THE OXYGEN CONSUMPTION OF THE TORTOISE HEART: ITS DEPENDENCE UPON DIASTOLIC VOLUME AND ON THE MECHANICAL CONDITIONS OF SYSTOLE.

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THE present investigation is an attempt to verify whether heart muscle behaves in respect to the liberation of energy in a way similar to skeletal muscle.

The amount of energy set free in a single twitch or a short tetanus is dependent on the initial circumstances of the muscle, as well as on those it encounters after the stimulus is over [Fenn, 1923]. The mechanical conditions of the muscle, in fact, throughout the duration of contraction, play a very important rôle; and it has been found that the performance of work is associated with the mobilization of extra energy, in an amount which, under certain circumstances, is nearly equal to the work done. Also the length of the muscle fibres, which had long been recognized to have at the moment of stimulation a great influence on the liberation of energy, has been found to play a part at later stages, or, more generally, throughout the whole period of the mechanical response of the muscle [Fenn, 1923; Hartree and Hill, 1928; Hill, 1930; Fischer, 1930].

While these facts are definitely established in the case of skeletal muscle the same cannot be said in the case of the heart. In the literature, in fact, there is no agreement on this point: recent work tends rather to show that the process of contraction in heart muscle is profoundly different, that in the heart (contrary to skeletal muscle) the amount of energy liberated in a systole is not affected in any way by the conditions under which the latter occurs, neither by the work performed nor by the fibre length throughout; but that it depends exclusively on the initial mechanical and physiological circumstances existing at the moment when stimulation occurs.

Rhode [1912] studied the oxygen consumption of the left ventricle

of the isolated mamalian heart, perfused with Ringer's solution under a variety of conditions. Comparing the isometric with the isotonic systole, he noticed that the latter used up less oxygen than the former, the difference being, however, very small, of the order of 5 p.c.; and he did not pursue the problem further.

Lüscher [1920] was the first to do the same research on the frog's ventricle with a strict control of the diastolic volume: he found that, all other conditions remaining constant, the amount of oxygen consumed in a systole was not fixed once for all by the diastolic volume, but varied according to the mechanical conditions of the systole itself. From his figures it may be reckoned that at the same initial volume an increase of the arterial resistance from say 10 to 40 mm. Hg would raise the oxygen consumption by as much as 20 p.c. about.

The results of Rhode and of Lüscher, however, were not confirmed by subsequent investigators; Starling and Visscher [1927], using the technique of the heart-lung preparation, investigated the oxygen consumption of the dog's heart at various diastolic volumes, various arterial resistances and different outputs; they found that when all other conditions of temperature, heart rate, etc., remained unchanged, the amount of oxygen consumed was determined only by the diastolic volume, while the arterial resistance and the output had no detectible effect upon it.

These results have been confirmed by Hemingway and Fee [1927] on the dog's heart.

Clark and White [1928 a], from a research on the frog's heart, have arrived at the same conclusions.

The essential difference in the regulation of the energy liberation in the two kinds of muscles, if definitely confirmed, would be of great theoretical importance for an understanding of the process of contraction. The facts described in the present paper, however, do not support the idea that such a difference exists. On the contrary they are in fairly good agreement with what has been found in skeletal muscle. The probable reason why some investigators failed to recognize this will be discussed below.

This research has been carried out on the isolated ventricle of the tortoise heart, whose oxygen consumption was taken as a measure of the energy mobilized; it deals with the energy associated with the performance of work. In a second series of experiments an attempt has been made to calculate the influence of the initial fibre length *per se,* i.e. independently of the work the muscle performs at any initial length. In order to follow the oxygen consumption in detail over long periods

of time, and also to check or modify the mechanical conditions of the systole without greatly interfering with the functioning of the organ, a new apparatus was used, to be described below.

METHOD.

For the study of oxygen consumption the method employed was that of estimating directly the amount of that gas taken up by the heart from a closed atmosphere of the same. The heart was surrounded by oxygen and perfused with Ringer in diffusion equilibrium with the atmosphere around the heart; the diffusion of oxygen into the organ, therefore, took place both directly through its external surface and indirectly through the perfusing fluid and the internal surface.

The CO_2 formed in the heart and escaping into the air was promptly absorbed by 20 p.c. KOH, and the volume of oxygen used was read in terms of diminution of pressure on a water manometer.

In the methods used by Weizsäcker [1911], Lüscher [1920], Clark and White [1928 a], the frog's heart, perfused with oxygenated blood or Ringer blood, was immersed in paraffin oil to prevent diffusion of oxygen from the external surface. In this way the outer layers of the ventricular wall are under rather unfavourable conditions, so far as both the supply of oxygen and the removal of CO_2 are concerned; and the case would be still worse for the tortoise's heart whose ventricular wall is much thicker. This would be so especially when, as was the case in my experiments, the heart is not perfused through the coronaries, but directly through its internal surface.

The same technical error is also present in the methods of Bodenheimer [1916] and in the second method of Clark and White [1928 a] in which the heart is surrounded by oxygen-free saline or Ringer; here too the outer layers of the ventricle are in unfavourable conditions as regards their oxygen supply, with the additional disadvantage that if the consumption of oxygen be small and consequently its tension on the outer surface above zero, oxygen diffusion will take place into the surrounding liquid, thus introducing a corresponding error in the calculation of the amount of that gas consumed.

In all the above-mentioned methods there is still another source of error, derived from the fact that whether the heart be perfused with Ringer's solution or with blood, there is always a filtration of colourless liquid from the heart independent of any mechanical damage of the heart walls. The amount of liquid transuding in this way is not at all negligible; it varies from heart to heart, and in the same heart it depends

on different conditions, such as the venous and the arterial pressure, the time which has elapsed from the beginning of the experiment, etc. In the case of a tortoise heart of 4 c.c. diastolic volume perfused with Ringer plus 10 p.c. blood it can amount to as much as 0·4 to 0·6 c.c. per hour, sometimes even more. Now the tension of oxygen in the escaped liquid is not the same as in the fluid remaining inside the heart; it is obviously less. It follows that when the consumption of oxygen is calculated from its tension in a known amount of liquid before and after perfusion of the heart, as is done in the methods of Weizsäcker, of Lüscher, and of Clark and White, the oxygen consumption itself will be reckoned smaller than it actually is, owing to the fact that the liquid at the end of the perfusion period is, so to speak, more concentrated than at the beginning; and the error will be the larger the smaller the volume of liquid employed for the perfusion. In the method used in the present investigation such a source of error has been avoided; moreover, by keeping the outer surface of the heart in contact with oxygen, a sufficient supply of this gas has been insured, as is shown by the fact that the heart could maintain at a constant level its mechanical performance and its oxygen consumption, throughout periods extending sometimes over several hours.

The apparatus used is shown in Fig. 1.

It consists essentially of two chambers A and B, the venous reservoir and the heart chamber respectively, in free air communication with each other through the connecting tube a. c is the venous and d the arterial tube. The two valves K and J allow the movements of the perfusing fluid in one direction only.

During diastole the liquid from A runs along the tube c into the heart which then increases in volume and forces an equal volume of air from chamber B into chamber A through the connecting tube a; during systole the air is drawn back into chamber B. In this way not only the pressure in the two chambers is maintained at the same level throughout, but also the air in the whole system is kept well stirred, thus quickening both oxygen equilibration and the absorption of CO_2. The stirring is further insured by the fact that the tube a is of a small bore (3 mm.), and thus the air enters the two chambers alternately at a considerable speed.

For the absorption of CO_2 filter paper soaked in 20 p.c. KOH is placed on the walls of chamber B and of the upper part of chamber A; moreover the small bulb inserted along tube a is filled with soda-lime renewed at the beginning of each experiment.

The venous reservoir can be raised or lowered according to the venous pressure wanted. The arterial resistance is increased by compressing the rubber portion of the arterial tube with a screw clamp. The contractions thus obtained are therefore of the so-called auxotonic type.
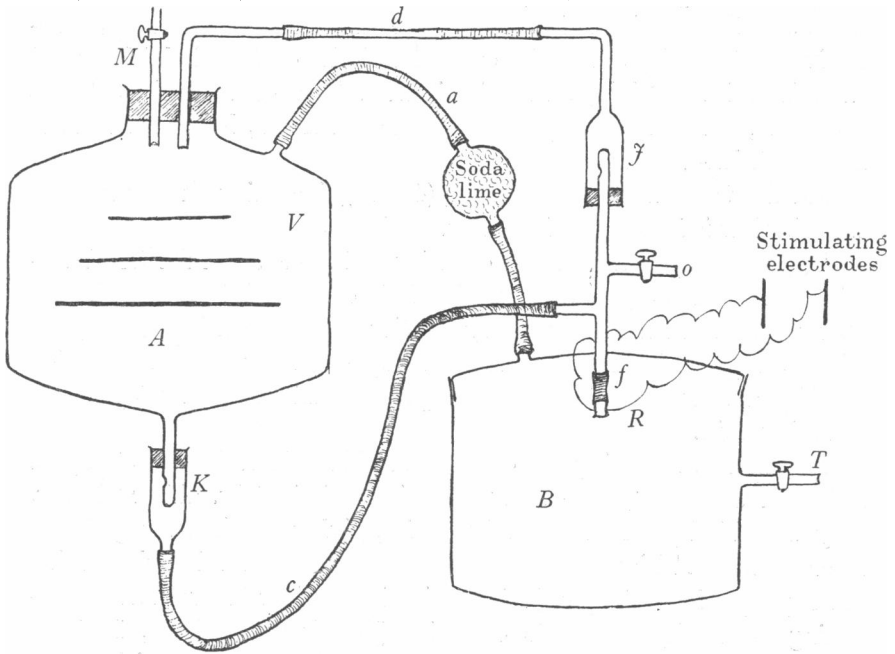

Fig. 1. Apparatus for measuring the oxygen consumption of the tortoise ventricle. *A*, venous reservoir, *B*, heart chamber, *c* and *d* respectively the venous and the arterial tube, with the two valves *K* and *J*. *A* and *B* are in free air communication through *a*. The lateral tube *o* on the arterial side, leads to a membrane manometer for recording the intraventricular pressure. Tube *T* connects the apparatus to a Barcroft differential manometer or to a piston recorder; the latter is the case when changes in volume of the heart are to be recorded; for this purpose *a* is temporarily clamped, and *M* opened to a large oxygen reservoir at barometric pressure and at the same temperature of the apparatus. The heart is tied round the short cannula *R* and fixed to the apparatus in *f* by means of a short piece of thick rubber tube. The perfusing fluid, on entering *A* from *d* spreads over the three small discs *V* before falling to the bottom of the vessel. The heart in all the experiments was driven at constant rate by means of single induction shocks.

The side tube *o* near the heart leads to a sensitive membrane manometer for recording the intraventricular pressure. When a record of the volume changes of the heart is wanted, tube *a* is clamped; chamber *A* is open to the air or to a large reservoir of oxygen at barometric pressure

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through tube M, and the heart chamber B thus transformed into an oncometer is put in communication with a piston recorder. The simultaneous records of volume and pressure changes during systole give an indication of the work done per beat. If now the venous inflow be temporarily stopped by clamping tube c so that fluid cannot reach the heart and the arterial resistance drops to zero, the organ at each successive beat expels some of its content and the cavity diminishes until the volume is zero giving a base line in the volume curve. The apparatus is of glass, except in some parts of the three tubes a, b and c which are made of thick-walled rubber tube.

All the tubes have a large bore (4 mm.), including the small glass cannula that is introduced into the ventricle.

The whole apparatus has a capacity of 170 c.c., and for the determination of the oxygen consumption it is connected to a branch of a Barcroft differential manometer, the other branch of which is connected with a compensating bottle of the same capacity as the apparatus which contains a volume of sterile water equal to that of the heart plus the perfusing fluid.

Before use everything was carefully sterilized. Tortoises of 5 to $5\frac{1}{2}$ in. in length were used, male and female indiscriminately. After pithing, they were bled from the carotid arteries, giving on the average 10 to 15 c.c. of blood. This was defibrinated and added to the Ringer's solution in the proportion of 10 p.c. (this dilution is sufficient to avoid the supervening of the hypodynamic condition [Clark and White, 1928 b]). A cannula was introduced into the ventricle through the auricles after the A.V. valves had been cut and a ligature tied around the A.V. groove. The small cannula is shown in Fig. 1, R; a short piece of rubber tube is attached to it, so that when the heart has been thoroughly washed inside and out, it can easily be fixed on to the apparatus at f.

Usually 30 c.c. of liquid of the following composition was employed for the perfusion; it was poured into the venous reservoir as soon as the heart was in the apparatus:

NaCl	...	...	...	...	0·65 p.c.
KCl	...	...	...	...	0·015 p.c.
CaCl$_2$	...	...	...	...	0·013 p.c.
P (as sodium phosphate)		...	...	0·010 p.c.
pH	...	...	...	...	7·4

The whole apparatus was then closed and immersed in a water bath at constant temperature together with the compensating bottle. Oxygen

was passed through for some minutes in order to replace the air with that gas and then the apparatus was connected with the manometer.

Every one or two hours the oxygen consumed was replaced from a reservoir in the same water bath.

As seen in Fig. 1 the manometer was connected with the heart chamber, and through tube *a* indirectly with the venous reservoir. Owing to the movements of the perfusing fluid from one chamber to the other during diastole and systole, there was always a small oscillation in the water manometer, but this was so small as not to represent any serious hindrance in the taking of the readings (0·2 to 0·3 mm.); there was, therefore, no need to cut off the manometer from the apparatus every time, although this could easily be done whenever the greatest accuracy was wanted.

The periods over which measurements were taken usually lasted from 40 to 60 minutes. During these periods manometer readings were taken every 5 minutes, and all conditions of temperature, heart rate, diastolic volume, arterial resistance and output remained constant; at the beginning and the end of each period pressure and volume records were taken. After a change in the arterial resistance or in the diastolic volume it generally took 5 to 10 minutes before steady readings were obtained.

The venous reservoir *A* has three small discs over which the liquid coming from the heart spreads before falling down to the bottom of the vessel, thus quickening equilibration with oxygen and liberation of CO_2; to further insure these two processes, the venous reservoir itself was kept shaken the whole time by means of a small motor.

If all the manipulations be carried out under rigid aseptic precautions and the perfusion fluid renewed every morning, it was possible to extend each experiment over several days. In such cases the heart (in the apparatus) was left overnight in a cold store at 2° to 3° C. In some experiments, in fact, a well-marked effect of work upon the oxygen consumption was still present on the fourth day of experiment on the same heart.

Tortoise blood was generally used, except in a few instances in which ox blood was employed instead, without any noticeable difference in the results.

To study the influence of work upon the energy liberated by muscle two methods have been followed by previous workers: (*a*) the comparison between the isometric contraction and the contraction in which the muscle is allowed to shorten and perform work, and (*b*) the com-

parison between contractions in which different amounts of work are done [Fenn, 1923; Hartree and Hill, 1928; Hill, 1930].

The first of these two methods assumes that the length of the single fibres in the isometric contraction remains absolutely constant throughout, and that consequently no work is performed. This, however, has been shown to be valid only in exceptional cases, such as that of the thin, parallel-fibred frog's sartorius when stretched to a certain extent; commonly, however, internal work is done by the muscle when contracting "isometrically."

In the present research the "isometric" systole has been studied only very little, since here the difficulty of getting a true isometric condition would have been great; the energy which accompanies the performance of work has been investigated by making the heart perform different quantities of work at the same diastolic volume. From the curve of the oxygen consumed plotted against the work it is then possible to study the relation between the two.

From the same curve, by extrapolation, the oxygen consumption of the heart contracting isotonically against zero resistance, and performing no work, can also be predicted. This last condition could best be compared with an ideal isometric systole; but it is not to be expected that the energy set free in the two cases will be the same owing to the different length of the muscle fibre which remains constant in one case while it undergoes considerable change in the other.

The Effect upon the Oxygen Consumption of Varying the Work at Constant Diastolic Volume.

In this series of experiments the work per beat was varied by varying the arterial resistance. In each experiment the diastolic volume was kept constant by adjusting the venous pressure to such a level that a period of diastasis should always precede the onset of systole; under these conditions the diastolic intraventricular pressure at the end of diastole remained the same, as long as the height of the venous column was not altered. This was about 10 cm. above the level of the heart, so the diastolic volumes investigated here were all submaximal.

In all the experiments several arterial resistances were used, ranging from a minimum of 12 to 15 cm. to a maximum of 45 to 60 cm. of water; beyond these last limits in most of the hearts the output was very small, resulting in the stagnation in the ventricular cavity of a large volume of liquid at diminished tension of oxygen and increased tension of carbon dioxide.

To avoid the establishment of such conditions, that as we know from the work of Gray [1924] and of Clark and White [1928 *b*] would have affected both the mechanical performance and the oxygen consumption of the organ, in every experiment the maximum arterial resistance investigated was such as would not interfere too seriously with the output per beat.

The periods of increased arterial resistance lasted from 40 to 60 minutes, and were alternated with periods of low resistance, the consumption of oxygen during the latter being then taken as a base with which to compare the oxygen used at the higher resistances. In this way the effects of fatigue were eliminated.

The temperature, which was constant for each experiment, varied from 12° to 18° C. Out of twenty-nine experiments, six gave negative results: the oxygen consumption was very little, if at all, influenced by the arterial resistance, and the only determining factor seemed to be the diastolic volume which had a very pronounced effect. The six hearts that behaved so exceptionally had been taken from very weak tortoises coming from an ill stock, as was realized afterwards. This is a very interesting fact, because all those hearts that gave a positive result on the first day of survival still showed the same behaviour of the oxygen consumption in respect to work several days after the removal from the animal. It would seem therefore that the conditions under which the hearts worked in the apparatus were very satisfactory in maintaining their normal physiological activities.

In all the other experiments, on the other hand, an increased consumption of oxygen was constantly observed on increasing the arterial resistance and therefore the work; and in most cases between increase of oxygen consumption and increase of work there was a very clear, constant relationship as is shown in Table I (*a*) and (*b*), where the results are given of two typical experiments taken from among a series of eighteen all similar experiments, differing from one another only in the value of the ratio (increase of oxygen)/(increase of work). Exp. (*a*) was performed on the day in which the heart had been taken from the animal; Exp. (*b*) was performed after 30 hours of survival of the organ. The work per beat was calculated from the simultaneous records of the volume and pressure changes during systole. Since the contractions were of the auxotonic type, *i.e.* the pressure was not constant throughout, both pressure and volume curves were first divided into smaller parts, each fraction of diminution of volume multiplied by the corresponding mean pressure and the separate small products finally summated. The

TABLE I. Data of two typical experiments to show increase of energy set free with increase of work at constant diastolic volume (from these data Fig. 2 and Fig. 3 were constructed).

(a) Exp. 6, on the first day of survival of the excised heart. Heart weight 1·40 g.; heart rate 14 per minute; temp. 17·5° C.; diastolic volume of ventricular cavity 3·25 c.c.

Mean arterial resistance: cm. H_2O	Output per beat: c.c.	Work: g.cm. Per beat	Work: g.cm. Per hour	O_2 consumed per hour: c.c.	Energy: g.cm. per hour	Efficiency W/E p.c.
15	3·10	46	38,500	1·30	280,000	13·7
25	2·95	74	62,000	1·56	328,000	18·9
30	2·80	84	70,000	1·63	348,000	20·0
45	1·95	88	74,000	1·66	357,000	20·7

(b) Exp. 17, on the second day of survival (similar results had been obtained the day before). Heart weight 0·60 g.; heart rate 9 per minute; temp. 13° C.; diastolic volume of ventricular cavity 1·30 c.c.

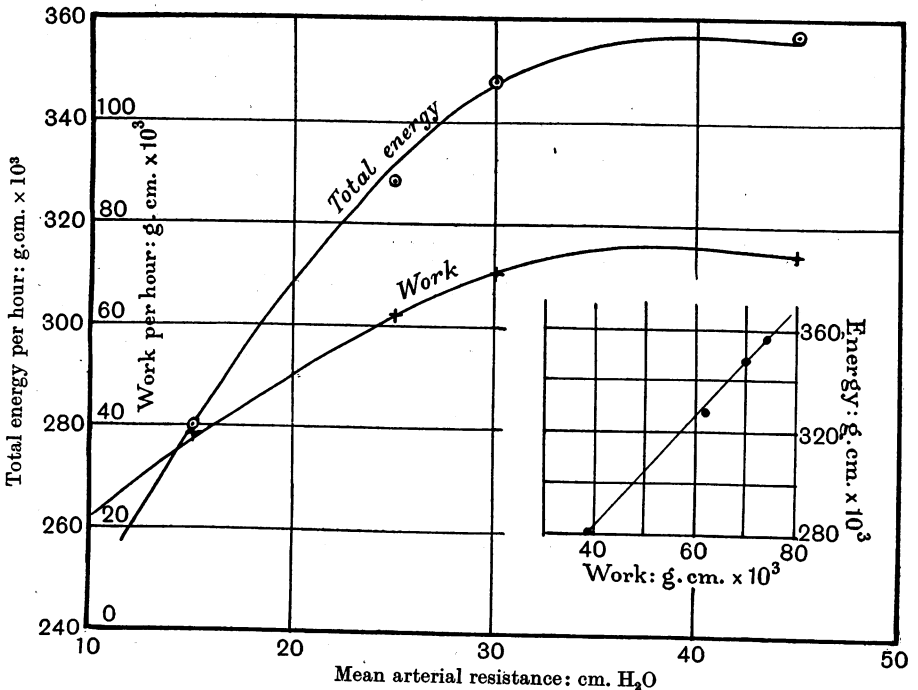|						
15	1·20	18	9,750	0·445	95,500	10·3
30	1·15	35	18,900	0·560	120,000	15·8
40	1·05	43	23,150	0·610	131,000	17·7
50	0·93	46	24,700	0·650	140,000	17·6
60	0·73	44	23,700	0·650	140,000	16·9

Fig. 2 [from the data of Table I (a)]. Variation of work and total energy with increasing resistance. The energy increases more than the work. Inset: total energy per hour plotted against work per hour to show the linear relationship between the two. The ratio (increase of energy)/(increase of work) was in this experiment 2·0.

value seen in the table under the heading "mean arterial resistance" is the quotient (work)/(output) and was given as a rough indication of the average arterial pressure during the period of systolic ejection.

The work is given in g.cm.; column 6 gives the total energy set free in an hour, calculated from the amount of oxygen used, on the assumption that 1 c.c. of oxygen corresponds to 216,400 g.cm., as would be the case if all the energy set free by a muscle were derived from glycogen. The ratio W/E is the "oxidative efficiency" of the heart.
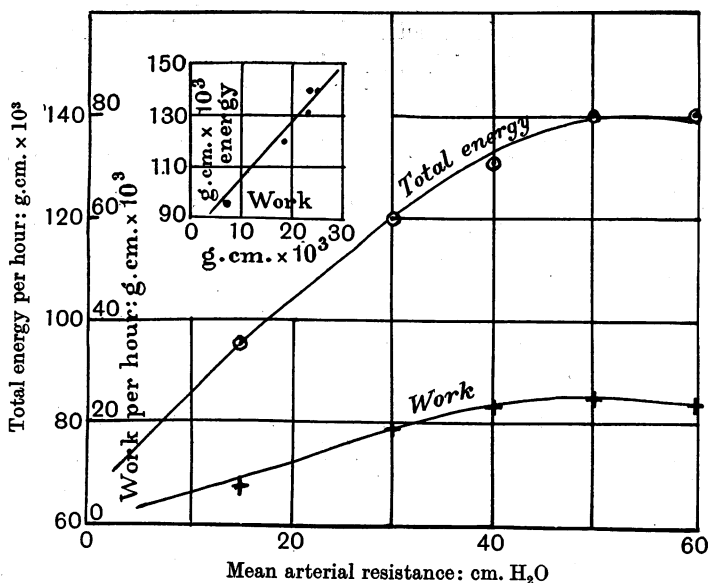

Fig. 3 [from the data of Table I (*b*)]. For description see Fig. 2. The ratio (increase of energy)/(increase of work) was here 2·65. The heart on which this experiment was performed had been working in the apparatus for 30 hours. The day before it had given results similar to those shown, and overnight it had been kept in a cold store at 2° C. with a small venous pressure and low arterial resistance in order to reduce for the time its energy expenditure.

Table I shows that as the work increases, both the oxygen used and the efficiency increase. In Exp. (*a*), for example, an increase of work per hour from 38,500 to 74,000 g.cm. caused an increase of the oxygen used from 1·30 to 1·66 c.c., and the efficiency went up from 13·7 to 20·7 p.c.

The relation between arterial resistance, work, and energy liberation is best seen in Figs. 2 and 3, constructed from the data of Table I (*a*) and (*b*) respectively. The figures show that with increasing arterial

resistance the work increases at first rapidly, then less rapidly, and becomes nearly constant at resistances of 40–60 cm. of water; beyond this it would fall again as is the case with skeletal muscle (and as was confirmed for the tortoise heart by E. Peserico [1928]). The curve of energy, calculated in the way described, follows a very similar course, only it rises more steeply than the curve of work; it reaches a maximum at about the same arterial resistance as the former, and after that it runs horizontal for the rest of the resistances investigated. It is not possible here to state with any certainty how the curve would run at still higher resistances, *i.e.* whether it would remain at the same high level while the work diminishes, or if it would drop down as the work does; a few experiments, however, in which the heart was made to beat isometrically at every second systole, by clamping the venous and the arterial tubes, seem to indicate in confirmation of the findings of Rhode [1912], that the energy does drop to some extent, but not to a level as low as that corresponding to the smaller resistances investigated. The difficulty, however, of obtaining true isometric contraction from the heart takes away much of the importance of this observation.

In the inset of the two figures the total energy has been plotted against the work. The relation between the two is very nearly linear over the whole range of work that the heart can perform, when made to contract against increasing resistances, from the same initial volume. From what has been said above, it is very likely that at resistances higher than the optimum, the work would decrease relatively much more rapidly than the energy and that the relation between the two would be quite different from that represented in the figures; this, however, does not diminish the importance of the results actually obtained, which clearly show that under the experimental conditions described when the heart performs work, an extra amount of energy is set free proportional to the work itself.

The ratio (increase of energy)/(increase of work) was 2 in the experiment of Fig. 2 and 2·65 in that of Fig. 3, the average value for all the experiments on the subject being 2·90. Thus the extra energy is about three times as large as the work, but we know [A. V. Hill, 1922] that in a contraction the energy available for conversion into mechanical potential energy and work is derived only from two-fifths of the total energy in oxygen (*i.e.* from the part that represents the anaerobic energy), the remaining three-fifths playing a part only in the recovery process. Therefore in order to get more information on how the extra energy is utilized, it is necessary to multiply by 2/5 the value of 2·90

given above for the ratio (aerobic energy)/(work): one thus obtains a value of the ratio (increase of anaerobic energy)/(increase of work) as low as 1·16: the extra energy is only slightly greater than the work.

Similar results have been described for the frog's sartorius by Fenn [1923] who, under favourable conditions, found a value for this ratio of 1·30. More recently A. V. Hill [1930], also on the frog's sartorius made to contract isotonically against increasing loads, often found a clear parallelism between the work and the anaerobic energy set free in a twitch.

There is evidently a very close agreement between the results for the sartorius of the authors just mentioned and those described here for the tortoise heart; the heart muscle, therefore, in this respect does not seem to differ essentially from skeletal muscle.

THE EFFECT UPON THE OXYGEN CONSUMPTION OF VARYING THE WORK AT CONSTANT ARTERIAL RESISTANCE.

In this series of experiments the arterial resistance was kept constant at a low level (12–15 cm. H_2O) and the work varied by varying the diastolic volume. This was done by leaving the venous reservoir stationary and screwing or unscrewing the venous tube leading to the heart. Only at the maximal diastolic volumes investigated was there a period of diastasis before the systole; in the case of all the smaller volumes, stimulation occurred during diastolic filling, interrupting the latter at different levels.

As in the experiments on the effect of the arterial resistance, each period of constant diastolic volume lasted from 40 to 60 minutes, and volumes and pressure records were taken at the beginning and end. As usual, manometer readings were taken every 5 minutes throughout.

According to Clark and White [1928 a] the relation between diastolic volume and oxygen consumption in the frog's heart is a linear one. Approximately the same result was obtained here on the tortoise heart, provided the arterial resistance was maintained constant; the relation, however, is not exactly linear, in fact the line showing the energy calculated from the oxygen used is slightly curved with the concavity towards the horizontal axis, as is the case in the experiments represented in Figs. 4 and 5; and still more in about 50 p.c. of all the experiments. The two figures show that as the initial volume of the heart increases both the work and the energy liberated per unit of time increase, the latter much more rapidly than the former; the efficiency

also increases, as can be reckoned from the ratio (work)/(energy) at any diastolic volume, but to a much smaller extent than in the case of the experiments described in the last section, where the work was always performed at the same diastolic volume. Under the experimental conditions an increase of the diastolic volume was always accompanied by the performance of a larger amount of work, which is itself capable of causing a greater output of energy, as was shown above. The effect
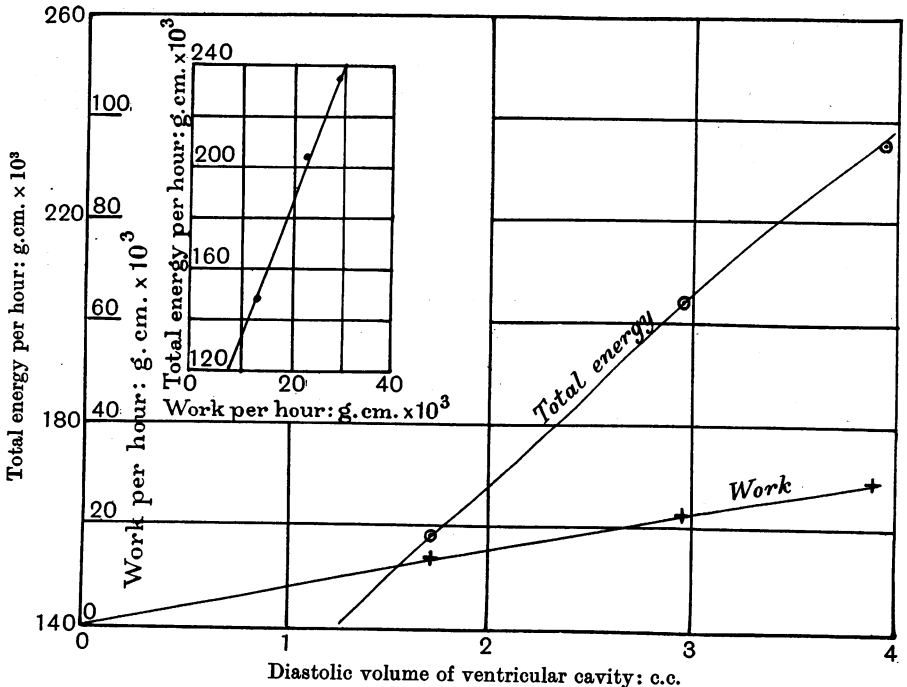

Fig. 4. Increase of work and of total energy with increasing diastolic volume. Arterial resistance constant at 15 cm. H_2O. Heart weight 1·00 g.; heart rate 9 per minute; temperature 13° C. Experiment performed on the first day of survival of the heart. Inset: total energy plotted against work.

therefore of an increase of initial volume on the liberation of energy is here to be ascribed to at least two factors (a) the greater length of the muscle fibres of the heart, and (b) the larger amount of work which has been made possible by the greater fibre length.

No experiments have been made on the influence of work upon oxygen consumption at constant diastolic volume except in the case of submaximal diastolic volumes, and it is therefore impossible to distinguish with certainty in the experiments of Figs. 4 and 5 what is to

be attributed to the work and what is to be explained as a direct effect of the fibre length, independently of the work they actually performed.

By analogy with what has been found in the case of skeletal muscle, it seems justifiable to assume that as long as the resistances against
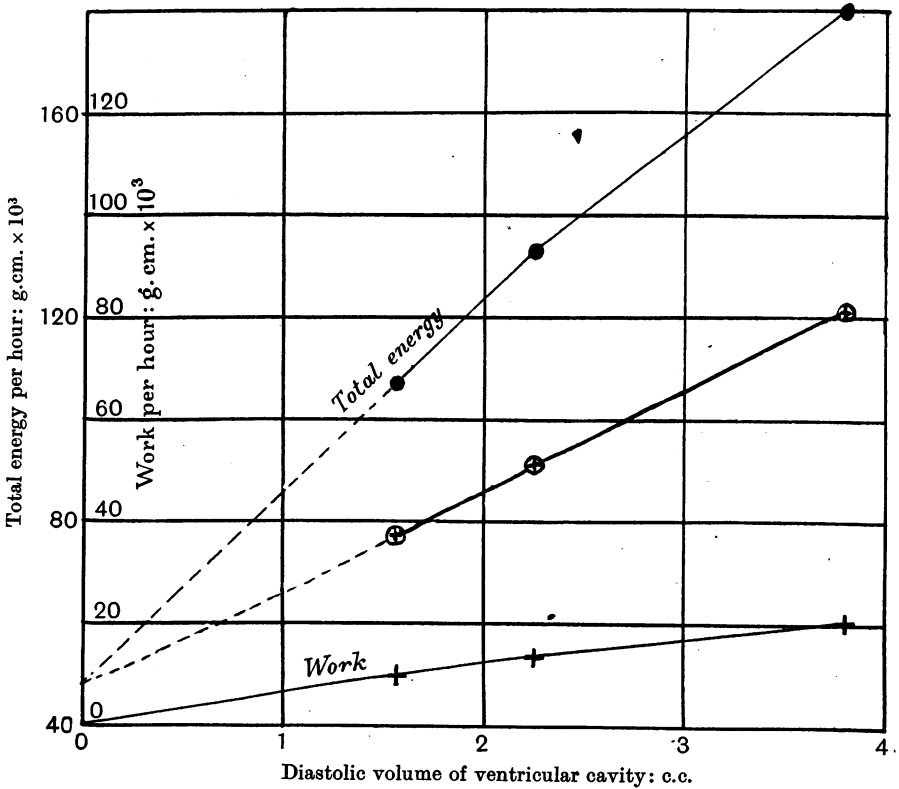

Fig. 5. Experiment similar to that of Fig. 4; heart weight 1·00 g.; heart rate 8 per minute; arterial resistance 12 cm. H_2O; temperature 13° C. The middle curve was calculated by subtracting from the total energy at any diastolic volume, the part due to the work according to the formula [(increase of energy)/(increase of work) = 2·9]; it represents how the energy would have increased if only the diastolic volume had been responsible for the increase; and shows the effect of the initial fibre length *per se*.

which the heart contracts are not above the limits at which the work begins to decrease, the relationship between work and energy does not alter to a great extent with altering the diastolic volume. In fact Hartree and Hill [1928] have described experiments on the frog's sartorius which show that in the case of short tetanic contractions the extra energy (anaerobic) is equal to work done, with various conditions

of initial length and of load; and very recently A. V. Hill [1930] has shown that in the case of single twitches also the frog's sartorius, under favourable conditions of load, liberates an extra amount of energy very nearly equal to the work performed (even at those initial lengths at which the energy liberated in a free isotonic contraction is smaller than that in the isometric).

Assuming now, that the extra energy set free by the heart to meet the demands of work always bears the same relation to the latter, namely 2·9 (as given above) whatever the diastolic volume, it is possible to get a rough idea of the pure influence of heart volume by subtracting from the total energy liberated at increasing initial volumes the part due to the work done at any volume. In Fig. 5 the top and bottom curves pass through the points actually observed, while the middle curve has been calculated in the way just described and shows how the energy would have increased if only the diastolic volume had been responsible for it. It thus represents, therefore, the amount of energy liberated by the heart at any diastolic volume when the arterial resistance is zero and the work zero too, or in other words when made to contract isotonically at tension 0. The influence of the diastolic volume upon the energy liberation is clearly considerable. The initial fibre length *per se,* however, is very likely not influencing only the amount of energy liberated in contraction, it is indeed more probable that the resting metabolism also is largely affected by the heart volume, especially since we know from the work of Clark and White [1928 a], that the latter plays a not insignificant rôle in the total metabolism of this viscus.

CONCLUSION.

The view put forward by Starling and Visscher [1927] that "under all conditions of load, output and fatigue the total energy liberated at each beat of the heart is determined by its diastolic volume and therefore by the fibre length at the beginning of contraction" is not confirmed by the results of the present research. It has been found in fact that here, as well as in the case of the skeletal muscle, the performance of work is accompanied by the liberation of energy; and consequently that the initial conditions of the organ are only some of the factors determining the total energy set free. Under the conditions studied here the extra energy associated with work was fairly well proportional to the work itself; this implies that the fibre length after the moment of stimulation had a much smaller effect; or in other words that the work represented the preponderant factor [Hill, 1930].

It seems, therefore, that in the special instance of the heart also, the idea that work is done by a muscle at the expense of its elastic potential energy can not be held [Fenn, 1923; Hill, 1930]. In Figs. 2 and 3 of this paper it is seen that there exists a range of arterial resistances within which the work and the energy vary only very little; presumably Starling and Visscher [1927] and Clark and White [1928 a] failed to detect any influence of changes of the arterial resistance upon the oxygen consumption, because they happened to keep within this region which is in fact quite large. Apart from the importance of the results here obtained, in so far as they show that no essential difference exists between heart muscle and skeletal muscle in relation to the mechanism of the contraction, the conclusions that can be derived from them as to the efficiency of the heart according to the conditions under which it works, are also of great interest:

(a) When the arterial resistance is moderate, the oxidative efficiency of the heart increases, although only slightly, as the diastolic volume increases from its minimum up to submaximal values.

(b) At the same diastolic volume there is an optimal arterial resistance at which the efficiency reaches its maximum; this arterial resistance corresponds to that at which the work per beat is also at its maximum.

(c) Comparatively large variations of the arterial resistance, above and below the optimum, affect the work and the efficiency only slightly (at constant diastolic volume).

(d) If, however, these variations are beyond a certain limit the work decreases considerably and the efficiency drops to a great extent. In the cases investigated the region of comparatively constant efficiency extended between 40 and 60 cm. of water; with resistances between 40 and 15 cm. of water the efficiency decreased by about one-half; it may be presumed that with resistances above 60 cm. of water the efficiency would go down even more for the same work. The significance of these results, if confirmed for the mammalian heart, need not be emphasized.

The maximum "oxidative efficiency" recorded in the present experiments was of the order of 30 p.c. In the majority of cases the optimum varied between 17 and 25 p.c. These figures are in good agreement with those given by Weizsäcker [1911] for the frog's heart.

As to the oxygen consumption per gramme per hour, it evidently undergoes large variations according to many different conditions, the diastolic volume of the heart being one of the most important factors. By way of comparison with what has been found on the frog's heart I

give here the oxygen consumption of one gramme of heart muscle when the heart has a diastolic volume corresponding to a diastolic pressure of 10 cm. of water, at the heart rate of 8 to 12 beats per minute, arterial resistance 15 cm. water, and at a temperature of 12° to 18° C. As calculated from all the experiments performed it corresponds to 1·05 c.c. per hour, a value very close to that given by Clark and White [1928 a] for the frog's heart under similar conditions.

A diminution of the heart volume to its minimum, while all other conditions remain constant, would reduce the oxygen consumption down to as little as 0·25 to 0·30 c.c. per hour; and an increase of the arterial resistance to its optimum would raise it to 1·20 c.c. per hour per gramme; the variations in the amount of oxygen consumed by one gramme of muscle in unit time are considerable.

SUMMARY.

1. A new apparatus has been described, for the study of the oxygen consumption of the tortoise ventricle working under well controlled and easily variable conditions.

2. The effect upon the total energy liberated during systole, of the mechanical conditions under which the latter takes place, has been investigated, and is found to be similar to that already described for skeletal muscle.

3. The performance of work has, in fact, been found to mobilize an extra amount of energy, fairly well proportional to the work itself.

4. An attempt to reckon the influence of the initial length of the fibres *per se*, independently of the work done, has also been made.

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