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CONTENTS.

Physiology. — *"On the heart-rhythm"*. By Dr. S. DE BOER. (Communicated by Prof. Dr. WERTHEIM SALOMONSON).

(Communicated in the meeting of Jan. 30, 1915).

1. *The a-v-interval and the refractory period.* [1])

The normal heart-rhythm is caused by a system of different factors, among which the irritability and the transmission of stimulation of the different parts of the heart are of great significance. I have now made a series of experiments on frogs, in which I have modified these two principal properties of the heart by means of veratrine. I followed in my experiments this method: the heart was suspended on the point, after I had removed the sternum, cut open the pericardium and cut the frenulum in two. The single suspension was used, because I intended to note down, after the poisoning, during

[1]) The experiments mentioned here were communicated by me in a lecture, held in the meeting of the biological section of the Genootschap ter bevordering der Natuur-, Genees- en Heelkunde at Amsterdam of November 19th 1914.

a couple of hours and longer, all systoles; this aim can be better reached with one lever than with two. By doing so I had to watch only one friction on the smoked paper, when noting down the systoles of the auricles and ventricles, so that their succession, with regard to time, can be better estimated and we obtain a better survey of the whole reproduction. The curves were noted down by the lever on an endless smoked paper which was wound round three kymographia; the motion was obtained in the usual way by making one of these apparatuses turn, whilst the two others with unscrewed axes followed the revolution. In this way I could note down during two hours and a half after the poisoning all the curves and obtained the entire reproduction of the poisoning; in order to make a comparison first about one hundred systoles of the unpoisoned heart were reproduced. To a maximum of ten drops of 1 % acetas veratrini were then injected into the abdominal cavity. About 10 minutes after the injection the systoles became larger and wider, the a-v-interval increased, the electric irritability of the ventricle diminished. When I fixed before the poisoning the weakest stimulation with which I could obtain an extra-systole after the beginning of the diastole, I had, after the poisoning, either to strengthen it or to apply it later, in order to obtain the same effect. This continued till in the end, during the whole diastole, I did not obtain any effect on the ventricle not even with the strongest stimulation.

In this stage of the poisoning I observed quite a new phenomenon: at the end of the diastole no extrasystole was obtained after-irritation, but a pause of the ventricle. The duration of this pause was always of such a nature that, added to the duration of the preceding heartperiod, they amounted together to two heart-periods. The pause began with an extrasystole of the auricle. The auricle was now irritable indeed, which was promoted by lengthening the a-v-interval. This extrasystole of the auricle was caused by retrogressive transmission of stimulation or with strong stimulation by current-loops.

The next-following irritation coming from the sinus venosus finds then the auricle refractory. The result is that one auricle- but likewise one ventricle-systole falls out of the normal rhythm, and so an extra pause takes place. Now it is remarkable to see, how strongly widened the postcompensatory systoles are after these extra-pauses without extra-systoles. This fact is indeed entirely in accordance with the law on the conservation of the energy of the heart (LANGENDORFF). In my case indeed pause of the ventricle i. e. rest of the ventricle appears without preceding extra-systole. The condi-

tions for the formation of a postcompensatory systole as wide as possible (according to LANGENDORFF) are then most favourable.

The irritability of the heart-muscle during the diastole has much improved again during the pause. This appears from the fact, that the next-following systole, after the postcompensatory one, occurs in the diastole of this postcompensatory systole. The ventricle consequently is now susceptible of the weak physiological irritation coming from the auricle, whilst, two heart-periods before during the diastole, it was still insusceptible of a much stronger, artificial stimulation. By artificial irritation in the diastole of the post-compensatory curve I could again bring about extra-systoles, which did not occur when, with the same strength of stimulation, I irritated at the same moment of the diastole in the normal rhythm. The refractory period however can be enlarged during this great systole without extending to the diastole. Experiments, in which I noted likewise the action-currents, taught me, that during the extra-pause the ventricle neither produced action-current.

I repeated this experiment more than a hundred times. An extra-stimulation occurring somewhat later caused again an extra-systole (vide Fig. 1 the 7th systole of the second curveseries).

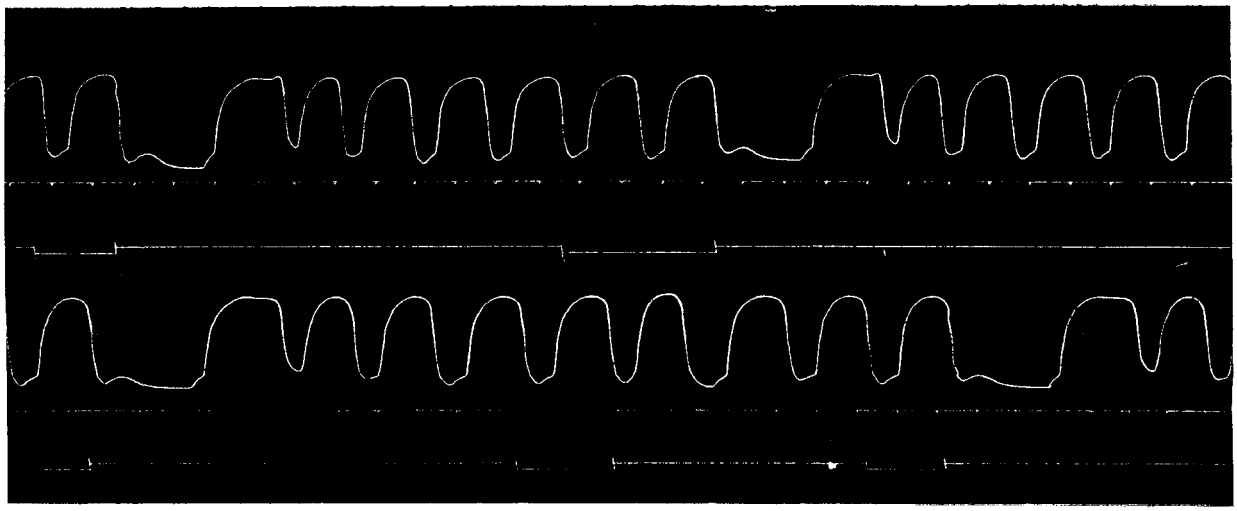

Fig. 1.

In a later period of the poisoning the rhythm of the ventricle is halved, after the extent of the systoles has first diminished. The cause of this phenomenon lies in the prolongation of the refractory period and of the a—v-interval. An auricle systole falls consequently at last in the refractory period of the preceding ventricle-systole, so that then every 2nd auricle-systole remains unanswered by the ventricle.

Both of auricle and ventricle the halving of the rhythm can also suddenly occur (i. e. with regard to the sinus-contractions).

After this rhythm-halving the a-v-interval is shortened again, the irritability of the ventricle has improved: an extra-stimulation during the diastole causes again an extra-systole, but now without compensatory pause; the row of the ventricle-curves has only been removed by one auricle-systole. The duration of this extra-period + the duration of the preceding period is now equal to the duration of $1^1/_2$ heart-periods.

When now this halved rhythm of the ventricle has existed for a short time, I can, with one induction-stroke during the diastole, reduce this rhythm to the original one, which can continue again for some time: consequently an artificial return to the original rhythm. This experiment can be explained as follows: In the first place it is irrefutable, that the metabolic condition of the heartmuscle was such as to allow the heart to pulsate in the normal rhythm; nor were the physiological irritations proceeding from the auricle wanting, for only the ventricle pulsated in the halved rhythm; and yet this halved rhythm would have continued, if I had not intervened by an extra-stimulation. The cause of this phenomenon is, that the systoles of the halved type are much larger and wider than those of the not halved one. Each systole in itself of the halved type has consequently a larger refractory period, so that each second auricle-systole cannot be answered by the ventricle. The ventricle is consequently, as it were imprisoned in its own rhythm; if there were only one narrower systole with a smaller refractory period between, then the normal rhythm would have been restored with the smaller systoles. Now I obtain this little systole as an answer to the extra-stimulation, and because the latter took place directly after an auricle-systole, the extra-systole is not followed by a compensatory pause, but after the extra-stimulation I detect a continual recovery of the original rhythm. If the extra-systole was followed by a compensatory pause, this recovery of the rhythm could not take place, for the postcompensatory systole would have been enlarged (= widened) again, and would thus restore again the halved rhythm. At the same time we have here consequently before us an example of an extra-systole without a compensatory pause. The ventricle can thus again pulsate c. g. about 5 minutes in the original rhythm and then pass again in the ordinary way into the halved rhythm. During the first time of halving the metabolic condition of the heartmuscle had certainly much improved, but every large systole of this type has in itself a larger refractory period than every little systole of the

normal rhythm. The pauses in the latter rhythm, however, are much shorter, so that after some time the refractory period, at a given moment, after a systole of the ventricle, no longer depends only upon the preceding systole, for on account of the insufficient restoration between the quick heart-periods the preceding systoles have also had influence upon it; the refractory period increases again in such a way, that once more a halving of the ventricle-rhythm takes place. I could also bring about this change artificially, by intervening exactly in the same manner, by which I could alter the halved rhythm. By an extra-stimulation during or a short time after the diastole I made an extra-systole; this was followed by a compensatory pause, after which the post-compensatory systole, as always, is enlarged and widened. The enlarged refractory period is the cause that the halved rhythm returns again, because the first-following auricle-systole takes now again place in this refractory period. I could consequently these variations of rhythm bring about discretionally when the ventricle-rhythm had been halved for some time.

I practised a second method of variation of rhythm according to a quite different principle and with as certain a result. When the ventricle pulsated after the veratrine-poisoning in the halved rhythm, I could by refrigeration of the sinus venosus make the impulses, originating in the latter, reach the ventricle in a slower tempo. Thus every second auricle-systole moved over the refractory period of the preceding ventricle systole, and restoration of the original ventricle-rhythm was the result. As a transition I obtained then heart-bigeminy and trigeminy. Consequently we obtained here by refrigeration of the sinus venosis an increase of the frequency of the ventricle, this is an exception to GASKELL's experiment which teaches us, that refrigeration causes a decrease of the rhythm. Calefaction of the sinus venosus causes, after the preceding experiment, a return of the rhythm to the halved one.

Another method of bringing about variations of rhythm is calefaction and refrigeration of the ventricle. Calefaction of the ventricle shortens the refractory period, and changes consequently the halved rhythm into the normal one; refrigeration of the ventricle causes then again a restoration of the halved rhythm. I could most quickly change the halved rhythm of the ventricle into the normal one by refrigerating the sinus venosis, and at the same time calefying the ventricle. Especially by this latter method the variation of the rhythm succeeds always. The variation by an induction-stroke succeeds only, when the halved rythm has not yet existed a long time, or when at the reaction of the poisoning, the halved rhythm was to change

again after the lapse of not too long a time into the not halved one.

I saw also repeatedly variations of rhythm occur spontaneously. When the poisoning-process increased these variations of rhythm resulted in the halved rhythm, which by further halvings applied to 1 ventricle-systole caused 4, 8 or sometimes 5, 6, or 7 auricle-systoles. At the reaction of the poisoning during the halving period these variations of rhythm are accompanied with varying lengthening and shortening of the a-v-interval. The lengthening occurs during the quick rhythm, the shortening by restoration during the slowly halved rhythm.

When the poisoning continues, no restoration takes place, but through lengthening of the a-v-interval and the refractory period further halving is the necessary result.

2. *The transmission of stimulation in the ventricle.*

We have seen that by poisoning with veratrine the transmission of stimulation between auricle and ventricle slackens. The mechanograms do not tell us anything about the transmission of the stimulation in the ventricle-muscle itself. In order to obtain more information about this subject I reproduced the action-currents before and at fixed times after the poisoning.

In Fig. 2 we have the suspension-curve and the electrogram of a not poisoned frog's heart. Time in $^1/_4$ sec. Electrodes auricle-ventrical.

Whilst leaving for the rest all the circumstances the same, I make 12 minutes after the injection of 5 drops 1% acet. veratrine (vide Fig. 3) another reproduction.

The R-top is raised and widened, it is somewhat split.

The T-top has become positive, the line of connection between R and the T is lowered. The heartrhythm has slackened. The pauses between the mechanograms have lengthened, but those between the electrograms have shortened. The electrograms before the poisoning lasted till the beginning, after the poisoning till the end of the diastole; the duration of the electrograms runs parallel with the duration of the refractory period.

Both are indications of the metabolic processes of the heart-muscle. After the poisoning the beginning of the R-oscillation goes much more in advance of the suspension-curve than before the poisoning. The period of the latent irritation has consequently considerably lengthened after the poisoning.

Directly after the halving of the ventricle-rhythm, 1 hour 20 min. after the injection I obtain the representation of Fig. 4.

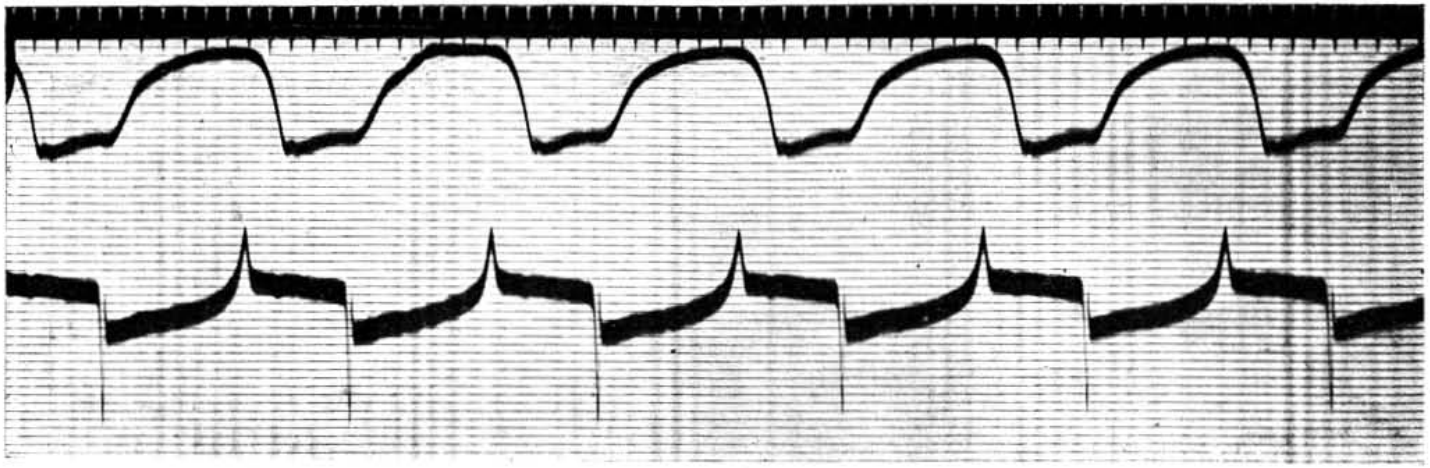

Fig. 2.

In Fig. 2, 3, 4, 5, 6, 7, 9, and 10 the time is at the top in $^1/_5$ sec.; then follows the suspension curve with the top directed towards the time; at the bottom the oscillations of the string (the negativity of the basis shows in all the curves an oscillation of the time, consequently downward).

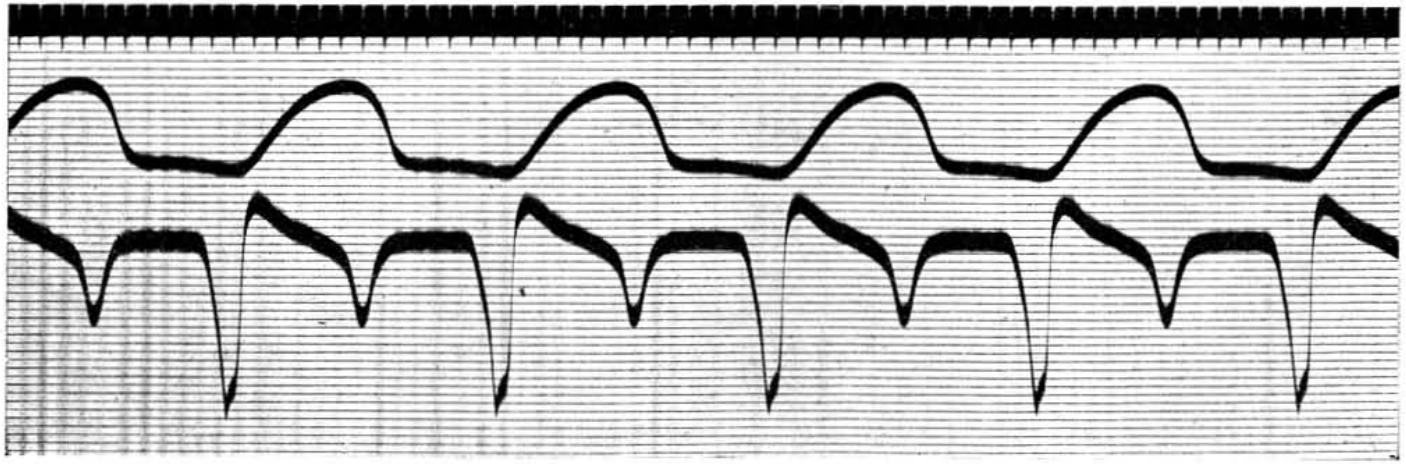

Fig. 3.

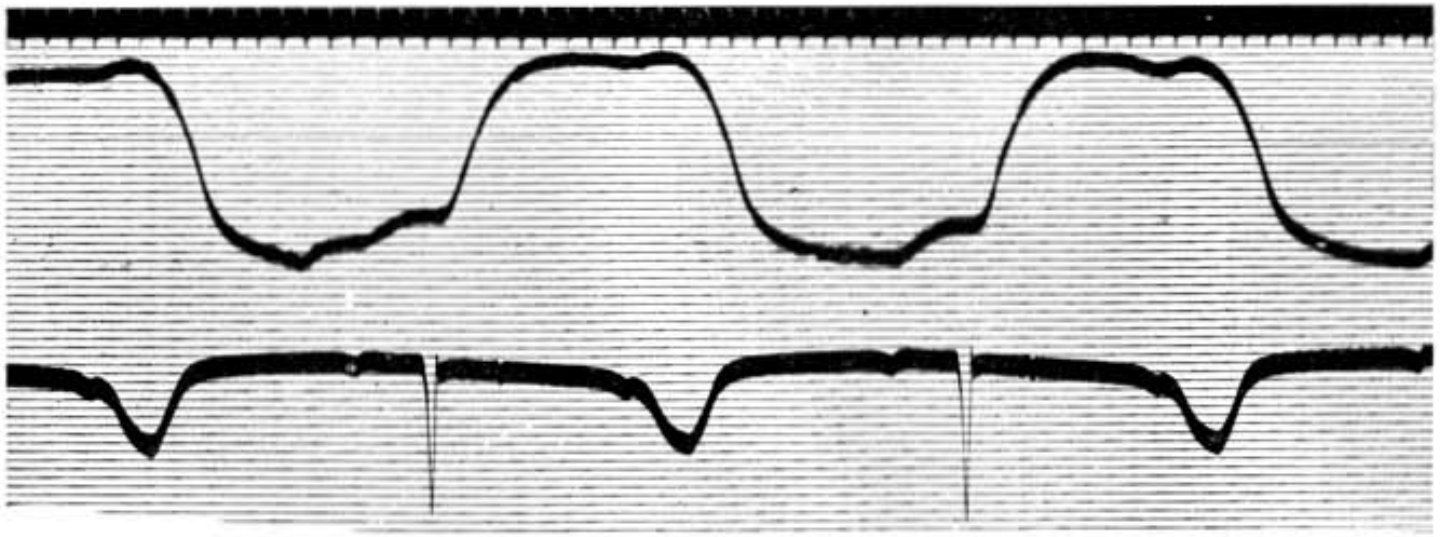

Fig. 4.

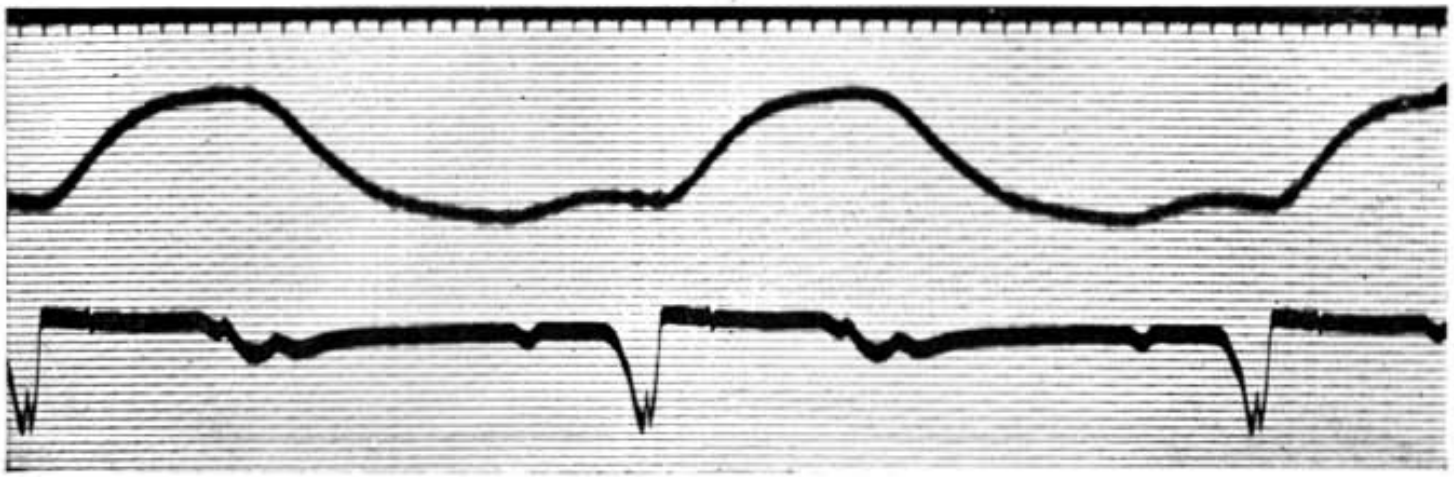

Fig. 5.

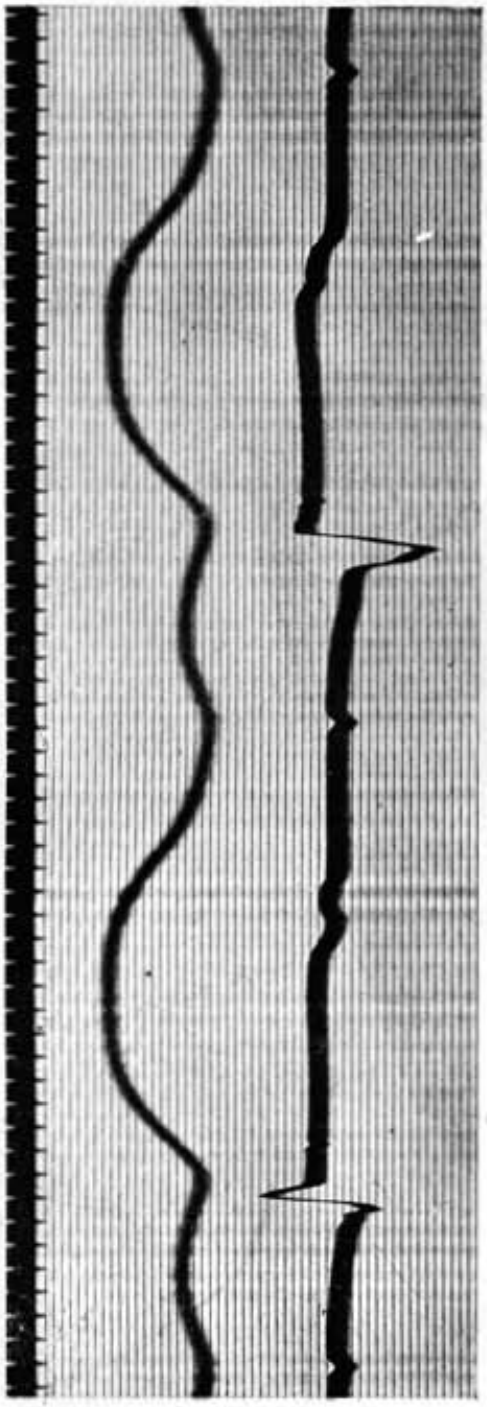

Fig. 6.

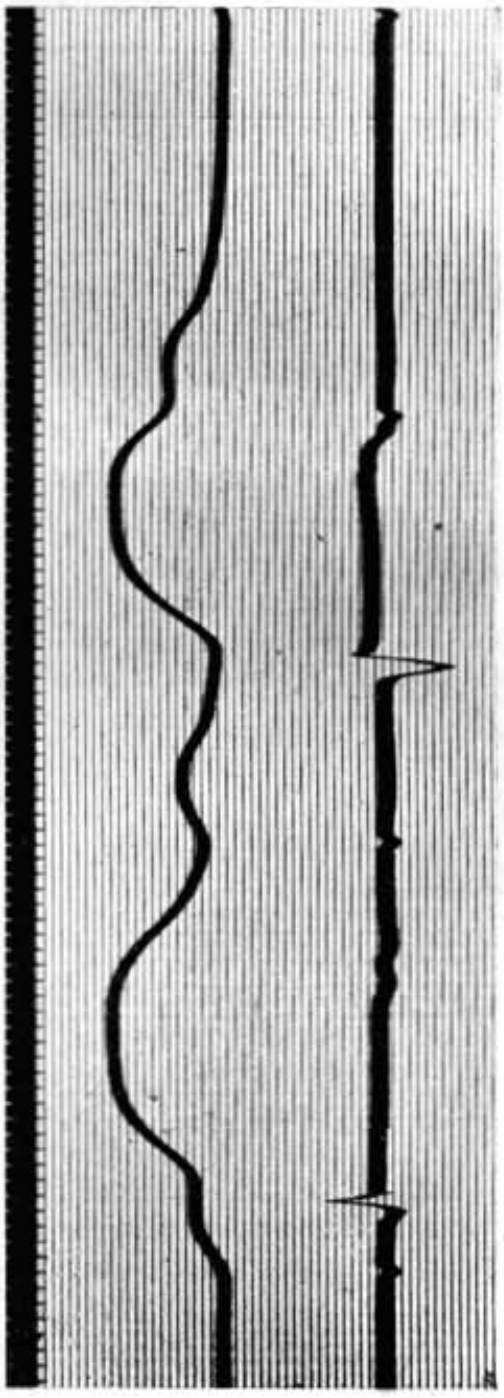

Fig. 7.

We see that with the restoration of the metabolic condition of the heartmuscle the variations indicated above have for the greater part regressed again. I call only the attention to the shorter duration of the R-oscillation. The a-v-interval is even again shorter than before the poisoning. Slackening of rhythm promotes shortening, poisoning lengthening of this interval.

Directly after the halving shortening prevails.

35 minutes after the reproduction of Fig. 4 I obtain representation Fig. 5. The R-branch has widened and split again, the a-v-interval has increased, and likewise the period of the latent irritation.

If now, in analogy with the duration of the action-currents for the striped muscles, we see in the duration of the R-oscillation a measure for the speed of the transmission of stimulation in the heart-muscle, then the variation of the duration of the R-oscillation becomes immediately intelligible. Through the poisoning the speed of the transmission of stimulation decreases, after the halving it improves again in the beginning, when the poisoning continues, the transmission falls afterwards off again into this halved rhythm.

We saw before, that the irritability of the heart muscle sustains the same oscillations during the poisoning and the halving-process. This cannot be otherwise, for transmission of stimulation means, that a level that is in irritation influences an adjacent level. The speed with which this influence can take place depends upon the irritability.

In a following period of the poisoning the basis and the point of the ventricle palpitate alternatively stronger (Vide Fig. 6). The a-v-time has increased again.

If now 25 minutes later I make another reproduction (vide Fig. 7) every 3rd systole has fallen out. In Fig. 7 we see consequently a bigeminusgroup, the point and the basis of which pulsate alternatively. With the naked eye this could be distinctly observed. We see after the long pause a short a-v-interval, after a short pause a long a-v-interval. On my suspension-curves of heart-bigeminy and -trigeminy, after veratrine-poisoning, of which I possess a great number, the increase of the a-v-interval in the bi- and trigeminus- gronps can be observed. As an example I give Fig. 8.

I have asked myself if we have here a strict, legal proportion. Is the transmission of stimulation after a long pause always better than after a short one?

With a quite different intention I have now made an extensive investigation concerning the potential differences occurring in the heart at extra-systoles. In a series of experiments I irritated the

auricle for this purpose. I could consequently make use of these curves for the measurements, and now I find the a-v-interval

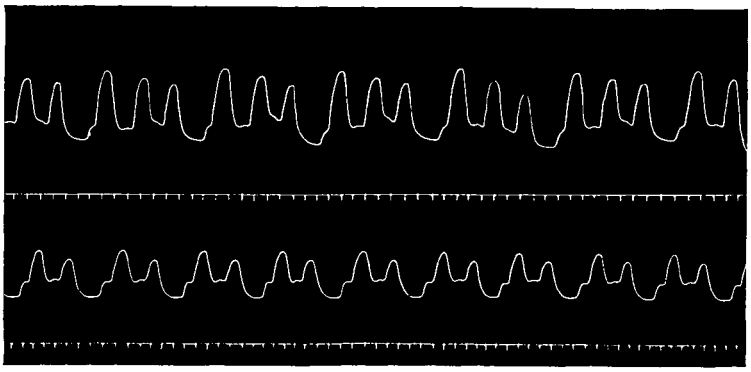

Fig. 8.

increased for the extra-systoles, decreased for the postcompensatory systoles, in comparison with the undisturbed rhythm. The duration of the R-oscillation behaved in the same manner[1]).

Herewith I suppose, that I have established a law of the conservation of the power of transmission, both for the connecting systems of the separate partitions of the heart and for the heart-muscle itself. In this way LANGENDORFF has established, that the extra-systole is smaller, the postcompensatory systole larger than the normal systoles, and saw in it a law for the conservation of energy for the heart-muscle.

When now, 20 minutes after the reproduction of Fig. 7, I make another reproduction, the basispulsations have ceased and with this again halving of rhythm has taken place, but now with systoles of the point-type. Between every two point-systoles there is now one auricle-systole that is not answered by the ventricle. This second way of halving of rhythm I saw also often in my suspension-curves. As a transition-stage heartpoly-, tri- and bigeminy were formed then.

The slackening of the transmission of stimulation by poisoning with veratrine caused the formation of a split R-top. As an example I give here Fig. 9.

I shall shortly indicate in what manner this electrogram was made.

[1]) The height of the R-top during the extra-systole was enlarged, during the postcompensatory systole diminished. In this manner it was, if the circulation of the blood was undisturbed. That was caused by the bloodfilling of the heart. This was small during the extra-systole, through which the potential differences are less exchanged and stronger during the postcompensatory systole, through which the potential differences are more exchanged. When the bloodcirculation was disturbed all the R-tops had the same height.

Fig. 9

Fig. 10

At half past 2 o'clock I injected the frog 8 drops 1 % veratrine into the abdominal cavity; at 10 minutes to three there was halving of rhythm, the electrogram shows a very quick R-top. In the following reproductions at 3 o'clock, 10 min. past, half past 3 and a quarter to four, the R-top remains unsplit, but at every reproduction it becomes wider. The duration of the R-top is in the last reproduction $1^1/_4$ time-unity of $^1/_5$ second. In the following three reproductions at 5 minutes, 20 minutes, and half past 4 o'clock the duration is $1^3/_4$, 2 and almost 3 time-unities.

With the increase of the duration of the R the splitting becomes more conspicuous after every reproduction. The reproduction of half past four o'clock is represented here in fig. 9. By this the formation of the splitting of the R-branch becomes obvious. By the slackening of the transmission of stimulation the influence of the apexnegativity comes constantly somewhat later (this influence is after all the cause of the decline of R). At last this influence comes so late, that the basisnegativity after the quick original oscillation increases again before the tonical slow oscillation of T.

By the next reproduction, which I made at 4.40, this connection becomes still more conspicuous. For this purpose I had amply cauterized the point of the heart with a red-hot probe. With a, for the rest equal, deduction (auricle-heartpoint) I obtained now the reproduction Fig. 10.

Here I see indeed again the same initial top. This explains the splitting of the top. The cause of it is to be found in the slackening of the transmission of stimulation and the manner in which the heart-muscle contracts.

At the same time we can see in these experiments an experimental proof that the two components, in the interference of which the definitive electrogram originates (at diphasical deduction) consist of a quick initial oscillation and a subsequent slow one. According to SAMOJLOFF, who saw likewise in his monophasical ventricle-curves the initial top, this would originate, because the deduction could never be obtained purely monophasically; he supposed the curves still to be partially diphasical, which would be the origin of the sharp initial top. In my curves, however, the initial top is detected before the influence of the apex-negativity is felt. The part of the ventricle-curve into which the sharp initial top falls is consequently purely monophasical. In the hearts of my frogs that were poisoned with veratrine, I always found this split R-top; it is however no special consequence of the effect of the veratrine, but wheresoever slackening of the transmission of stimulation takes place

the split R-top appears, as likewise with the extra-systoles of mammals.

The latter experiments indicate likewise, how, also with other methods, the splitting of the R-branch can be brought about. For the genesis of the electrocardiagram this fact is of great significance. There is, in my opinion, likewise great probability that the purely diphasical electrogram of the ventricle consists of a quick diphasical R-oscillation, and a T-branch that is either positive or negative. This conception would then at the same time afford an explanation of the formation of the S-branch.

Zoology. — *"The physiology of the air-bladder of fishes"*. By Dr. K. KUIPER Jr. of the Physiological Laboratory at Amsterdam. (Communicated by Prof. MAX WEBER).

(Communicated in the meeting of November 28, 1914).

I. *The air-bladder as a hydrostatic organ.*

For a long time it has been held that fishes possessing an air-bladder could modify its contents by muscular action, which would enable them to regulate, within certain limits their own specific gravity.

If the fish wanted to go down to lower strata a decrease in the contents of its air-bladder would enable it to increase its specific gravity. To rise to the surface it needed only to relax the tension of the muscles of the air-bladder; the gases in the air-bladder expanded and this increased volume carried the fish upward.

In the latter half of the 19th century, this view, which was established more especially by BORELLI, and which prevailed during some centuries without being sufficiently tested by experiment, was declared erroneous by A. MOREAU. Some simple but ingenious experiments convinced him that a modification in the S.G. by an active muscular action was out of the question.

A fish which, placed in a cage of thin wire, is submitted to modifications in the pressure on the water in which it is, behaves exactly like the cartesian diver.

He caused a fish to swim round in a glass vessel which was closed hermetically, and which was entirely filled with water. The stopper was pierced by a bent glass tube in which the water-meniscus, when the fish was at the bottom, was found at a certain point, A for instance. When the fish swam upward, the meniscus moved slowly forward, that is to say a decrease of the water column