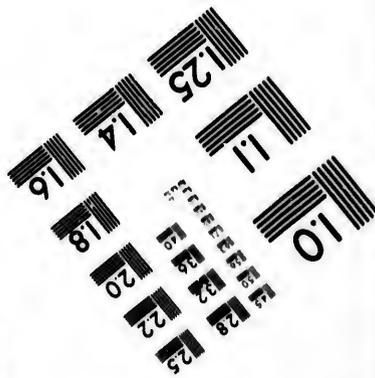
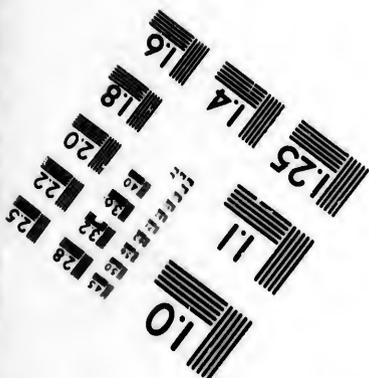
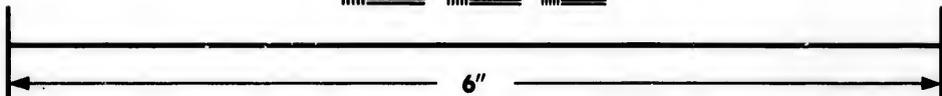
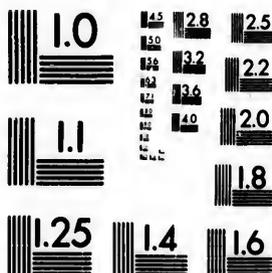


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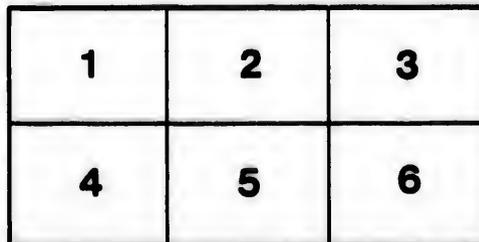
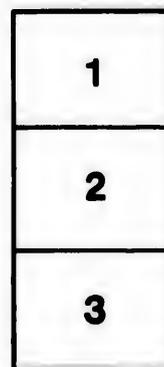
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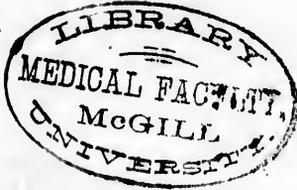
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MARCH, 1886.



THE ACTION OF CERTAIN DRUGS AND POISONS
ON THE HEART OF THE FISH.

By T. WESLEY MILLS, M.A., M.D., L.R.C.P., ENG.
Lecturer on Physiology, McGill University.

Last summer I was able to make an investigation on the physiology of the heart of the fish, Professor Brooks having kindly allowed me the advantages of the marine laboratory of the Johns-Hopkins University at Beaufort, North Carolina.

Part of this work consisted in an examination of the action of certain drugs and poisons on the heart, and so far as I know, for the first time for *this* animal.

Exceedingly little, if anything, is known of the action of such agents on the hearts of the cold-blooded animals, except in the case of the frog. This investigation demonstrates that in the fish the action of the drugs and poisons used is similar to what it has been shown to be for the frog by other investigators. (Ringer, Brunton, &c.) The results will be presented exactly as stated in my notes taken at the time, and without comment in most cases, leaving the reader to draw his own conclusions as to *mode* of action.

The fish chiefly used for these experiments was *Batrachus Tau*, popularly known as the "toad fish," a term indicating well its general appearance. It is a fish of great vital tenacity, and well suited in every way for physiological experiments generally. The hearts of most fishes are so easily rendered abnormal that the attempt to investigate them proves abortive; but the

heart of *Batrachus* seemed so well suited for testing the action of drugs, etc., that a considerable number of experiments were made to ascertain their influence when directly applied to the heart. The drug was either applied in solution with a camel's hair pencil, or simply dropped over the heart; the fish meanwhile being kept under normal conditions (on its back, with sea-water bathing its gills, etc.) That the effect witnessed on the heart was not due to indirect influence through the extrinsic nervous system of the fish was shown by isolating the heart and treating it with the same drug or poison as the heart *in situ*. The results have always been harmonious.

It may be remarked at the outset that almost all the drugs and poisons used by me have had, as a first effect, the production of an increased rhythm, owing, probably, to the exciting effect of a foreign substance before the specific action had time to manifest itself. To this general rule the auricle proper has often proved an exception. I have constantly found that its beat is arrested with the greatest ease while the sinus extension remains comparatively unaffected.

It will be borne in mind that the heart of the fish consists of a sinus and sinus-extension (as in the tortoises, turtles, etc.), one auricle, and one ventricle.

PILOCARPIN AND ATROPIN.

The following extracts from my notes will give a general idea of the action of these drugs:

" AT 2.30 P.M.—Fish prepared as usual. Pilocarpin Mur. in solution of 1 per cent. applied freely to heart, which has a rhythm of 30; vigor soon diminished, the beat lacking in decision; is a lazy heart; diastolic relaxation increased; heart more readily arrested; *e.g.*, wiping it over with a moistened sponge arrests heart for two minutes, which is much longer than the usual stop under such circumstances.

3.05.—Pilocarpin removed with a sponge, and Atropin applied; at once the rhythm, which had sunk, rose to 32; manifest increase of force in both auricle and ventricle; original decision of action restored."

The above notes are meant to be merely illustrative; space does not admit of all being given without undue distension of the paper.

Summary of the results of the action of Atropin and Pilocarpin.

1. Pilocarpin and atropin are antagonistic in action. The former is a cardiac depressor, tending to lower the excitability of the heart, render its action sluggish, and to stop it in diastole; the latter to improve a sluggish or weakened heart, and heighten the excitability of this organ under all circumstances. While pilocarpin tends to slow the rhythm, atropin quickens it, and increases the force of the beat. It manifests its action rapidly.

2. Atropin freely applied to the heart annihilates the possibility of arresting the heart reflexly.

Atropin applied to the conus arteriosus, arrested by a ligature between conus and ventricle, excites it to pulsation.

SODIUM AND POTASSIUM CARBONATE.

The following extract from my notes shows the opposing action of these two agents :

"Fish prepared as usual. 10.15 A.M.—Sod. Carb. in solution of 5 per cent. applied. Rhythm at once gets very rapid; diastole of ventricle very short and imperfect; auricle proper arrested.

10.25.—Auricle has recovered, and leads the rhythm of the ventricle.

10.30.—Pot. Carb. in solution of 5 per cent applied; (1) Auricle at once arrested; (2) Ventricular beat enfeebled. (This preceded by an increased rhythm.) Later, auricle begins and then again stops; an independent rhythm of auricle and ventricle.

10.36.—Rhythm of auricle 40, but weak; rhythm of ventricle 25, and also weak."

Sod. Carb. and Pot. Carb. were alternately applied in this case several times, always producing decidedly opposite effects.

Summary of the results of the action of Sodium Carbonate and Potassium Carbonate.

Sod. Carb. and Pot. Carb. are antagonistic in action on the fish's heart; the former quickens rhythm and diminishes diastolic relaxation, and heightens cardiac excitability, but is in this respect inferior to Atropin. Potassium Carbonate diminishes excitability, weakens the heart's action, and tends to arrest it in diastole. This agent seems to be a poison to the fish's heart.

LACTIC ACID.

In 5 per cent. solution, this acid proves a speedy poison. Its effects in 1 per cent. solution will be clear from the following extract from my notes :

Exp.—R. 56. Lactic acid 1 per cent. freely applied.

Its effects :

- (1) Slows rhythm.
- (2) Auricle affected before ventricle.
- (3) In ten minutes, whole heart arrested in well-marked diastole.
- (4) The heart cannot be excited to action by mechanical means (prick with seeker). Neither Acetate of Strychnia in 1 per cent. solution, nor Digitalin applied in the usual manner, cause any improvement.

It is thus seen that lactic acid in 5 per cent. solution is a rapid poison, while in solution of 1 per cent. it depresses the heart and gradually kills it in diastole.

DIGITALIN, IN SOMEWHAT LESS THAN 1 PER CENT. SOLUTION.

Of all the drugs and poisons used, none has produced such decided manifest, rapid and constant action as digitalin. It was used in a solution of rather less than 1 per cent., and the results were precisely the same whether applied to the isolated heart or to the heart *in situ*, though, as is to be expected, much more rapid in the former case, on account of the better state of nutrition in the heart under normal conditions, enabling it to resist longer all kinds of foreign influences. This principle applies in all cases, so far as I have observed, of the action of cardiac drugs and poisons.

The action of digitalin may be stated thus :

1. Digitalin, when applied to a rapidly-beating heart, slows it.
2. *Its invariable action, no matter what the condition of the heart, is to produce gradually increasing systolic contraction, the diastolic relaxation getting less and less till the heart is finally arrested in most pronounced systolic tetanus.*
3. The peculiar action of the drug requires a short period before there is any decided manifestation of its effects ; but when the latter do appear, they rapidly advance to a maximum.

4. It is not possible to stimulate a heart brought to stand still by digitalin, to beat by mechanical means.

5. When the action is well pronounced, a large part of the time occupied in the systole of the ventricle is taken up in *maintaining* contraction when that is complete.

6. Digitalin neutralizes the action of various chemical agents which, when applied to the heart, tend to cause undue diastolic relaxation—(e.g., Pot. Carb.)

7. A ventricle brought to stand still by digitalin is unusually small, hard and pale ("tonic" contraction).

NICOTIN IN 1 PER CENT. SOLUTION.

The effects of this agent I have found somewhat variable. A comparison of my different experiments will, I think, justify the following general statement :

1. The effect of nicotin has generally been arrest of the heart in diastole for a variable, but brief, interval ; when actual arrest has not taken place, the beat has been much weakened and the rhythm slowed.

2. This condition is usually followed by irregularity and an increased rhythm, without much damage to the force of the beat.

3. The different parts of the heart may not act with their usual proportionate force or frequency. There may be two or more beats of the auricle for one of the ventricle, etc. (In-coördination.)

4. The fish's heart shows a remarkable power to recover entirely from the effects of nicotin.

VERATRIA IN RATHER LESS THAN 1 PER CENT. SOLUTION.

It is much more difficult to define the action of Veratria than that of Digitalin, though the *eye* readily appreciates differences. In general, the beat has that sluggish appearance seen after pilocarpin is used, but in other respects veratria is very unlike that drug in action. One of the most marked effects is the tendency to throw the parts of the heart and even parts of the ventricle out of harmony with each other, e.g., the central portion of the

ventricle is sometimes seen to be more relaxed than the rest of it ; the auricle often, after the action has lasted some time, gives several beats to one of the ventricle. It is also clear that the diastole takes place in a very sluggish way, quite unnatural to the fish's heart.

The effect on the diastole is certainly much greater than on the systole. In some phases of this action, at least, the systole is strengthened. In consequence of this effect on the diastole, the rhythm is slowed. We may put the salient points of its action thus :

The principal action of veratria is on the diastole, which it renders more sluggish ; the effect on the systole is slight, and possibly variable with the phase of action of the poison ; as a consequence of its effect on the diastole, the rhythm is slowed. Want of harmony between the different parts of the heart and different fibres of the same part is liable to manifest itself.

CHLOROFORM (UNDILUTED.)

Attention is asked to the following extract from my notes, with a view of showing the action of this drug, and of pointing out how different is the behaviour of the auricle proper and the sinus-extension (connecting sinus proper and ventricle) :

Exp.—Four to five drops of chloroform applied to heart. Auricle stopped at once ; ventricle continuing to act longer ; latter gradually getting weaker, stops ; later sinus-extension beating. A second application, especially to the sinus-extension and sinus, leads at once to a dead stop of the whole heart in diastole. Ventricle recovers first, and sets up by its rhythm a beat of the auricle (*i.e.*, after its own beat.)

Generally the whole heart recovers from the effects of the drug.

It is thus seen that undiluted chloroform is a powerful cardiac depressor ; that its readiest effect is on the auricle proper ; that it can arrest the heart in diastole, but that this organ has considerable ability to recover from the effects of this agent.

ACETATE OF STRYCHNIA IN 1 PER CENT. SOLUTION.

From a limited number of experiments with this poison, it appeared that it had the power to shorten the diastole and

lengthen the systole, and slow the rhythm ; after arrest of the heart, it was still excitable by mechanical means.

It may be stated that in an area of the ventral wall of the ventricle, extending across it from the point of junction of the auricle, a behaviour, under the use of drugs, is witnessed different from that of the rest of this part of the heart. Sometimes it seems more dilated ; at all events, it appears to be more susceptible to the influence of certain drugs and poisons (nicotin, chloroform, etc.) than the rest of the ventricle, but whether there is here difference in structure has not been determined. On hearts so sensitive as those found in the sharks and skates, drugs and poisons act with remarkable celerity.

