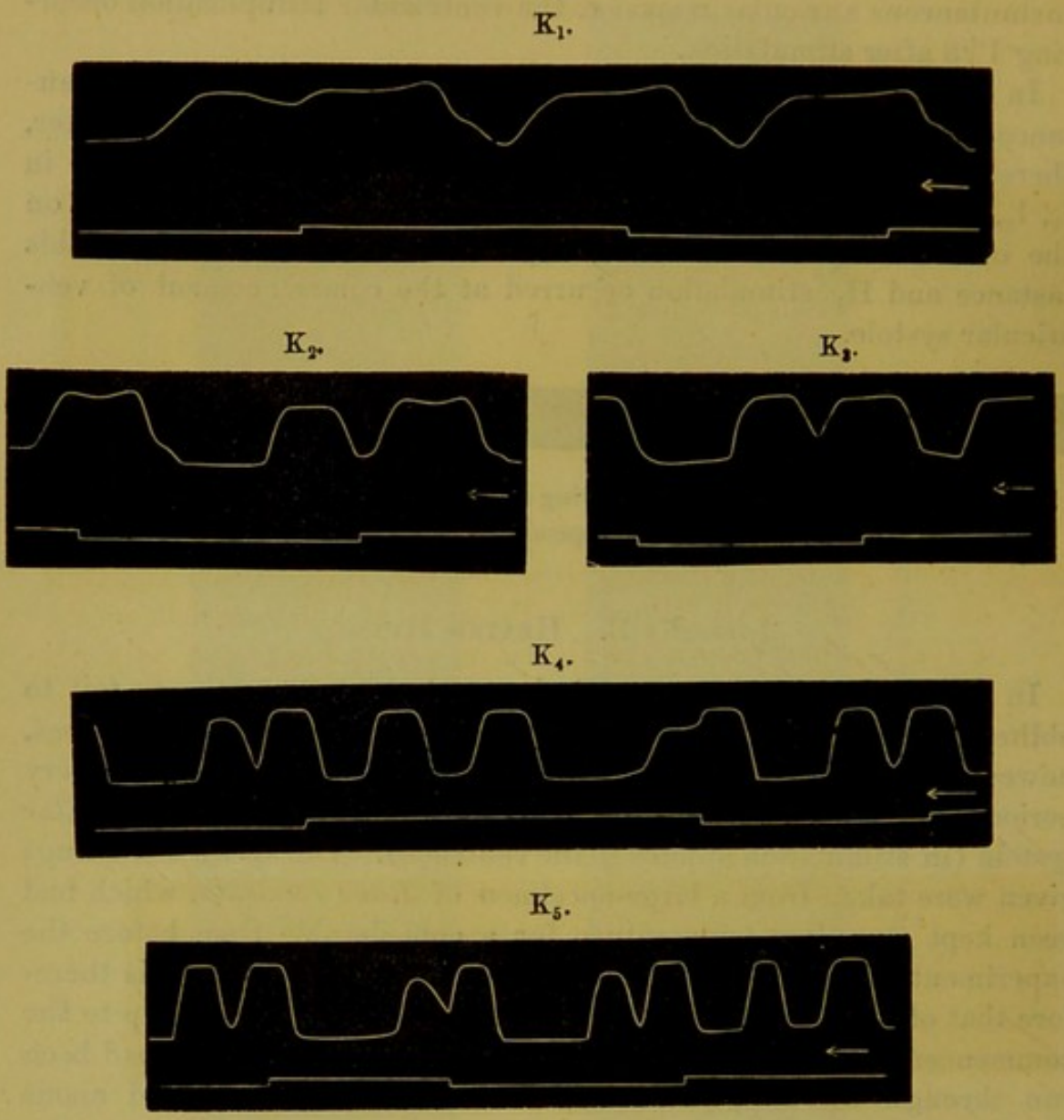
In the case of maximal stimulation, the usual result is an instantaneous auricular systole succeeded by a ventricular. The latter, therefore, has a latency equal to the auricular beat: this is seen in I_1, I_2, in both of which the latency is about ·7″; but in I_3 we have, on the other hand, no auricular reduplication for 1″·1. In both this instance and H_1 stimulation occurred at the commencement of ventricular systole.

Time tracing. Electro-magnet recording seconds. Applicable to all tracings in Appendix A.

Appendix B. Heated Heart.

In some cases, heating a frog's heart through 4°·5 C. may fail to obliterate entirely the period of resistance to stimulation. Heat, however, in the same experiment may be shown to shorten the refractory period much, and to limit it to the very commencement of ventricular systole (in stimulation applied to the ventricle). The series of tracings given were taken from a large specimen of *Rana esculenta*, which had been kept at a low temperature for a considerable time before the experiment. The tracing obtained at room temperature (K) is therefore that of a cold heart, and the refractory period extends up to the commencement of relaxation after systole. After hot water had been run through the support for 5′, and the temperature raised about 2° C., we find diastole increased and systole much shortened; at the same time there is a refractory period as extensive as in the cold heart, that is to say, extending to the commencement of relaxation K_2.

In K_3 after heat had been applied 10′, and the temperature raised another degree, stimulation at an earlier phase produces reduplication. Heated still further, K_4, there is reduplication at systolic maximum, and at K_5 everywhere except at the very commencement of systole. After heating through about 5° we still have a refractory period, whilst the curve has been reduced from 1″·4 to ·4″. In many cases, however, the same extent of heat may obliterate the refractory period completely. The heart which yielded these curves passed into rigor without showing the abolition. In the heated heart, of which the ventricle is stimulated, we may find that the auricle does not in any way participate in the ventricular excitement, but continues to beat in its usual rhythm. Thus, when the heated heart yields a series of contractions in answer to a single stimulation—a result not unfrequently obtained—the auricle does not reduplicate, but may



Stimulation of Ventricle (maximal stimulation).

K_1. Heart at room temperature, frog long kept in cold room.
K_2. Temperature raised 2° C.
K_3. Taken 10′ later than K_2, during which time temperature was raised 1° C.
K_4. Temperature raised again 1° C.
K_5. Temperature raised 1° C., making about 5° C. altogether above K_1.

Drum of more rapid rotation used in tracings given in Appendix B. The electromagnet marks seconds.

give its systole in due place, whilst the ventricular contractions are still occurring. Not only is this indifference to ventricular action observed on the part of the auricle, but the counterpart may be occasionally seen in the ventricle, failing to follow the normal systole of

the auricle L. This is in part due to the fact that the auricle has only shared imperfectly in the heating.

L.

Stimulation of Ventricle (maximal). Heart heated about 7° C. Time as in K.

There is thus a disturbance of both muscle-wave and nervous impulse produced by the heating to which the auricles and ventricle have been exposed. This failure on the part of the ventricle occurs only after there has been a reduplication of its beat, and does not often occur, so far as we have seen, when stimulation, applied to the auricle itself (M), originates a systole there, for then the

M.

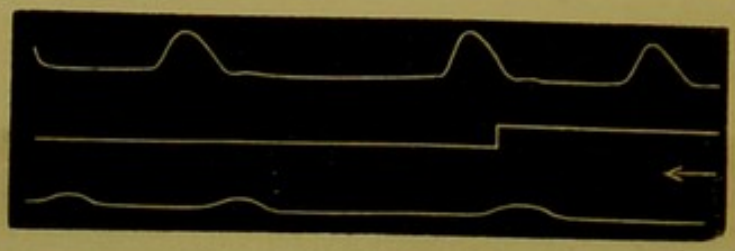
Stimulation of Auricle (maximal). Heart heated about 6° C.

ventricle follows in due course; we should therefore regard the exhaustion of the ventricle after its unusual activity as the cause of its quiescence after the normal auricular beat. Should stimulation be applied to the auricle during ventricular diastole, a reduplicated auricular beat succeeded by a ventricular at once occurs. In all phases this natural sequence is maintained, though sometimes at the end of its systole the auricular reduplication may be ·5". Whilst a long pause follows this reduplication, it is very rarely that a stimulation of the auricle produces omission of the succeeding auricular and ventricular reduplication.

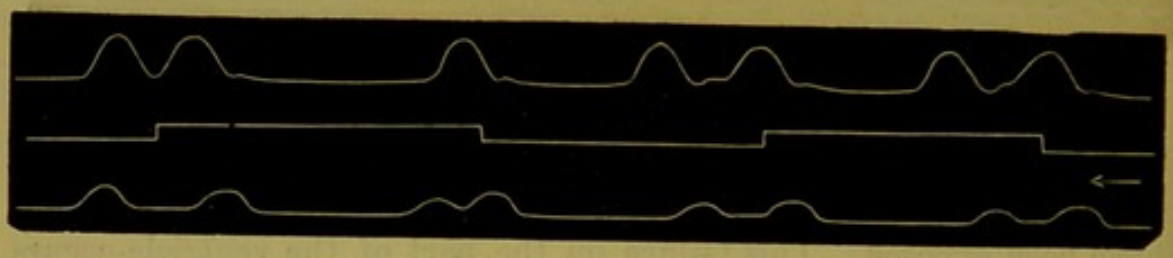
In stimulating the venous sinus, however, omission of the following ventricular beat is frequently produced when the shock falls at the commencement of ventricular systole (N_1), but we may find that there is an impulse propagated to the auricle, for this may reduplicate whilst the ventricle remains quiescent (N_2).

A little later, and up to the maximum of systole, the auricular

N_1.



N_2.



N_3.

Stimulation of Venous Sinus (maximal).

reduplication is succeeded by a ventricular (N_2), and after the maximum, and during the diastole of the ventricle, the induced auricular beat may occur synchronously with the ventricular, or it may precede it in regular course.

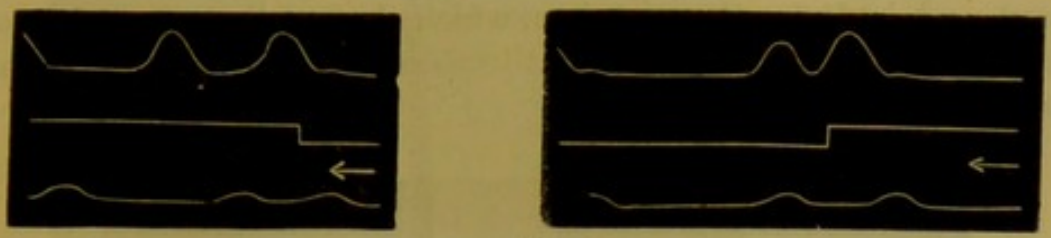
Both of the charts N_1 and N_2 are taken from a heart warmed through about 5° C., and N_3 gives a tracing of the same, in which stimulation does not occur.

In the stronger tendency to cause omission of a ventricular beat, as well as in the frequent occurrence of an auricular contraction coincident with or succeeding the ventricular, when stimulation fails after ventricular maximum or in diastole, we see a marked contrast in the reaction of the venous sinus and the auricle to stimulation.

From the charts O_1, O_2, O_3 we see that the latency of the auricular beat varies. Thus stimulation occurring just at the end of auricular relaxation (O_1) causes an instantaneous reduplication, whilst during diastole proper it has a reduplication with a latency of ·2″. In the former case auricular induced systole precedes the ventricular, in the latter they occur at the same moment (O_2, O_3).

Contrast this result with the stimulation of the auricle itself in which reduplication occurs at once on stimulation, and ventricular

O_1. O_2.



O_3.

Stimulation of Venous Sinus (maximal).

reduplication succeeds or occurs occasionally (stimulation at the end of auricular relaxation) in ·5″, followed by ventricle.

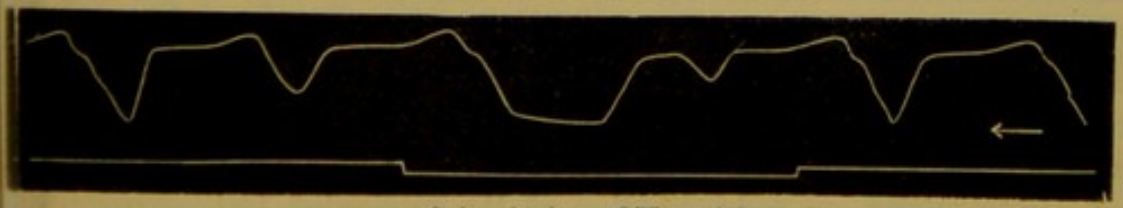
Appendix C. Strychnia on Frog's Heart.

In order to test the correctness of the conclusion that strychnia lengthens the refractory period, we placed frogs in which the medulla and cord only existed on the cardiograph. The effects of stimulation were then observed, and subsequently a small dose of strychnia was injected into the dorsal lymph sac; as soon as the resulting spasm was well developed, stimulation was again applied, the strength of stimulation and the position of the electrodes remaining constant.

Thus, in fig. P_2, a frog's heart, in which active circulation was present, showed a refractory period through about one-half of the

P_1.

P_2.



Stimulation of Ventricle.

1. Before injection of strychnia. 2. After injection of strychnia.

maximal maintenance of systole. In 3′, after the injection of a small dose of strychnia into the dorsal lymph sac, distinct spasm was present, and in 5′ fig. P_1 was taken, which showed that the refractory period had become prolonged, until relaxation of the ventricle had commenced.

Time-marker recording seconds. All tracings in Appendix C taken at this speed, except S and T.

It may happen that stronger stimulation before the maximum of systole is reached, causes an auricular beat, which precedes in normal rhythm the induced ventricular contraction. This is observed when the electrodes are placed near the base of the ventricle, or when stimulation is passed through the same portion of the heart from the float to an electrode placed beneath the heart upon the supporting shelf. After the maximum of systole, however, the auricular contraction succeeds the induced ventricular. Both these facts are demonstrated in fig. Q, in which this occasional increased auricular excitability is shown.

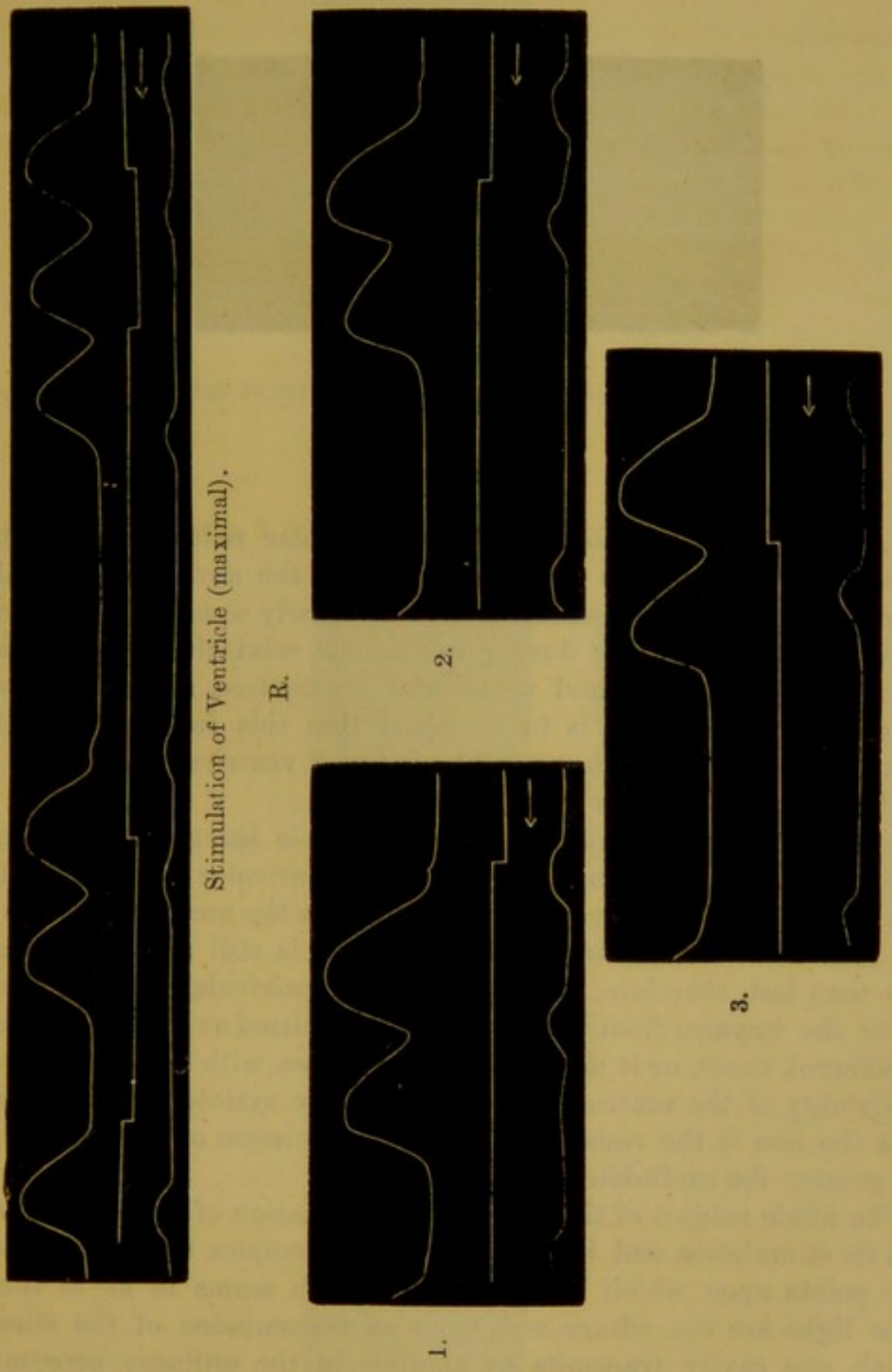
Auricular Stimulation.

Occasionally maximal stimulation applied to the auricle produces at all times an auricular contraction succeeded by a ventricular; more usually, however, this relationship exists only up to the maximum of systole (ventricular), and thereafter the induced auricular beat succeeds the ventricular.

Should stimulation cause an instantaneous auricular systole, then the ventricular reduplication has a latency of *nearly* equal value at all times at which it may occur, but should there be, as in fig. R_1, a considerable auricular latency (about 1″) then the ventricular latency is liable to great variations.

At the maximum of auricular systole, fig. R_2, we have an immediate auricular response, and a ventricular latency of ·4″; and in fig. R (3) there is an almost instantaneous ventricular systole, with an auricular latency of about 15″. The diastolic pause is the longer the later stimulation falls. In fig. R_1 it is ·9″; in fig. R_2 it is 1″·9; in fig. R_3 it is 2″·3.

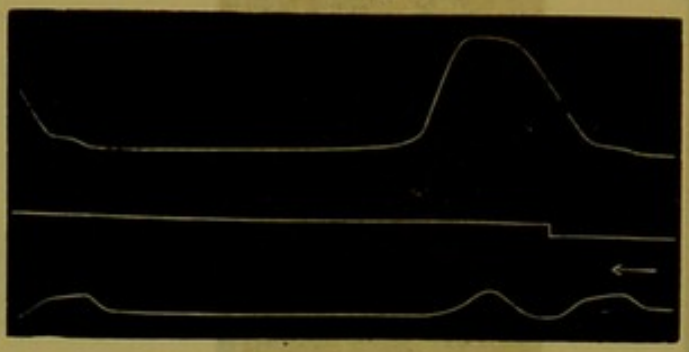
Stimulation falling just after maximum of auricular systole, and at the commencement of ventricular systole, may cause in addition to the results enumerated, omission of the succeeding auricular and ventricular contractions, or reduplication of the auricular, but omission of the succeeding ventricular (fig. S).



Thus the induced auricular contraction in this instance, instead of passing a motor impulse downwards to the ventricle, appears not only to check the reduplication, but greatly to prolong the diastole.

It is easily recognised from the auricular tracing that the induced contraction is one of the unfilled cavities (fig. S), but though little or no blood passes into the ventricle, a positive effect upon the latter is still produced.

S.



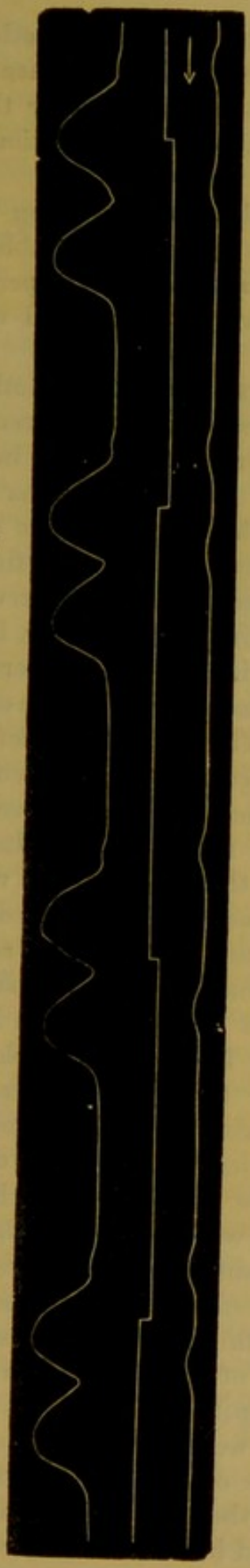
Stimulation of Auricle (maximal). Levers as in fig. Q.

Venous Sinus.

As regards the relationship of the auricular reduplication to the time of stimulation, we find the latency of the auricle occasionally varying in length, but usually it has very nearly equal values, except when the shock, falling during ventricular relaxation, calls forth a simultaneous auricular and ventricular contraction, and in this case latency is reduced. It is to be noted that this induced auricular contraction does not cause another induced ventricular systole: its further effects seem to be lost or dissipated.

At two points in Chart T, ventricular systole being advanced half-way and ·6 of the way to its maximum, the auricular latency is equal, and when at the end of ventricular relaxation the auricle contracts at the same time as the ventricle, the latency is still about the same. The time lost, therefore, in this case is in ventricular reduplication: either the impulse from the auricle is transmitted at different speeds at different times, or it meets at different times with variation in the excitability of the ventricle. The later in the systole the stimulation falls the less is the resistance to the transmission of the impulse or the greater the excitability of the ventricle.

The whole subject of the rhythmical contraction of the frog's heart and its stimulation and inhibition is a very complex and difficult one. The points upon which our present research seems to us to throw some light are the nature and mode of transmission of the stimuli which one cavity transmits to another in the ordinary process of rhythmical contraction. Marey's researches have shown that in the ventricle itself there is a time when stimulation applied to it has no apparent action; this time is, however, in many cases of very short duration and limited to the commencement of ventricular systole. At the commencement of ventricular systole stimulation without provoking contraction causes often a positive effect, namely, a greatly prolonged diastolic pause, which we have been inclined to regard as due to omission of a ventricular contraction.



T.

Stimulation of Venous Sinus (maximal).

It seemed of interest to ascertain whether a similar condition occurred in the other cavities of the frog's heart. We find that in the auricular stimulation about or shortly after the period of maximum contraction of the auricle may cause inhibition of the next auricular beat.

We have not yet succeeded in registering the contractions of the venous sinus with sufficient accuracy to enable us positively to determine the occurrence of a similar refractory period in the venous sinus itself, but the results we have obtained lead us to hope that we shall soon be able to do so.

Another interesting consideration is, whether the stimulus which each cavity of the heart transmits to the succeeding one, consists in the propagation of an actual muscular wave, or in the propagation of an impulse along the nerves. The observations of Gaskell have given very great importance to the muscular wave occurring in each cavity of the heart of cold-blooded animals as a stimulus to the contraction of the next succeeding cavity. Our observations appear to us to show that while this is an important factor, it is not the only one in the transmission of stimuli. We have observed that stimulation of the auricle rarely or never causes contraction of the ventricle unless the auricle also contracts. When stimulation of the auricle causes both itself and the ventricle to contract, the auricular contraction precedes the ventricular one in such a way that we might be justified in regarding the ventricular contraction as due to the propagation of the contractile wave from the auricle to the ventricle. It would also appear that a contractile wave may be propagated backwards, for on stimulation of the ventricle we have observed the contraction of the ventricle produced by stimulation has been succeeded by an auricular contraction such as might be supposed to be due to propagation of the contractile wave back from the ventricle to the auricle. While these observations appear to show that the propagation of the contractile wave from one cavity of the heart to another is of importance in keeping up the rhythmical sequence, we consider that stimuli are also propagated from one chamber of the heart to another through nervous channels:—thus we find that irritation of the venous sinus will sometimes produce simultaneous contractions of the auricle and ventricle, instead of the ventricular beat succeeding the auricular in the usual way. This we think is hardly consistent with the hypothesis that a stimulus consists of the propagation of a muscular wave only from the auricle to the ventricle.

As additional evidence we may notice the occurrence of an auricular beat followed by absence or inhibition of a ventricular beat as the result of stimulation of the auricle, or venous sinus. Moreover, we have noticed in the heated heart the occurrence of groups of regular beats in the ventricle in consequence of a single stimulation applied

to it, while the auricle has continued to beat with its ordinary unaltered rhythm undisturbed by the ventricular excitement.

It is not however our purpose to do more in this paper than state the results we have hitherto obtained, and we shall therefore reserve to a future communication the consideration of this and some other questions of importance closely allied to it.

Another question is the nature of the inhibitory influence exerted by one cavity of the heart upon another. Marey had shown that stimulation of the ventricle during a great part of the refractory period exercises an inhibitory instead of a motor action upon the ventricle itself. It might be supposed then that a stimulus of either kind, whether proceeding from the auricle in the form of a contractile wave, or a nervous impulse, might produce inhibition of the ventricle, provided the stimulus reached it during that part of the refractory period in which stimulation usually causes inhibition. From our observations it seems that the inhibition of the ventricle which may follow stimulation of the auricle is not due to the muscular wave propagated from the auricle and striking the ventricle during the refractory period. In fig. 6, we notice that the auricular contraction succeeded by ventricular inhibition occurs after the refractory period of the ventricle has passed; we must, therefore, look upon the inhibition as due to the propagation of a nervous impulse from one cavity to another. In the auricle we find that stimulation may produce inhibition of the auricular and ventricular beats, or of the ventricular beats alone. We may, therefore, suppose that the stimulus applied to the auricle acts upon two different nervous mechanisms; seeing that it is enabled to inhibit the ventricular beats without affecting the auricular ones, we are unable to say precisely what the effect of a single stimulus applied to the venous sinus is upon the sinus itself, but here we note that the same result will follow stimulation of the sinus, as of the auricle, viz., inhibition of the ventricular without inhibition of the auricular beat, or inhibition of both together.

As has been already pointed out by Professor Marey, the refractory period is increased when the heart is artificially cooled. We have also found that there is a prolongation of the time during which stimulation causes an inhibition or omission of the following systole.

It is very seldom that stimulation of the auricles or of the venous sinus causes a ventricular contraction without auricular systole preceding it in the ordinary rhythm. In this respect the action of the heart offers a contrast to the normal. Though the muscular wave started in the auricle is usually succeeded by a ventricular contraction, it may occasionally be succeeded by a ventricular inhibition, or auricular stimulation may be followed by inhibition of both auricle and ventricle.

The propagation of the wave in an upward direction, viz., from ventricle to auricle, is not so regular as in the normal heart, the time elapsing, when it does occur between the ventricular and auricular systole, bearing a relationship to the degree of cold produced. Whilst the ventricle is reduplicating in response to direct stimulation, the auricle may maintain its regular rhythm. Stimulation of the venous sinus almost invariably gives an auricular contraction at all times preceding the ventricular. It has been already shown that in the case of the normal heart stimulation in advanced diastole frequently causes a spontaneous auricular and ventricular contraction, or a ventricular beat preceding the auricular.

In the heated heart we have noticed, in addition to the excessive diminution or abolition of the refractory period in the ventricle already observed by Marey, that usually the refractory period in the auricle entirely disappears. A single stimulation of the ventricle sometimes gives rise to a series of contractions with incomplete relaxation intervening. After this has occurred, or after a simple reduplication has been caused, it often happens that the auricular beat occurring in normal sequence is not followed by ventricular, which seems to show a temporary state of exhaustion of the ventricle. In the heated heart the duration of a systole is so short that two beats immediately succeeding one another may be perfectly distinct, while, in the normal heart, the second one would have fallen within the time of the systole of the first, so that it could only have appeared, if it were possible at all, as an increase either of the height or length of the first systole. Inhibition occurs in the heated heart as well as in the normal, which is most frequently observed upon stimulation of the venous sinus, and it is frequently at this time associated with a reduplicated auricular contraction. The effect of strychnia is to prolong the refractory period of the ventricle. Stimulation of the ventricle is frequently succeeded by contraction of the auricle. There is an increased tendency for stimulation of the ventricle to induce a beat of the auricle preceding the ventricular systole. There is less tendency for the stimulation of the venous sinus or auricle to induce a beat of the ventricle succeeded by one of the auricle; and, indeed, this only occurs when the stimulus falls just at the end of the ventricular systole, *i.e.*, when the ventricle itself is most sensitive. These facts seem to indicate that the nervous channels are more active in transmitting stimuli, both downwards from the venous sinus to the auricle and ventricle, and from the ventricle back to the auricle.

In its effect upon the refractory period, and in the tendency it produces to maintain the regular rhythm, the action of strychnia agrees with that of cold, as shown in the present series of experiments; but, as we have already shown in a former paper,* its effect in causing

* "St. Bartholomew's Hosp. Reports," vol. xvi, p. 229.

the ventricle when arrested by a ligature applied around the junction of the venous sinus with the auricles to recommence pulsation resembles that of heat.

There are many other points on which we think that a fuller consideration of our experiments will throw light, but to take them up at present would involve too lengthy a discussion of doubtful points in the physiology of the frog's heart, and so we must reserve them for a future time.

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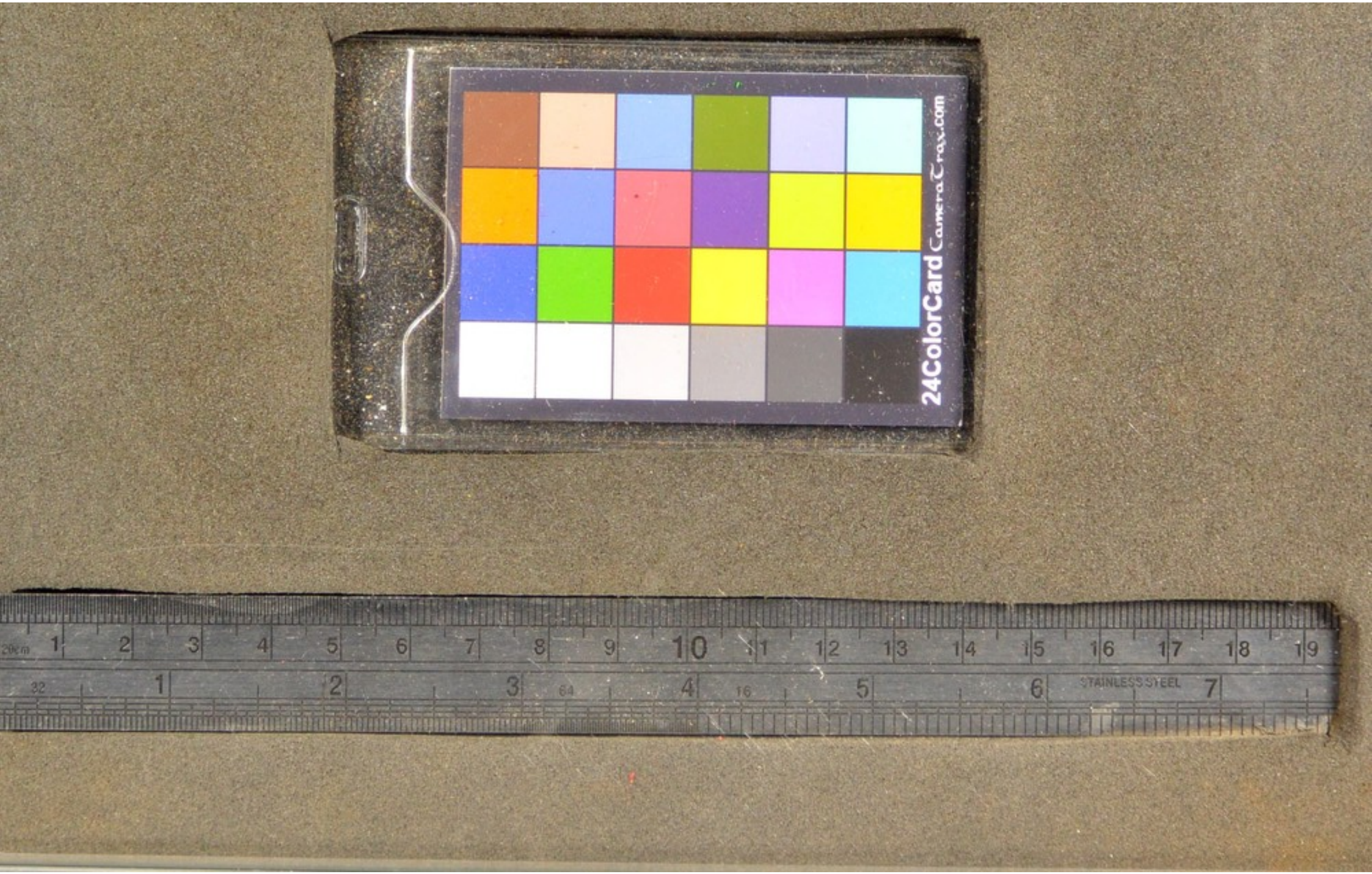
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