THE EFFECT OF VARIOUS MECHANICAL CONDITIONS ON THE GASEOUS METABOLISM AND EFFICIENCY OF THE MAMMALIAN HEART.

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The experiments which are described here were commenced two years ago by one of us in continuation of a previously published paper, and have recently been taken up again by both of us. In the interim the work of Patterson, Piper and Starling(1), which has thrown much light on the effect of various mechanical conditions on the work of the heart, has appeared, and has modified our point of view considerably.

In the previous paper(2) the gaseous exchanges of the heart and lungs were studied in the heart-lung preparation, and these results, in so far as the respiratory quotient and other chemical relationships were concerned, have since been confirmed and extended. The statements made in that paper however now require some revision as regards the influence of various mechanical conditions on the gaseous exchanges, and especially on the efficiency of the heart. The most important of these is the effect of alteration of work by change of output, as well as by change of arterial pressure; only the results of the latter were dealt with, at the time of publication of the earlier paper; the great range of outputs which were easily possible was not then known. There are also new points to be added with regard to the influence of venous pressure and heart volume.

Methods. The methods used were similar to those previously employed. The heart-lung preparation was prepared in the manner described by Patterson and Starling(3) with the exception that the warming spiral for blood was replaced by the inner tube of a double surface condenser, which being of thin glass had the combined advantages of more rapid and uniform heating of the blood by the warm water, of

diminished resistance to the passage of blood, and of diminished content. The first rendered it easier to maintain the blood inflow at a constant temperature—a most important point in gaseous metabolism experiments; the second effected a diminution of the minimum obtainable arterial resistance, so that we were able to obtain large outputs at low arterial pressures; while the last diminished the volume of blood essential in the artificial circuit. Better results are obtained in metabolism experiments by reducing the volume of blood as much as possible, since the possibility of the tissue drawing extensively on the blood oxygen and less on the atmospheric oxygen in the lungs is restricted. The necessary volume of blood in circulation was further diminished by the employment of a longer and narrower venous reservoir (30 cm. × 9 cm.). This was covered with felt in which a slot was cut to observe the blood level. If the heart dilated the blood level in the reservoir was lowered and *vice versa*. It was therefore possible to observe the effect of rapidly altered mechanical conditions on the volume of the heart cavities by taking note of the immediate changes of blood level in the venous reservoir which resulted when the mechanical conditions were changed. Slower changes could not be followed with any accuracy owing to the constant slow leakage of blood away from the circulation both between the ligatures and by small but evident collaterals. This slow leakage was especially marked during periods when high arterial pressures were employed.

The gaseous metabolism was determined by means of the apparatus described in the earlier paper by one of us. Generally only the oxygen usages have been determined; the carbon dioxide production is of less interest, but has been taken in a few cases, and the resulting respiratory quotient given.

The results given for the oxygen usage of the heart are in all cases corrected for the metabolism of the lungs and blood. It has been shown by Evans and by Evans and Starling(4) that for each gram of heart the corresponding lung tissue uses 1 c.c. of oxygen per hour. The heart was therefore weighed (auricles and ventricles) and deduction for the lungs made accordingly from the observed metabolism of the preparation. From the oxygen consumption of the heart we can calculate its total energy usage; Voit, and more recently Benedict and Joslin(5), find that the calorific value of one gram of oxygen is 3·4 cal. on the average. Hence if 1 cal. = 425 kilogram metres, 1 c.c. oxygen = 2·07 kgm. The oxygen figures are multiplied by 2·07 in order to obtain the energy usage in kilogram metres. The previous

value of 2·34 kgm. employed by Evans and that of 2·6 kgm. by Rohde are too high, and therefore give too low efficiency results.

The amount of work done by the heart was found from measurements of the output and arterial pressure. That for output requires a slight correction for the coronary flow.

In some of the experiments the venous pressure was determined by means of a water manometer connected with a cannula inserted into the inferior cava near to the right auricle.

The calculation of the work done by the heart.

The amount of work done by the heart in a given time can be found by the well-known formula

$$W = QR + \frac{wV^2}{2g}$$

where W = work done in kgm.; Q = volume of blood expelled in litres; w = weight of blood in kilos; R = arterial resistance in metres of blood (*i.e.* arterial pressure in mm. Hg. × 0·013); V = velocity of blood at root of aorta in m.p. sec.; g = acceleration due to gravity = 9·8 m.

The greater part of the expression is always QR, which gives the work done in expelling the blood. The expression $\frac{wV^2}{2g}$ represents the work done in imparting velocity to the blood expelled, and it has often been said that it is so small as to be negligible in comparison with the value of QR, less than 1% in fact. A consideration of the facts shows that this is only sometimes true, and that very often the velocity factor forms an important fraction of the total work. Since the value of the expression increases as the square of the velocity, and since the velocity increases (roughly) as the output, it follows that whereas QR varies directly as the output, $\frac{wV^2}{2g}$ must vary as the cube of the output because it varies as the products of w and V^2, *i.e.* as Q^3. Thus if the output is increased ten times, the arterial pressure remaining the same, the product QR is also increased ten times, but $\frac{wV^2}{2g}$ is increased one thousand times. The output of the heart-lung preparation can readily be increased thirty-fold from a small initial output, *e.g.* from 100 c.c. per minute to 3000 c.c. per minute, and this leads to a 27,000-fold increase in the velocity factor, which obviously can be no longer negligible. The following examples will show this:

(*a*) Let the output be 100 c.c. per min. (6 litres per hour), and the arterial pressure 100 mm. Hg. With a cannula of 5 mm. diameter in the innominate artery the velocity of the blood is 0·085 m. per sec. in passing the cannula. Thus we have

$$W = (6 \times 100 \times \cdot013) + \frac{6\,(\cdot085)^2}{2 \times 9\cdot8}$$
$$= 7\cdot8 + \cdot00223 \text{ kgm. per hour.}$$

The velocity factor is 0·029 % of the whole work.

(*b*) Let the output be 1500 c.c. per min. The velocity will be about 1·27 m. per sec. Let the arterial pressure remain constant; then

$$W = (90 \times 100 \times \cdot013) + \frac{90\,(1\cdot27)^2}{2 \times 9\cdot8}$$
$$= 117 + 7\cdot4 \text{ kgm. per hour.}$$

The velocity factor is now nearly 6 % of the total work.

The cannula which we used had a diameter of 5 mm. at its narrowest part and the greatest velocity of blood would be in passing this narrow point. In order to simplify the calculations of work done by the hearts we made out a table for use with this cannula. The table is given below, and gives the values of $\frac{wV^2}{2g}$ for various outputs from 3 to 120 litres per hour. In making the calculations we neglected the velocity factor in those cases where the output was less than 400 c.c. per min. (24 litres per hour), at which amount it has a value of ·14 kgm. per hour.

TABLE I.

Values of $\frac{wV^2}{2g}$ *in experiments where a 5 mm. cannula was used, with differents outputs.*

Output c.c. per min.	Output litres per hour	Velocity m. per sec.	$\frac{wV^2}{2g}$ kgm. per hour
50	3	0·042	·00027
100	6	0·085	·00223
200	12	0·169	·018
400	24	0·338	·14
500	30	0·423	·28
600	36	0·51	·48
700	42	0·59	·75
800	48	0·67	1·1
900	54	0·76	1·6
1000	60	0·845	2·19
1100	66	0·93	2·4
1200	72	1·02	3·83
1300	78	1·1	4·82
1400	84	1·18	6·02
1500	90	1·27	7·45
1600	96	1·35	8·95
1700	102	1·44	10·8
1800	108	1·52	12·8
1900	114	1·61	15·2
2000	120	1·69	17·5

Under normal conditions *in vivo* it is probable that the velocity factor is somewhat smaller with large outputs than it is here because of considerable distension of the aortic orifice and aorta, but in cases of aortic stenosis and arterio-sclerosis this physiological complication would be lacking or much reduced, compensation during exercise being rendered more difficult thereby.

It is evident that the value of the velocity expression becomes relatively greater in relation to *QR* the smaller the arterial pressure. Thus in the right ventricle, where, as Führer and Starling have shown, the pressure is about one-sixth of that on the left side, it forms a considerable proportion of the total work of the right side when the output is large, often amounting to 25–30 % or more. We have allowed for the velocity factor on the right side as on the left, the two being taken as equal.

The correction of output for coronary flow is made in accordance with that found in the experiments of Starling and Evans(4), viz. as 60 % of the weight of the heart per minute. This only represents a mean value and is probably rather too small for most periods, and much too small when the arterial pressure is high and when the heart, by doing heavy work, is producing much metabolites. This is shown by the results of Exp. 1 (see Protocols at end of Paper), where the coronary flow was directly measured by collection of the coronary sinus blood and subsequent calculation. Here the coronary flow amounts to as much as 212 % of the heart weight when the work of the heart is much increased.

The arterial pressure taken for the calculation of *QR* was the mean pressure given by a mercury manometer connected with the side tube of the innominate cannula. The tension set up by the systole, *i.e.* the endocardiac pressure in the left ventricle, is about 20 or 30 mm. greater than this, but for the calculation of mechanical work done we require only to know the arterial resistance against which the blood volume is expelled.

The endocardiac pressure would be a measure, though not a direct one, of the tension change in the muscle cells, *i.e.* of the energy liberated in systole. As a matter of fact the tension varies roughly as the endocardiac pressure and as the square of the radius of the heart cavities so that the endocardiac pressure would only be a measure of the tension if the volume of the heart were not altered. Even if the tension energy could be measured by the endocardiac pressure the mechanical work done would not be identical with the energy set free, since as pointed

out by A. V. Hill, some of it, or perhaps even the greater part of it, may be lost by conversion into heat unless it can be *rapidly* converted into work.

The pulmonary arterial pressure has been taken as one-sixth of the aortic, in accordance with the observations of Führer and Starling(6). The work on the right side of the heart was therefore equal to $\frac{QR}{6} + \frac{wV^2}{2g}$ where R is the aortic pressure and where $\frac{wV^2}{2g}$ is taken as the same as that on the aortic side, so that the total work of both ventricles is

$$W = \frac{7 \cdot QR}{6} + \frac{wV^2}{g}$$

which was the formula used in calculating the mechanical work in our experiments. In these experiments Q represents the output corrected for coronary flow. The values of $\frac{wV^2}{g}$ were got by doubling the figures in the last column of Table I.

It might be thought that the viscosity of the blood would be a factor that would need to be taken into consideration in estimating the work done. This is not the case however, although it is certainly an important factor in causing a difference between the energy liberated on contraction and the work which can be done by the contraction.

Evans and Ogawa(7) have shown that when the viscosity of the blood in the heart-lung circulation system is increased, the inflow into the right heart is diminished; the outflow is therefore lessened so that less mechanical work is done when it is expelled against the same arterial pressure, though it is not known whether the energy expended to do the work is increased or diminished. It is certain however that if the inflow were kept constant by suitable adjustment when the viscosity was raised, the mechanical work done would be the same, while the energy expenditure would be increased since the endocardiac pressure would need to be higher—in other words, the mechanical cardiac efficiency is lowered by increase in the viscosity of the blood. If the blood had no viscosity at all, then the mechanical work done would be at its maximum and would be more nearly equal to the energy liberated by the contractile process, because the contents of the ventricle would be instantly expelled at the end of the isometric period and the tension energy developed would be more completely converted into work. The mechanical efficiency of a heart working under such conditions would be at a maximum; it would however not reach nearly

100 %, since all of the chemical potential energy would not necessarily be converted into tension energy if the whole cardiac cycle be taken into account.

Patterson, Piper and Starling find that when the work of the heart is increased by augmented output, or more especially by rise of arterial pressure, the duration of systole is increased quite appreciably. The rate of rise of pressure in the presphygmic interval is likewise increased with high pressures, and calculation from their results indicates that the total duration of the isometric phase is not altered, so that the alteration is mainly in the period of expulsion. We suggest that the blood viscosity is a factor at work in prolonging this phase of the cardiac cycle, though we do not pretend that it is of first importance.

Weiss(8) has quite correctly pointed out that what we require to know is not merely the work done but the total effort made by the heart, what he calls the "static effort" as well as the "dynamic effort." The sum of these two would give us the total amount of tension energy set free. He indicates that the static effort is in direct relation to the area of the intraventricular pressure curve, but at the present stage of our work we can see no hope of investigating this side of the question with any accuracy. Rohde(9), it is true, has said that the energy usage of the heart is related only to the number of beats and to the tension set up under isometric conditions, but it is not easy to apply these results to the heart beating under normal conditions with execution of mechanical work.

The effect of alteration of arterial pressure.

Some experiments of this kind have been already published by one of us, but the experiments here given are more complete, and have been undertaken with a different object in view. Our present aim has been not only to show what are the effects of increased arterial pressure, but also to obtain results which would enable a comparison to be made between the effects of altered pressure and altered output. The arterial pressure was, as far as obtainable in practice, the only variable in these experiments; the output was as nearly constant as could be arranged: in some cases the conditions of inflow were kept uniform in order to ensure constancy of the total output including the coronary circulation, as shown by Markwalder and Starling(10). Exps. 2 and 3 were carried out in this way; in the other experiments no special precautions were taken to keep the level of the blood in the venous reservoir constant, though it probably did not alter more than one or two centimetres, while the other inflow conditions were not adjusted in any way;

the output was here measured in each case and the same allowance made for coronary circulation in all of them. This method gives somewhat too low results for output and efficiency at high pressures, since the coronary flow is variable with the arterial pressure, as Markwalder and Starling showed. In the example which we gave in Exp. 1 the coronary flow was increased more than fourfold, the difference amounting to nearly 5 litres per hour, though no allowance can be made for that difference here since we cannot directly measure the coronary flow, nor know the extent of its variation. The results of Exps. 2 to 4 (see Protocols) are typical of the kind of results obtained. We have not been able to investigate the effects of such high pressures as might be desirable, owing to the ease with which lung œdema comes on at high pressures; we have however been able to reach 170 mm. and maintain it for a sufficient length of time to enable an observation to be taken (Exp. 3).

The mechanical work done by the heart when the output is constant is proportional to the arterial pressure, and the oxygen consumption also increases with the pressure, as is well seen in Fig. 1 (Exp. 2). Most of the experimental results give similar curves when plotted. Sometimes the concavity of the curve is upwards, sometimes downwards, the latter being usually the case when the heart is in good condition. In either case the gaseous metabolism seems to tend sooner or later to a maximum, beyond which the heart tends to fail from inability to sustain further pressure. All the experiments of which we now speak were made with the pericardium intact, so that the diastolic volume could not pass a certain limit; this has an effect on the mechanical conditions and gaseous metabolism, as will be shown later.

The most interesting results of these experiments are those which give the efficiency values.

The mechanical efficiency figure, as already pointed out, is a measure of the completeness with which the energy expended in the muscle fibres is turned into mechanical work. In the case of skeletal muscle it has been proved by A. V. Hill(11) that the tension produced on contraction bears a constant relation to the energy expenditure. There is no reason for thinking that cardiac muscle differs from skeletal muscle in this respect. Starling, Patterson and Piper found that with increase of arterial pressure besides an elongation of the muscle fibres there was an increase in the duration of the systole, this being occupied apparently by a prolonged period of expulsion during which the endocardiac pressure rose to a maximum. One result of the increased duration of systole seemed to be that the tension change

was more completely converted into arterial pressure since their figures show a smaller difference between maximal endocardiac pressure and arterial pressure at high than at low arterial tensions. On the other hand, there was but little difference in the duration of the isometric phase in their experiments at high and low pressures. The net result of these altered conditions, as judged by our gaseous metabolism experiments, is at first an increase in mechanical efficiency with increase of arterial pressure, as may be seen from Fig. 1 (Exp. 2). We may

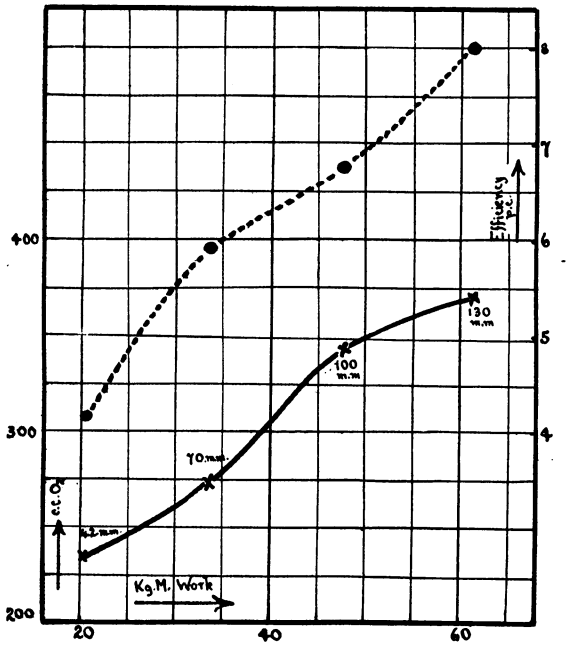

Fig. 1 (Exp. 2). Relation between work done and oxygen usage and mechanical efficiency with variable arterial pressures. Oxygen usage c.c. per hour = continuous line. Percentage efficiency = dotted line. The arterial pressures are indicated on the oxygen graph

assume that as a result of its increased length the cardiac muscle fibre sets free more energy on contraction and uses proportionately more oxygen in its recovery process, just as a skeletal muscle produces more heat and tension on isometric contraction as its initial length is increased (Evans and Hill(12)). The heart during the early part of its contraction is also under isometric conditions, and we believe our results to be in agreement with the assumption that it is during this first part of the systole that the whole of the chemical changes leading

to tension developments are consummated, the time of maintenance of a high endocardiac pressure not influencing the energy usage. When the arterial pressure is raised we have therefore two results. Firstly, the fibres elongate in order to be able to develop more tension—hence an increase in oxygen usage. Secondly, owing to the increased duration of systole there is a more complete conversion of tension energy into work and hence greater efficiency. If it were otherwise we should expect the efficiency to be lowered with rise of pressure. As a matter of fact, it does appear to fall off somewhat at high pressures, as is seen in Exp. 5 (Fig. 2). This would be explainable as due to an actual

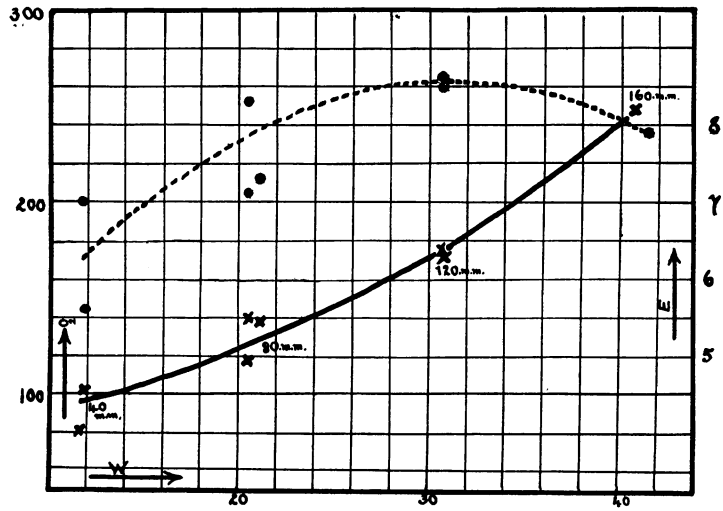

Fig. 2 (Exp. 5). Work, oxygen usage and mechanical efficiency of heart with varied arterial pressure. The oxygen used steadily increases, while the efficiency attains a maximum and then declines a little. The arterial pressures are shown on the oxygen curve.

diminution of the efficiency of the individual fibres owing to dilatation, a high energy expenditure being insufficient to set up the requisite tension in the fibres, and the duration of systole possibly being too brief for its development and conversion into work under the new conditions.

The conditions of tension production on isometric contraction in the slowly beating heart of the tortoise have recently been investigated by Kozawa (13). He finds that with increasing length of fibre there is at first an increase but on further distension a diminution in the pressure produced. Since the pressure produced varies approximately in the

inverse ratio to the square of the radius of the heart, such diminution of endocardiac pressure at increased volume does not necessarily mean that there is a diminution of tension production such as occurs in voluntary muscle. In the latter case Evans and Hill found that there was also a diminished heat production. We can find no such evidence of diminished metabolism in the mammalian heart, perhaps because it is only to be obtained under strictly isometric conditions and with such elongations as are not attainable with the mammalian heart, or perhaps because cardiac muscle does not show this phenomenon.

The results of gaseous metabolism experiments also give information with regard to the occurrence of fatigue in heart muscle. Such fatigue is of course always only relative, and is seen by lowered efficiency when a high pressure is maintained, or when the pressure is restored to a low level, the efficiency is found to be lower if fatigue is present, than it was in a previous period at corresponding pressure. Not all hearts show fatigue equally; thus in Exp. 2 there is little evidence of it, and Exp. 3 even shows an improvement, whereas in Exps. 4 and 6 there is an indication of some degree of fatigue. In Exp. 5, on the other hand, lowering of pressure in the 3 and 4 periods leads to increased efficiency in the fifth period, when the original pressure was established.

The respiratory quotient in those cases where it was determined shows considerable variation, as might be expected from the changing mechanical conditions. The general tendency is for there to be a fall of quotient with any circumstance causing an increase in the oxygen usage of the heart, and *vice versa*, and an explanation may be sought along the lines indicated by Evans and Ogawa(14) for the case where the heart's metabolism is accelerated by adrenalin. According to this explanation, the phenomenon is due to the fact that time is required to carry out the oxidative processes to completion, so that the production of carbon dioxide lags behind the oxygen intake and thus causes a temporarily lowered quotient with increased oxygen consumption and *vice versa*. This phenomenon is well seen in Exps. 3 and 4, but is also to some extent shown by Exp. 2.

The effect of alteration of output.

When the rate of inflow of blood to the heart is altered, the output alters, within very wide limits, by the same amount. The work done at different outputs is roughly proportional to the output in each case. The volume of blood which the heart can expel in unit time can be varied

over a greater range than the pressure; thus a twenty or thirty-fold increase from a minimal output is often possible, whereas pressure can only be raised about five-fold from its minimum of 30 or 40 mm.

Exps. 7, 8 and 9 were made by maintaining pressure and temperature constant, with varying rates of output. The results given below show that the increased output results in increased gaseous metabolism of the heart tissue. The increase of oxygen usage is not proportional to the increase in the work done, but is rather less, so that the graph relating gaseous metabolism to work done does not rise very steeply

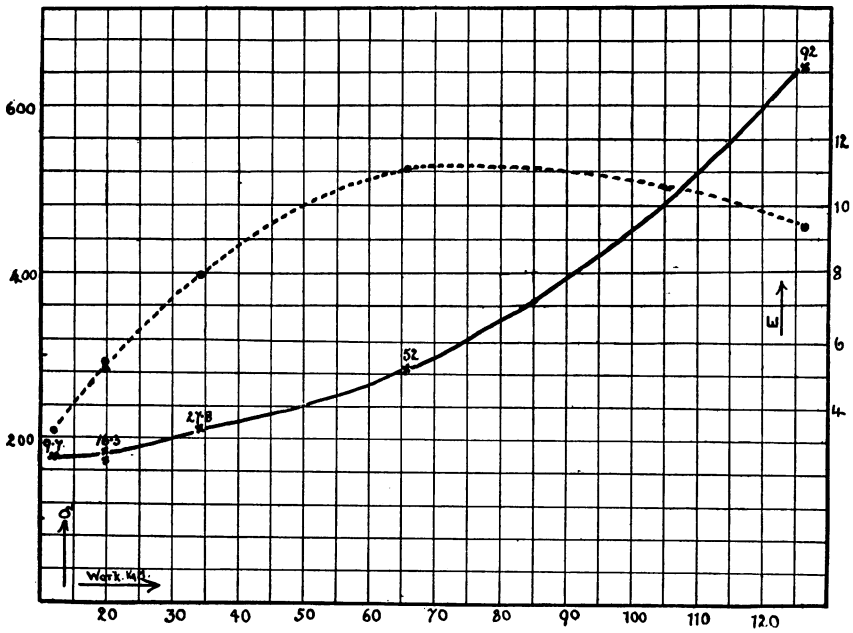

Fig. 3 (Exp. 7). Effect of varied output on oxygen usage (continuous line) and efficiency (dotted line). The figures on the oxygen curve indicate the output in litres per hour (mean values).

(Fig. 3). The efficiency values therefore increase considerably at first with increasing outputs; thus in Exp. 7 it rises from 3·2 % at about 10 litres per hour to 11·5 % at 52 litres per hour, and in Exp. 8 from 3·25 % at 6·4 litres per hour to 13·3 % at 53·4 litres per hour, while in Exp. 9 it reached 16 % with an output of 70·8 litres per hour. The increase of work is therefore very economically done. But beyond a certain limit the oxygen usage increases more rapidly and the efficiency curve now becomes markedly convex to the abscissa; additional work

is now done less economically, so that the efficiency values fall again, as shown in Fig. 3. In Exp. 7, for example, the efficiency fell from 11·5 % at 52 litres per hour to 9·4 % at 92 litres per hour; similarly in Exp. 9 the efficiency at 91·4 litres per hour output was the same as that at only 29·7 litres per hour, namely, 11·7 % average.

When we look for a physiological explanation of these phenomena we must again refer to the work of Patterson, Piper and Starling, who have shown that an increase in output at constant arterial pressure results in an increase in the maximal endocardiac pressure, *i.e.* in the tension developed in the contracted fibres, as well as an increase in both systolic and diastolic cardiac volumes, *i.e.* in the length of the muscle cells. Their experiments show that the heart responds to the call for extra work by such lengthening of its fibres and the elongated fibres, as in the case of skeletal muscle, develop more tension during the isometric phase. The present experiments show that there is a further resemblance to skeletal muscle in the utilisation of more energy by the elongated fibres and in the form of the efficiency curve which shows an increase up to a certain limit, beyond which it falls away again.

The fact that the heart is able to work better over wider ranges of output than of arterial pressure would lead us to expect that indications of fatigue should be less easy to find in the former case than in the latter. As judged by the criterion expressed in the previous section, there is in fact little definite evidence of fatigue to be found in the experiments under discussion. Sometimes, as in Exp. 7, there is evidence that the heart is even more efficient at the close of a prolonged period than at its commencement; thus from periods 4 to 6 and from 9 to 10 there is slight improvement, while in 7 and 8 there is a slight fall in efficiency. Exp. 9 shows variability in the efficiency which probably corresponds with alterations in the state of the heart through some undetermined causes. In the last two periods at the output of 91·4 litres the falling away in efficiency is probably due to fatigue. The onset of fatigue phenomena in the heart has been shown by Patterson, Piper and Starling to present itself as a dilatation or loss of tone of the heart. After hard and prolonged work the fibres usually elongate sufficiently to enable them to do the mechanical work which they could previously perform at a shorter length. When the fibres elongate it is necessary for more tension to be produced in order to produce a given pressure with an increased volume of heart. Still greater lengthening is therefore necessary than would suffice if the tension change which previously

prevailed were adequate to carry out a given amount of work, so that a vicious circle tends to be established. At this greater length they also necessarily use up more potential chemical energy just as skeletal muscle does. The variable efficiencies found in the above experiments correspond to fluctuations in the "tonus" of the heart muscle, and this in its turn is very probably due to variations in the adequacy of the coronary supply. The rise in efficiency which occurs frequently when the work is kept raised for successive periods is exactly in accordance with the demonstration by Patterson, Piper and Starling, that on increasing the work the heart first dilates and then partially recovers. In cases where the arterial pressure and output are both low, the coronary supply is often inadequate, even although it may not be as low as to cause the heart to fail; in this case there is a progressive dilatation and a steady fall in efficiency. It is likely that some of the earlier results obtained by Evans, where the oxygen usage steadily increased in the course of prolonged experiments, are to be explained in this way as due to increasing loss of cardiac tone.

With regard to the possible influence which the increased endocardiac pressure accompanying increased output at constant arterial pressure has upon the gaseous exchanges, we are of the opinion that the phenomenon is of an incidental nature and has no direct effect on the energy used. It is in fact a simple mechanical consequence of the increased output, which necessitates a greater tension development. It is the result and not the cause of the increased expenditure of energy. Starling and his collaborators found that there was no great prolongation of the contracted state here such as was observed with increase of arterial pressure; the primary factor is the increase in the length of the fibres and the increase of endocardiac pressure is a necessary consequence.

Comparison between the effects of altered arterial pressure and altered output.

In the same heart it is easy to study successively the effect of altered output and altered pressure, the other factor being kept constant in each case.

Exp. 10 is an example of such an experiment. As previously stated, it is not possible, under the conditions of experiment, nor in all probability under natural conditions either, to alter the arterial pressure over such wide ranges as the output. This is partly due to the fact

that very low pressures result in imperfect blood supply to the heart. It is particularly difficult to obtain low pressures unless the output is also low. This is because even if we are able to maintain the heart with a pressure of say 15 mm. Hg. and a low output, the pressure immediately rises when the output is increased. In order to maintain a constant low pressure it is essential that there shall be a reserve of arterial resistance in hand, which we can reduce when the output is raised. It was found more expedient in the present case to carry out the variations of output at pressures sufficiently high to ensure this margin of reserve, say at 80 mm. Hg. High outputs are not compatible with very low arterial pressures in these experiments, and the same is true of the intact heart. The converse also holds true in both conditions.

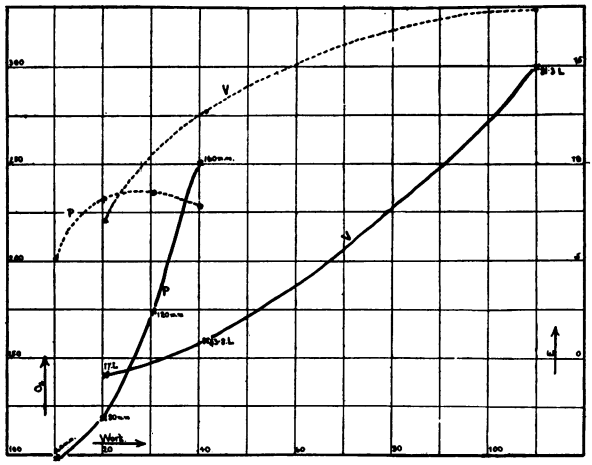

Fig. 4 (Exp. 10). Effect of alteration of arterial pressure (P) and of output (V) on the oxygen usage (continuous line) and efficiency (dotted line) of the heart. The pressure in mm. and the output in l. per hr. are indicated on the respective curves.

Experiment shows that a given increment of work is more efficiently done when it is brought about by raising the output than when it results from increased arterial pressure. The curves relating oxygen usage to work done therefore have different slopes, the curve for alteration of pressure sloping the more steeply (Fig. 4). Similarly efficiencies are higher for increase of output than for like augmentation of work by increased pressure. Thus in Exp. 10 a three-fold increase of pressure (periods 7 and 10) increased the efficiency from 5·1 % to 8·5 % and a four-fold rise actually lowered the efficiency again to 7·8 %, whereas (periods 2 and 3) a two-fold rise of output caused a rise of efficiency

from 7·1 % to 12·7 % and a four to five-fold increase further raised it to 17·8 % (periods 5 and 6).

These results are in accordance with those of the two previous sections on each change separately, and the explanation is to be sought along the lines there indicated. We may assume that the diastolic volume of the heart is not increased so much in order to produce a given increment of work by increase of output as to produce the same increment by increase in arterial pressure. This brings our observations on the heart into line with those of A. V. Hill on skeletal muscle. In both cases there is a relation between the tension set up on contraction and the metabolism of the contractile tissue. The case of a heart working against high pressure is somewhat like that of a muscle contracting against a strong spring, *i.e.* it more nearly approaches to isometric conditions, while the ventricle with a high systolic output is comparable to a muscle executing considerable shortening against a weak spring, *i.e.* it is more nearly isotonic. The tension developed is greater in the former case. The tension is more completely converted into work in the latter case.

The conditions under which the heart works *in situ* in the body are in accordance with these results. Increased cardiac work, as in muscular exercise, usually means a moderate increase of arterial pressure (not usually exceeding 50 %) and a largely increased output (up to 500 %). This is easily done, and even if often repeated does not necessarily lead to marked dilatation or hypertrophy of the myocardium. With this we may contrast the extreme hypertrophy seen in cases of aortic stenosis and arterial hypertension and the acute dilatation met with in those of sedentary habits who take unwonted exercise and in whom the vasomotor mechanism is unable to accommodate the extra output so that abnormal rise of arterial pressure follows.

The effect of simultaneous alterations of pressure and output.

It has been shown that there are optimal conditions of both pressure and output at which the cardiac efficiency reaches maximal values. We should naturally expect from this that there would be optimal values when the two are increased simultaneously and that the maximal efficiency thus obtained would be higher than that reached when either factor was augmented singly. Of the possible combinations of alterations of pressure and output, we have already studied those in which one factor is high and the other low, and have learned that lower

efficiencies are to be obtained in those cases where the pressure is high and the output low than when the reversed conditions hold.

When output and pressure are raised simultaneously and early in the experiment the efficiencies often reach relatively high values, nearly 20 % in some cases. This is well seen in Exps. 11 and 12. There is however an optimum beyond which further increases lead to a diminution in the efficiency, as in Exps. 12 and 14. In other cases the efficiency never reaches a very high level; this may be due to a bad initial condition of the heart (Exp. 13) or to fatigue. It is especially easy to demonstrate the occurrence of fatigue in experiments of this type. Exp. 15 is a good example; the mechanical conditions in the sixth and seventh periods approximated to those in the third and fourth, yet the efficiency is very much lower; on raising the pressure and inflow to the same as in period 5 the heart became extremely dilated, the venous pressure rose rapidly, showing a falling off of output, and the efficiency was now reduced to 4·7 %—the heart was pathologically dilated and incapable of doing the work set before it.

It was not found possible to determine any optimal conditions which were generally applicable to all dogs' hearts; each heart seems to have its own optima for pressure and output. But for the reasons already stated the maximal efficiency cannot be got with very high arterial pressures. Roughly speaking, we can expect to get the greatest efficiency by raising the pressure to 100–140 mm. Hg. and then increasing the output to the highest value that can be got without increasing the venous pressure very greatly. Examples are Exp. 10, periods 5 and 6, and Exp. 14, periods 5 and 6. In Exp. 15 it is clear that the heart was incapable of dealing with very high outputs efficiently at high pressures, since the venous pressure rose from 60 mm. H_2O in period 4 to 210 mm. in the following period as a result of increasing arterial pressure to double and raising the output slightly—hence the lower efficiencies in this experiment.

In the earlier experiments of Evans, the mechanical efficiencies obtained were much lower than those we now find, but we are now able to explain these low figures. They are due (i) chiefly to the small outputs which were used then, (ii) to the onset of fatigue resulting from too high arterial pressures with insufficient output, (iii) to the use of rather high coefficients for calculating the caloric value of the oxygen consumed, (iv) to the fact that the coronary circulation was not allowed for. The suggestion that the mechanical conditions in the heart preclude the attainment of such high efficiencies as may be obtained

with skeletal muscle we believe still to hold good—cardiac muscle acts at a considerable disadvantage as compared with most skeletal muscles.

The highest efficiency yet reached in any of these experiments is 19·7 % (Exp. 11)[1]; this is of course by calculating, in the usual manner, on the total metabolism of the heart. Some writers have used a different method of calculation by subtracting the work done and energy used at high from those at low work. Rohde bases his calculations on determinations of the basal metabolism of a heart brought to rest by calcium lack. Such methods naturally give higher efficiency values; thus Exp. 12, periods 1 and 2, would give an efficiency value of 41 % in this way. We do not think that such methods of calculation are legitimate or helpful.

The fact that the efficiency is so low under conditions where the work done is small is an interesting physiological point. The heart is liberating energy in excess of its immediate (subnormal) requirements; if now it is suddenly called on to do more work it can immediately respond without very much increase in its metabolism. If it were unable to do this, failure would be inevitable.

The fact must not be lost sight of that in these experiments the heart is free from nervous control and is therefore beating much more rapidly than when *in situ*, so that its efficiency is proportionately less. The acceleration which occurs when exercise is taken would under normal conditions enable the heart to deal with larger outputs, and this would probably raise the efficiency or at all events prevent it from being so low as it would be if there were acceleration without augmented output.

The oxygen requirement of the human heart.

The oxygen usage of the heart has often been estimated, on rather insufficient data, to be about 4 or 5 % of that of the whole body at rest. Unpublished experiments by Evans and Moorhouse indicate that for the dog this value is about right. The oxygen usage of the heart of the dog under conditions approximately to those of bodily rest were found as a mean of 51 experiments by Evans and Starling(15) to be 3·24 c.c. per gram per hour. Taking the weight of the human heart at 200 grams[2] and assuming its gram per hour metabolism to be the same

[1] The high value in the last period of Exp. 10, viz. 26·3 %, is not regarded as reliable.

[2] The measurements of the weights of human hearts by Lewis(16) shows that much of its substance is non-muscular, whereas in dogs the heart consists chiefly of muscle. The

as in the dog, the human heart should use about 10·5 c.c. of oxygen per minute under conditions of rest. This amount is about 3·0 % of 350 c.c., which may be taken as a fair average for the minute oxygen usage by the whole body. Our present experiments indicate that under conditions of exercise the oxygen usage of the heart may be increased at least three times, *i.e.* it may easily reach 30 c.c. per minute in man.

The relation between gaseous metabolism, heart volume, and venous pressure.

In many cases there is a close relationship between the gaseous metabolism of the heart and the venous pressure as measured in the inferior cava. Exp. 10 shows this very clearly (Fig. 5), and several experiments showing a fairly close relation between the two are given in various parts of this paper (Exps. 14–16). In other cases the relationship is not so constant. According to Patterson, Piper and Starling the factor determining the amount of energy liberated is the heart volume, *i.e.* the length of the individual fibres. Although the venous pressure in most cases varies directly with this, it does not necessarily do so. In order to investigate the relation between the gaseous metabolism and the volume of the heart we adopted the method of observing the change in level of the blood in the reservoir when the mechanical conditions were altered; the method is only a rough one and has certain inaccuracies. The chief of these are that in the first place it only enables us to determine a sudden change of volume, and in the second place it gives rather too high readings for the increase in volume accompanying increased output owing to the increased capacity of the lung capillaries under this condition.

Nevertheless the method was more practicable than cardiometric observations for our experiments. Exps. 15–18 are examples of the results obtained. These experiments show that as the work of the heart is increased the mean volume of blood in it and (usually) the venous pressure augment also. But as in the graphic experiments of Starling, Patterson and Piper, the volume of the heart is a much better indication of the energy being set free than is the venous pressure. This is especially well seen in those experiments where the pericardium is opened in the course of the observations. In Exp. 16 the pericardium

weight of the two ventricles and septum in normal human hearts was found by Lewis to be about 150 grams when freed from non-muscular structures. In the above calculation we allow 50 grams for the weight of the two auricles, and neglect the metabolism of the non-muscular tissues.

was removed at the commencement of the experiment, and even here there is a closer relationship between oxygen usage and volume than between oxygen use and venous pressure, since in the earlier periods the venous pressure did not alter much. When the pericardium is opened during an experiment there results a *fall* in the venous pressure (Exp. 18) provided it is not already very low (Exp. 17). At the same time there is a *dilatation* of the heart and an *increase* in output if the

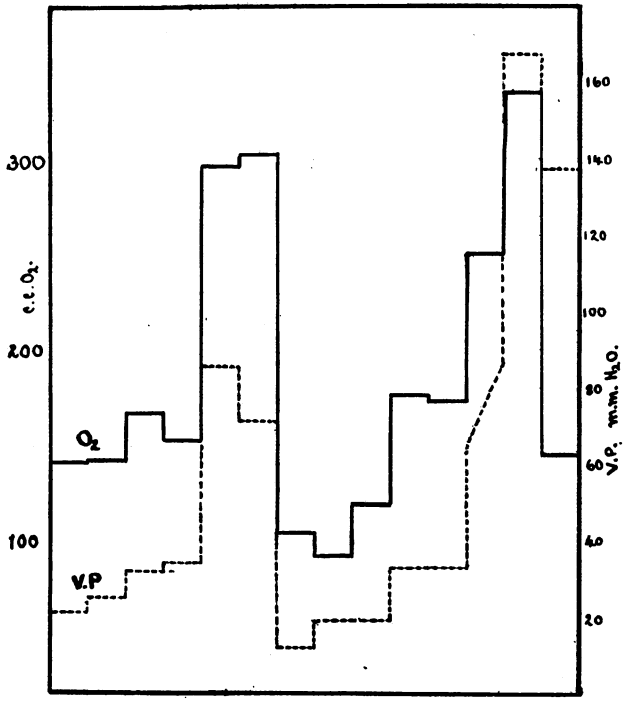

Fig. 5 (Exp. 10). Showing the close relationship which is frequently present between oxygen usage and venous pressure.

inflow conditions are unaltered and there is an increase in the oxygen usage of the heart. This is well seen in Exps. 14 and 18 (and Fig. 6).

The length of the cardiac cells would increase as the surface of the heart, *i.e.* as the square root of the volume change and not directly as the volume. In Fig. 6 the square roots of the volume changes have accordingly been plotted instead of the volumes.

Here then we have clear proof that the factor determining the energy usage of the heart is its volume; the venous pressure is an

incidental phenomenon related to the rate and extent of the diastolic filling.

We may regard the pericardium as limiting the diastolic filling of the heart. When we remove it, the filling is facilitated, so that with constant inflow conditions there will be an increase in output and a fall of venous pressure. These changes will be the more pronounced the more nearly the previous output with intact pericardium approached

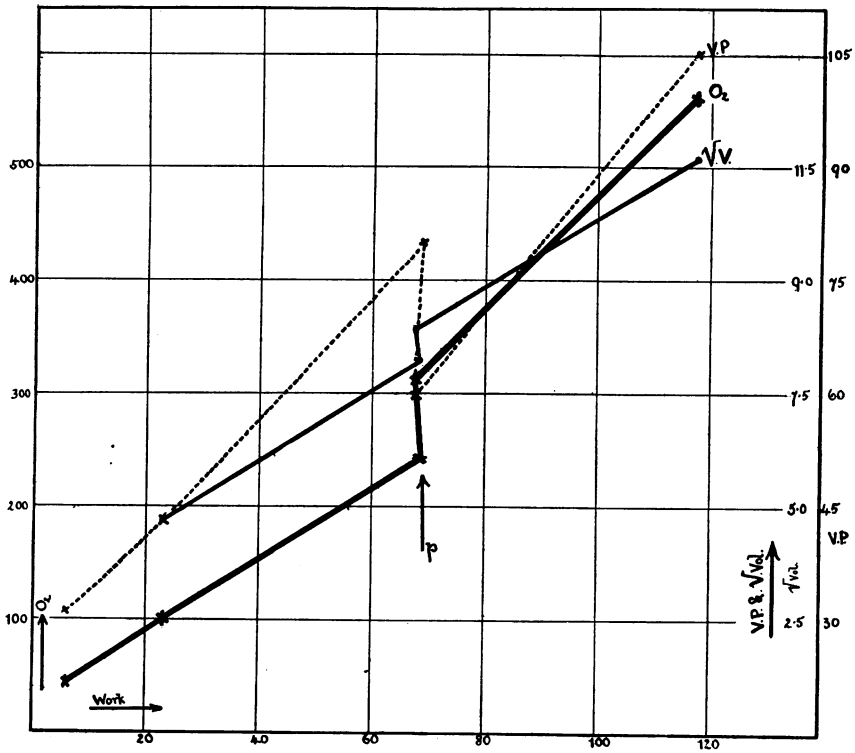

Fig. 6 (Exp. 14). Relation of oxygen usage to venous pressure and to the square root of the volume change of the heart. At *p* the pericardium was opened; oxygen usage and volume of heart increased while venous pressure fell.

a maximal value. The increase of work obtained under these conditions however is not usually economically done; the heart volume has now increased beyond its physiological limits and there is always a danger of irrecoverable dilatation. Thus in Exp. 17 the removal of the pericardium with a moderate output led to increased efficiency and to no appreciable change of heart volume or venous pressure; when the

output was raised the efficiency and the venous pressure were lower than at the same output with intact pericardium, while the heart volume was much increased.

Some of these experiments have clinical interest in connection with pericardial effusions. With a chronic pericardial effusion the pericardium steadily distends and its capacity increases without there being necessarily great cardiac embarrassment. If now the fluid is removed by tapping we have an enlarged pericardium which will be no longer able to confine the heart within physiological limits. Acute dilatation would therefore be extremely likely to follow.

When on the other hand the effusion is rapid as in hæmopericardium due to rupture of a vessel in the pericardium or on the heart surface, the pericardium cannot accommodate itself to the volume of fluid within it and the diastolic filling of the heart is seriously hampered. In experiment 20 such a condition of hæmopericardium was obtained experimentally as the result of an accident.

We have already indicated that as the heart becomes exhausted its volume increases and its gaseous metabolism is increased. Supposing now that the heart ultimately fails, how does its gaseous metabolism behave? The answer is that the heart may fail in one of two ways, and that the gaseous metabolism will be influenced by the mode of failure. The first method of failure is that the heart is confronted with work which is too great for it, it dilates maximally and ceases to expel its contents, thereby dying of asphyxia; if we reduce the inflow or pressure and empty the heart by massage or by drawing blood from veins before it succumbs it will resume work. There is every reason to suppose that in such a case the energy usage of the heart is maximal until it is asphyxiated. There is no slowing until asphyxial symptoms set in in the heart tissue. Exp. 14, which was terminated by lung œdema, is a case of such threatened failure; the dilatation was facilitated by the removal of the pericardium in the seventh period. The result of one of our experiments suggests that there is a second method of failure, viz. by exhaustion, in other words by failure of its metabolic processes[1].

Such a heart shows a progressive slowing of rate as a characteristic feature. Here naturally the heart fails and therefore dilates *because* of a diminution in its metabolic processes. Exp. 19 is an example

[1] This is of course the terminal condition in the other mode of failure if the condition of stress is not relieved sufficiently early. We speak now of a primary failure.

of this method of failure, which is very rare under experimental conditions. The heart had previously been given very heavy work, which it had efficiently done.

Conclusions.

1. In calculating the work of the heart, the velocity factor $\frac{wV^2}{2g}$ must be allowed for when the output is high, as it may be more than 5 % of the total work.

2. When the arterial pressure is raised the gaseous metabolism is increased. The mechanical efficiency of the heart is thereby raised up to a certain limit, beyond which it diminishes again.

3. When the output of the heart is increased, the gaseous metabolism is markedly increased up to a certain maximum, falling off again with further increase of output.

4. Increase of output is more economically performed than a comparable increase of pressure. The maximal mechanical efficiency is about 20 % and is obtained by moderate increase of both output and pressure.

5. Fatigue phenomena are seen in a lowered efficiency accompanying cardiac dilatation.

6. There is usually demonstrable a parallel between the oxygen usage of the heart and the heart volume, *i.e.* the length of the cardiac fibres, just as there is, as shown by Patterson, Piper and Starling, a close parallel between cardiac work and volume. Usually the venous pressure also runs parallel to the oxygen usage, but this is not always the case. The most striking exception to this is seen in the effect of removal of the pericardium while the heart is doing considerable work when volume and oxygen usage increase and venous pressure diminishes.

7. When the heart fails it is in our experimental condition usually because, in spite of high expenditure, it is unable to perform the excessive work offered it. But it may fail from the exhaustion, *i.e.* a lowering of its metabolism; a phenomenon of such failure is that it commences by a retardation in the pulse rate.

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REFERENCES.

(1) Patterson, Piper and Starling. This Journal, XLVIII. p 465. 1914.
(2) Evans. Ibid. XLIV. p. 213. 1912.
(3) Patterson and Starling. Ibid. XLVIII. p. 363. 1914.
(4) Evans and Starling. Ibid. XLVI. p. 413. 1913.
(5) Benedict and Joslin. Metabolism in Diabetes Mellitus. Carnegie Inst Washington, p. 166. 1910.
(6) Führer and Starling. This Journal, XLVII. p. 286. 1913.
(7) Evans and Ogawa. Proc. Physiol. Soc. 1915, p. ix (This Journal, XLIX.).
(8) Weiss. Journ. de Physiol. et de Path. XV. p. 999. 1913.
(9) Rohde and Ogawa. Arch. f. exp. Path. und Pharm. LXIX. p. 200. 1912.
(10) Markwalder and Starling. This Journal, XLVIII. p. 348. 1914.
(11) A. V. Hill. Ibid. XLII. p. 1. 1911.
(12) Evans and Hill. Ibid. XLIX. p. 10. 1914.
(13) Kozawa. Ibid. XLIX. p. 233. 1915.
(14) Evans and Ogawa. Ibid. XLVII. p. 446. 1914.
(15) Evans and Starling. Ibid. XLIX. p. 67. 1914
(16) Lewis. Heart, v. p. 367. 1914.

PROTOCOLS.

All the experiments were made on dogs.

EXP. 1. Heart 55 grams. Temp. 36° C. Periods of 20 min. Cannula in coronary and sinus flow along coronary sinus measured.

Period	Art. Press. in mm. Hg.	Total Output Litres per hr	c.c. O_2 per hr by heart	Kg. m. energy per hr	Kg. m. work per hr	% Efficiency	Output from aorta, l. per hr	Coronary sinus flow, l. per hr	Remainder flow in Coronary System, l. p. hr (calc.)	Total Cr. flow c.c./min. as percentage of weight of heart
1	80	7·7	111	229	9·3	4·1	6·2	1·02	0·51	46
2	80	24·4	168	347	29·9	8·6	22·5	1·23	0·62	56
3	80	8·3	131	271	10·0	3·7	6·0	1·56	0·78	71
4	106	25·6	188	388	41·4	10·7	21·3	2·86	1·43	130
5	120	30·6	188	388	56·2	14·7	23·7	4·62	2·31	212

EXP. 2. Heart 57 grams. Temp. of blood 37° C. Constant inflow conditions. Output at 40 mm. Hg. = 485 c c. per min. Output including coronary flow = 31 litres per hr. Periods of 15 min.*

Period	Art. Press. in mm. Hg.	Total Output Litres per hr	c.c. O_2 per hr by heart	Kg. m. energy per hr	Kg. m. work per hr	% Efficiency	R. Q.
1	42	31	239	496	20·2	4·07	·84
2	70	—	260	538	33·5	6·24	·74
3	100	—	325	673	47·6	7·07	·78
4	130	—	375	775	61·3	7·9	·71
5	100	—	371	768	47·6	6·2	·78
6	70	—	296	613	33·5	5·47	·79
7	42	—	229	475	20·2	4·25	·88
8	70	—	266	550	33·5	6·08	·69
9	100	—	335	695	47·6	6·85	·73
10	130	—	367	759	61·3	8·1	·57

* In the curves given in the text plotted from this and other experiments, mean values of periods made under same conditions were used.

Exp. 3. Heart 71·5 grams. Temp. of blood 37° C. Output at 50 mm. pressure = 540 c.c per min. Output including coronary flow = 35·1 litres per hr. Periods 15 mins.

Period	Art. Press. in mm. Hg.	Total Output Litres per hr	c.c. O_2 per hr by heart	Kg. m. energy per hr	Kg. m. work per hr	% Efficiency	R. Q.
1	50	35·1	214	442	27·6	6·25	·86
2	80	—	228·5	472	43·6	9·3	·795
3	110	—	282·5	584	59·5	10·2*	·71
4	140	—	404·5	839	75·7	9·1*	·64
5	170	—	396·5	820	92·1	11·3†	·638
6	140	—	318·0	658	75·7	11·5	·765

* Mean of periods 4 and 6 = 10·3 %.

† Output probably diminished at high pressure, so that 11·3 % efficiency was in all probability not reached.

Exp. 4. Heart 32·5 grams. Temp. 37° C. Pulse rate 143 per min. Periods 20 min., except last four, which were 15 min.

1	40	30·2	180	372	18·9	5·2	1·28
2	40	30·2	181	373	18·9	5·2	1·06
3	60	30·2	195	402	28·1	7·0	0·88
4	80	30·2	213	440	37·3	8·5*	0·78
5	80	30·2	233	483	37·3	7·7*	0·94
6	100	30·2	273	564	46·4	8·2	0·76
7	120	25·0	263	543	45·7	8·4†	0·77
8	120	30·2	275	569	55·5	9·8†	0·73
9	40	29·4	211	436	18·4	4·2	0·91

* Mean 8·1. † Mean 9·1.

Exp. 5. Heart 46·5 grams. Temp. 34° C. 15-min. periods. Pulse rate 134–150.

							Venous pressure mm. H_2O
1	80	17·4	139	288	21·1	7·3	38
2	80	16·8	140	290	20·5	7·1	42
3	40	17·1	103	213	11·9	5·6	35
4	40	16·9	81	168	11·7	7·0	36
5	80	16·8	118	245	20·4	8·3*	36
6	120	16·3	175	362	30·7	8·5*	50
7	120	15·6	172	356	30·7	8·6*	50
8	160	14·7	249	518	40·8	7·9*	80–103

* Constant inflow. Work done calculated from output of 16·8 litres per hour.

Exp. 6. Heart 53 grams. Temp. 30° C. Periods of 15 mins. Pulse rate 83–84.

1	60	13·9	87	180	12·7	7·1	2
2	120	12·9	120	248	23·5	9·5	6
3	60	13·0	115	238	11·9	5·0	5

Exp. 7. Heart 59 grams. Temp. 36·5°. Arterial pressure 80 mm. Hg. Periods of 15 mins. Pulse rate 143–146.

1	80	10·1	201	415	12·3	3·0	—
2	—	9·3	155	321	11·3	3·5	—
3	—	9·6	181	375	11·7	3·1	—
4	—	16·6	212	437	20·0	4·6	—
5	—	16·2	189	392	19·6	5·0	—
6	—	16·2	155	321	19·6	6·1	—
7	—	27·8	207	427	34·1	8·0	—
8	—	27·8	217	448	34·1	7·6	—
9	—	52·0	297	614	65·6	10·7	—
10	—	52·0	277	572	65·6	11·5	—
11	—	92·0	649	1343	126·3	9·4	—
12	—	16·4	175	363	19·3	5·3	—

Exp. 8. Heart 26 grams. Temp. 37° C. Arterial pressure 80 mm. Hg. Periods 15 mins., except last, which was 10 mins. Pulse rate 172–181.

1	80	6·4	114	236	7·8	3·3	—
2	—	6·4	118	244	7·8	3·2	—
3	—	18·9	134	277	23·0	8·3	—
4	—	18·9	124	257	23·0	9·0	—
5	—	53·4	247	509	67·9	13·3	—

Exp. 9. Heart 42 grams. Temp. 36·5°. Arterial pressure 80 mm. Hg. Periods 15 mins., except last, which was 10 mins. Pulse rate 131–143.

1	80	14·6	94	195	17·7	9·1	—
2	—	14·6	100	207	17·7	8·6	—
3	—	29·7	156	323	36·6	11·3	—
4	—	29·7	122	252	36·6	14·6	—
5	—	29·7	178	369	36·6	9·9	—
6	—	42·3	196	406	53·1	13·1	—
7	—	42·3	206	426	53·1	12·5	—
8	—	70·8	284	589	92·2	15·7	—
9	—	70·8	278	578	92·2	16·0	—
10	—	91·4	458	950	125·9	13·2	—
11	—	91·4	582	1207	125·9	10·4	—

Exp. 10. Heart 46·5 grams. Temp. 34°. Periods of 15 mins.

1	80	17·4	140	21·1	291	7·1	21*
2	80	16·7	141	20·3			25*
3	80	33·8	166	41·7	329	12·7	32*
4	80	33·8	152	41·7			34*
5	80	71·0	296	93·9	620	17·8	85*
6	80	91·6	302	126·1			71*
7	40	17·1	104	10·4	202	5·1	12†
8	40	16·9	92	10·3			19†
9	80	16·8	119	20·2	247	8·2	19†
10	120	16·8	176	30·6	360	8·5	33†
11	120	16·8	173	30·6			33†
12	160	16·8	250	40·2	517	7·8	63–86†
13	160	37·7	334	92·6	693	13·4	167‡
14	160–110	37·7	145	78·9	300	26·3	137§

* Altered inflow with constant pressure. † Altered pressure with constant inflow.
‡ Inflow raised. § Pericardium removed. Lung œdema.

Exp. 11. Heart 58 grams. Temp. 36°.

1	100	37·9	230	476	58·7	12·3	—
2	140	63·1	410	850	138·6	16·4	—
3	180	73·9	517	1070	210·8	19·7	—

Exp. 12. Heart 90 grams. Temp. 36·5–37° C. Pulse rate 146–150 per min. Periods of 15 mins.

1	100	20·4	213	442	31·2	7·1	—
2	126	67·2	334	690	133·2	19·3	—
3	134	100·2	636	1310	223·0	17·0	—

Exp. 13. Heart 54 grams. Temp. 35° C. Periods of 10 mins.

1	110	20·7	307	633	30·6	4·8	—
2	110	21·2	298	616	31·3	5·1	—
3	145	44·7	624	1290	104·4	8·1	—
4	145	61·9	660	1363	146·1	10·7	—

Exp. 14. Heart 28·5. Temp. 36°. Periods 15 mins., except last one, which was 5 mins. only.

Period	Art. Press. in mm. Hg.	Total Output Litres per hr	c.c. O_2 per hr by heart	Kg. m. energy per hr	Kg. m. work per hr	% Efficiency	Venous pressure mm. H_2O	Volume change of heart c.c.
1	42	9·3	47	91	6·0	6·6	31	—
2	42	9·4	42				31	—
3	80	19·4	88	208	23·2	11·1	43	+ 22
4	80	18·7	114				43	+ 22
5	120	37·1	252	504	68·5	13·6	74–80	+ 68
6	120	37·1	234				85	+ 68
7	120	36·5	312	644	67·4	10·5	65–55	+ 80*
8	130	57·5	562	1160	117·7	10·1	105	+136†

* Pericardium removed. Output adjusted. Immediately on removal of pericardium the output rose to 61 l. per hour without any alteration of inflow. At the same time the arterial pressure rose to 130 mm.Hg. and the venous pressure fell to 70 mm. H_2O, while the heart became very dilated (+110 or more). The output was immediately restored by alteration of inflow screw, to approximately its former value. This caused the arterial pressure to return to 120 mm. and the heart volume to + 80, while the venous pressure fell to 65 mm., afterwards falling slowly to 55.

† Inflow increased. Lung œdema coming on. In this period the inflow was increased to what it would have been in last period if not altered. There were signs of lung œdema after 5 minutes of last period, so the experiment was stopped. The venous inflow was stopped and arterial pressure reduced to zero. The volume of blood entering reservoir from heart was 92 c.c., but some still remained behind in heart, which was permanently dilated.

Exp. 15. Heart 39·5 grams. Temp. 35° C. 15-min. periods. The experiment was commenced with low arterial pressure and small output. After two periods, output and pressure were each doubled; this was again repeated after two more periods.

1	30	16·8	85	176	7·6	4·3	40	—
2	30	17·1	94	194	7·8	4·0	40	—
3	60	36·2	165	341	34·0	10·0	60	+ 40
4	60	34·8	189	390	32·7	8·4	60	+ 40
5	120	47·6	388	804	88·8	11·1	210–240	+ 98
6	60	35·4	234	485	33·1	6·8	102	+ 69
7	60	33·5	240	496	31·3	6·3	113	+ 69
8	120	13·2 (mean)	247	509	24·0	4·7	290	+134 or more*

* Full inflow allowed, but output rapidly fell off. Heart very dilated. Lung œdema came on soon after end of period 8. At the end of the experiment the venous inflow was stopped and the arterial pressure reduced to zero. The level of blood in the reservoir then rose by 79 c.c., but there was still a considerable volume remaining in the dilated heart and 12 c.c. were recovered from the heart after excision.

Exp. 16. Heart 32 grams. Pericardium removed. Temp. 34·5°. Periods of 15 mins.

1	130	16·9	128	265	33·4	12·6	22	—
2*	150	16·9	170	352	38·5	10·9	23	+9·5
3*	90	16·9	109	226	23·1	10·3	21–25	−8·5
4*	30	16·9	65	135	7·7	5·7	26	−19
5*	90	16·9	127	263	23·1	8·8	25	− 1
6	90	57·3	372	772	82·0	10·6	72	+65
7	90	67·8	370	767	97·4	12·7	142–170	+84

* Inflow constant.

Exp. 17. Heart 53 grams. Temp. 30° C. Periods of 15 mins.

Period	Art. Press. in mm. Hg.	Total Output Litres per hr	c.c. O_2 per hr by heart	Kg. m. energy per hr	Kg. m. work per hr	% Efficiency	Venous pressure mm. H_2O	Volume change of blood in heart in c.c.
1	60	13·9	87	180	12·7	7·1	2	—
2	120	12·9	120	248	23·5	9·5	6	+ 24
3	60	13·0	115	238	11·9	5·0	·5	+ 5
4	60	47·0	180	372	44·9	12·1	15	+ 48
5	60	62·0	331	682	60·8	8·9	70–80	+ 86
6	60	20·7	180	372	19·0	5·1	40	+ 27
7	60	19·4	109	226	17·8	7·9	35	—
8*	60	22·8	67	139	21·1	15·2	34	—
9	60	62·0	375	775	60·8	7·9	65	+102

* Pericardium opened.

Exp. 18. Heart 44 grams. Temp. 35·5° C. Periods 1 and 2 = 15 mins., 3 = 40 mins.; the remainder 20 mins. each.

1	60	51·4	332	686	49·3	7·2	50	+65
2	60	56·1	234	486	54·7	11·3	51	+65
3	60	17·1	111	229	15·6	6·8	30	+37
4	145	13·5	214	444	29·5	6·7	65	+ 0
5*	145	13·2	322	664	28·9	4·4	36	+60?
6	60	56·1	244	507	54·7	10·8	45	?
7	60	14·6	158	327	13·3	4·1	30	?

* Pericardium removed.

Exp. 19. Heart 47·5 grams. Temp. 35° C. 15-min. periods. The temperature of the entering blood was constant throughout.

									Pulse rate
1	80	8·4	213	10·2	442	2·3	—	—	143
2	80	37·7	325	46·7	673	6·9	14	+31	137
3	80	76·7	487	102·3	1008	10·1	23	+72	146
4	90	109·2	501	174·7	1040	16·8	40	+97	150
5	80	58·1	375	74·6	776	9·6	37–102	+78	Slows to 102;
6	80–20	9·6	95	7·3	197	3·7	117	+31 to +66 at first, then more and more dilated until it failed	slows to 0 after end of period 6

Exp. 20. Heart 60 grams. Temp. 37° C. Arterial pressure 120 mm. The experiment was commenced and a period of observation of 15 mins. taken. The output was measured every five minutes and the venous pressure every three minutes. The following values were obtained.

Duration of period	Pulse rate	Output Litres per hr	Venous pressure
3 min.	177	—	200 mm. H_2O
5	,,	52·1	—
6	,,	—	285 mm. H_2O
9	,,	—	305 ,,
10	,,	27·8	—
12	,,	—	315 mm. H_2O
15	,,	16·1	340 ,,

It was now discovered that the pericardium was tensely distended with blood which had leaked into it. It was immediately opened and the output and venous pressure at once returned to the values which they had at the commencement of the experiment. There was a small arterial twig found to be ruptured at the root of the aorta.