Energy Production in Cardiac Isotonic Contractions

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ABSTRACT The energy output of rabbit papillary muscle is examined and it is shown that there is more energy liberated in an afterloaded isotonic contraction than in an “equivalent” isometric contraction. This statement holds true regardless of whether equivalence is based on the proposition that tension or the time integral of tension is the best index of muscle energy expenditure. Besides the external work performed there is additional heat production in isotonic contractions and this heat increases as the afterload is decreased. The additional heat is more evident when tension rather than the time integral of tension is made the determinant of energy expenditure. It is shown in single contractions that the rate of isotonic heat production, regardless of afterload size, never exceeds the heat rate recorded in an isometric contraction at the same initial length. Experiments reveal no simple linear correlation between isotonic energy output and contractile element work. Problems associated with the compartmentalization of the energy output of a contraction are discussed.

INTRODUCTION

It was reported by Gibbs, Mommaerts, and Ricchiuti (1967), that in an afterloaded isotonic cardiac contraction more energy is liberated than the isometric heat vs. tension plot predicts. This energy, above that required in an equivalent isometric contraction, could be divided into energy associated with external work and additional heat which we suggested might be associated with shortening. The results reported in the literature since the myothermic experiments were performed have been in broad agreement with that study. (See Pool, Chandler, Seagren, and Sonnenblick (1968), Coleman, Sonnenblick and Braunwald (1969).)

Hill (1964 b) and Jöbsis and Duffield (1967) have recently reemphasized for skeletal muscle that tension maintenance contributes significantly to the energy cost of contraction. It seemed therefore worthwhile to repeat the myothermic experiments, using not only peak tension as an index of equivalent isometric energy expenditure but also the tension-time integral and to subject the results to more rigorous statistical analysis. The problem of the best
mechanical index of isometric energy expenditure is being examined by us at present, and statistically at least there is no clear benefit to be derived from selecting one or the other of the parameters.

Britman and Levine (1964) have proposed that myocardial oxygen consumption is a linear correlate of contractile element work (C.E.W.). Although this proposal has not been universally accepted (McDonald, Taylor, and Cingolani, 1966; Coleman, 1968) it seemed desirable to measure both external and internal work and to check whether the calculated C.E.W. did correlate with the total isotonic energy output ($E_T$).

**METHODS**

Papillary muscles were obtained from the right ventricles of rabbits. They had a mean weight of 5.8 mg and a mean length of 7.1 mm under a resting tension of 0.5 g. Their mean cross-sectional area was 0.82 mm$^2$ and ranged between 0.49 and 1.41 mm$^2$. The mean tension per cross-sectional area was 520 g/cm$^2$ (23 muscles). There were no consistent changes from this latter value that could be related to cross-sectional diameter. The muscles were suspended vertically in a chamber containing 55 ml of Krebs-Henseleit solution which was aerated with 95% O$_2$:5% CO$_2$. The first series of 15 experiments was conducted at temperatures ranging from 18.10 to 24.00°C and the second series of 8 experiments was run at 23.0°C. After dissection the muscles were stimulated to contract isotonic at 15 beats per min under a 0.5 g load. This period of preloaded isotonic contractions normally lasted at least 2 hr during which time there was generally a continual improvement in contractility. Experiments were only commenced when a stable state had been achieved.

**Mechanical Measurements**

Each preparation was fixed at both ends with braided noncapillary silk, and the silk at the ventricular end of the preparation was clamped 2 mm from the muscle. The tendinous end of the muscle was connected via a light stainless steel tube to the transducers.

In the first series of experiments the isometric transducer was a Sanborn FTA-100 and the isotonic lever was a modified Brush Metripak (Clevite Corp., Cleveland, Ohio). When operating isometrically, the total compliance of the transducer, stainless steel tube, and silk ties was $1.2 \times 10^{-4}$ cm/g wt. The isotonic lever had a ratio of 20:1 and the equivalent mass of the lever plus stainless steel tube was 780 mg. It was calculated that under isometric conditions muscles could shorten about 3% of the distance they could when maximum isotonic shortening took place (0.5 g load).

In the second series of experiments simultaneous measurements of both tension and length changes were made using a modified version of an isotonic lever described by Norris and Carmeci (1964). Tension was measured using two Ether (Ether Ltd., Stevenage, Herts, England) 35P type, strain gauges and a bridge circuit (Jewell, Kretzchmar, and Woledge, 1967). The magnesium alloy lever had a 20:1 lever ratio and the equivalent mass of the lever plus the stainless steel tube was 510 mg. The total system compliance (transducer, stainless steel tube plus silk ties) was about $1.6 \times 10^{-4}$ cm/g wt. Quick release experiments were performed using the technique of Wilkie (1956). The preparations were stimulated at a constant rate (15/min) and
were prevented from shortening by means of a mechanical stop. After nine control
isometric contractions the solenoid-activated stop was withdrawn after a preselected
delay (timed for the contraction peak) so that the muscle could now shorten against
some preselected afterload. These experiments were repeated using a wide range of
afterloads applied in random order. The load-extension curve so obtained was similar
to that recorded by Parmley and Sonnenblick (1967). No attempt was made to sepa-
rate out the extension due to equipment distensibility. The resultant curves were
graphically integrated to obtain a measure of the internal work performed by the
contractile elements.

Heat production was plotted against peak developed tension and also against
tension integral. In order to measure the tension integral of a train of contractions
two procedures were adopted. If the resting tension base line remained stable the
output of the tension transducer was integrated using a Burr-Brown Operational
Amplifier (Burr-Brown Research Corp., Tucson, Ariz.). If there were base line
changes then recordings were made at a fast chart speed and the area under the ten-
sion wave forms was measured using a planimeter. It was also essential to know the
tension-time integrals in the afterloaded contractions. These cannot be obtained
directly in cardiac muscle by making simultaneous measurements of length and ten-
sion, because the resting tension is not an insignificant fraction of the peak isometric
tension. At rest this tension is supported by the parallel elastic elements of the muscle
but when the muscle shortens during an afterloaded isotonic contraction, part or all
of the preload will be transferred to the contractile elements. The transducer cannot
discriminate between passive or active tension and if we take the worst case, that is
when the afterload is zero, no additional tension is recorded above the established
base line during an isotonic contraction although it is evident that the contractile
elements have been under a tension of 0.5 g (the preload) for the greater part of the
isotonic phase of contraction. In order to make a correction for this effect it is necessary
to obtain a passive length-tension curve. Then knowing the length change that has
occurred at any given moment it is possible to calculate the tension that the contractile
elements are bearing. This correction is quite large when the afterloads are small and
the isotonic shortening distance is large but becomes smaller as the afterloads are in-
creased and the shortening distance diminishes. When the afterload becomes so large
that the contraction is isometric then no tension correction is called for as the trans-
ducer is effectively recording solely the behavior of the contractile elements. In Fig. 1
a schematic representation of the correction procedure is shown. In making this
correction it is assumed that during isotonic shortening the passive length-tension
curve has not changed its configuration from that determined in static measurements.

In most of the first series of experiments it was not possible to record a tension-time
integral during an isotonic contraction although it was possible to plot heat produc-
tion against the tension-time integrals obtained from isometric contractions at
different muscle lengths. In order to compute the tension-time integrals during the
isotonic contractions a relationship between load and the tension-time integral was
obtained from the second series of experiments (Fig. 2). Each load was expressed as
a fraction of the peak isometric tension and each tension integral was expressed as a
fraction of the tension integral measured in a peak isometric contraction. Note that
provided we know the peak developed tension and the time integral of this tension it is
possible with only small errors to work out the isotonic tension-time integral when any given load is lifted. Tension-time integrals were estimated in this way for 11 muscles in the first experimental series. The other four experiments were carried out with equipment which allowed simultaneous measurement of length and tension changes.

Isometric and Isotonic Contractions During isometric contractions tension was altered by changing muscle length. The muscle length under a resting tension of 0.5 g was taken to be $l_0$ and the tension generated at this length at a stimulus rate of 30/min was taken to be $P_o$. In order to simplify the analysis and presentation of data, values for work, total energy, and equivalent isometric heat were always selected that corresponded to certain load values (i.e., 0.1, 0.2, 0.4, 0.6, and 0.8 $\times$ $P_o$). Since the loads used were generally not exact fractions of $P_o$, graphs of the experimental data were made and the appropriate values (e.g., at 0.2 $P_o$) were interpolated from these graphs. Between 5 and 10 different afterloads were used for the isotonic contractions.

Normally during isotonic relaxation, the energy which appears as mechanical work is converted to heat when the muscle lowers the load. As the load hits the afterload stop some energy is dissipated as heat in the afterload stop and is not converted to heat.
by the muscle. In the slow cardiac contractions that occur at 23°C such a heat loss from the muscle thermopile systems was generally negligible but with some muscles for certain load ranges, small corrections had to be made (up to 8% of the potential energy of the load).

In order to randomize the effects of fluctuations in muscle performance, in some experiments the isometric measurements were done first and in others the isotonic measurements were done first. The stimulus rate within a train of contractions was always kept constant (30/min), but the duration of the train was varied between 30 and 60 sec in different experiments. However, the duration of the train was held constant within any one experiment. Both the isometric and isotonic measurements were run in mirror-image fashion; i.e., started at high loads (isotonic) or normal muscle length (isometric) and progressed to light loads or short muscle lengths, followed by the reverse procedure, after which the results were averaged. The quick release experiments were carried out after the heat measurements were concluded, while the muscle was still on the thermopile.

Stimulation The preparation was stimulated by two flexible platinum electrodes cantilevered from the thermopile frame. The stimulus voltage was adjusted to
be 10% above threshold (range 3 to 6 v) and the stimulus duration was kept at 0.5 msec. Heat liberated in the muscle by the stimulus must be corrected for and details of the procedure employed have been published previously (Gibbs and Vaughan, 1968).

**Heat Measurements** Three thermopiles with "protected regions" and having outputs of 3.48, 3.03, and 2.43 mv/°C, respectively, were used in conjunction with an Astrodata Model 120 Nanovolt Amplifier (Astrodata Inc., Anaheim, Calif.) whose frequency response was reduced to 20 Hz by a filter network. The heat loss from the muscle thermopile system was practically exponential. It averaged 12.8%/sec and was corrected for electrically.

An absolute calibration of heat production was made after each experiment by a technique described previously (Gibbs et al., 1967). The possible sources of error which have been outlined recently (Gibbs [1969]) generally lead to an overestimate of the actual amount of heat produced by the muscle and individual muscle errors as high as 10% are possible. The mean error should be considerably less but even a mean error as high as 10% would not produce marked errors in the analysis for a "shortening heat" component (see Results).

No attempt has been made to correct the time course of the heat records for conduction delays. Because of the relatively high heat capacity of the thermopiles and the unknown distribution of adhering fluid any such analysis would not be warranted. Comparative studies of the rate of heat production made under the same physical conditions are still valid but the heat records cannot be compared directly with the mechanical records; the former are undoubtedly too slow. The heat associated with the contractile response has been called the fast phase heat and there is evidence that this heat corresponds to the initial heat of skeletal muscle (Gibbs [1969]). In order to measure the total heat (i.e., initial plus recovery heats) with reasonable accuracy it is necessary to measure the total heat liberated in a train of contractions and then to divide the summed heat by the number of stimuli in that train. The contractions can be either isometric or isotonic. The average total heat value per contraction can then be plotted against the average developed tension or the average work done. In the graphs and tables presented in this paper the measured heat (or energy) is always the average total heat per contraction. It should be noted that in afterloaded isotonic contractions the load is allowed to stretch the muscle out to its original length. This work done by the load upon the muscle appears as heat and hence the total heat measurement alone gives the total energy output of the muscle, i.e. (external work + active heat production).

**Extra Heat Production in Isotonic Contractions** Apart from total heat energy \( (E_T) \) and external work \( (W_e) \) three different measures of energy output were plotted against load or tension (both expressed as fractions of the average peak isometric tension at \( l_0 \)). Since \( E_T \) includes heat equivalent to the degraded external work \( (W_e) \), we subtracted the latter quantity to obtain the heat production \( (H) \) associated with contraction but not due to external work; i.e., \( H = E_T - W_e \).

By altering the length of the muscle it is possible to determine the relationship between isometric tension and the amount of heat produced (Gibbs et al., 1967).
and so to estimate the isometric heat associated with given levels of tension development, this estimate being designated \( H_i \).

Similarly it is possible to determine the relationship between the isometric tension-time integral and heat production and to estimate the isometric heat associated with given levels of this integral. Heat estimated in this way has been designated \( H_a \).

Thus for the isotonic contractions we found values for \( W \), \( H \), and \( H_i \), as well as having two estimates of the equivalent isometric heat, one \( (H_i) \) being based on the idea that tension is the best index of heat production and the other \( (H_a) \) based on the idea that the tension-time integral is more important.

Statistical Analysis  Data were handled using analysis of variance as for a randomized complete block design (Steel and Torrie, 1960, Chap. 8), each muscle preparation being considered as a block to which each of 15 treatments were applied. The treatments were in a factorial arrangement (Steel and Torrie, 1960, Chap. 11), there being five levels of load \( (P/P_o = 0.1, 0.2, 0.4, 0.6, \text{ and } 0.8) \) at each of which three different estimates of heat production \( (H, H_i, H_a) \) were considered. For each muscle at each load a single train of contractions was studied. \( H, H_i, \) and \( H_a \) were determined for this particular train of contractions by the methods described above.

RESULTS

The results of the first series of experiments at 18.1–24.0°C are given in Table I and Fig. 3. Different muscle preparations differed widely in their heat production (block effect, \( P < 0.001 \)) as well as in their relative amounts of heat determined in three different ways \( (B \times E \text{ interaction, } P < 0.001) \) and in their relative amounts of heat produced at different loads \( (B \times L \text{ interaction, } P < 0.001) \). The main point to note is that the heat actually produced in an isotonic contraction \( (H, \text{ the isotonic heat, which excludes external work}) \) was consistently greater than the heat predicted on the basis of isometric contractions, whether the prediction was based on the peak tension developed \( (H > H_i, P < 0.001) \) or on the time-tension integral \( (H > H_a, P < 0.01) \). In this comparison the isotonic heat is being compared with the “equivalent” isometric heat. Now in order to obtain the equivalent isometric heat we have altered tension development by changing muscle length (see Methods). We believe this comparison is valid because there is evidence that it is mechanical output and not muscle length, per se, that determines cardiac energy output (Sarnoff, Gilmore, Skinner, Wallace, and Mitchell, 1963; Gibbs et al., 1967). The differences between the heats were more noticeable at lower loads than at high loads \( (E \times L \text{ interaction, } P < 0.001) \) and further analyses were carried out to examine this interaction more closely. An analysis was done within each load so that the different error variances which occurred at different loads could be used in testing significance, rather than using an estimate pooled across loads. These analyses showed that the isotonic heat, \( H \), was greater than the equivalent isometric heat, \( H_a \), at all loads \( (P \text{ always } < 0.001) \) whereas \( H \) was greater than the equivalent isometric tension integral heat, \( H_a \).
at lower loads \((P/P_o = 0.1, 0.2, 0.4, 0.6, P < 0.01)\) but was not significantly greater when \(P/P_o = 0.8\).

In the second series of experiments carried out at 23°C and for which the isotonic tension-time integral was obtained directly (see Methods), the results were similar to those for the first series (Table II, Fig. 4). Again the main effect

### Table I

The amount of heat produced by papillary muscles during isotonic contractions \( (H = E_T - W_e) \) compared with the amounts predicted (neglecting shortening) on the basis of tension developed \( (H_i) \) or time-tension integral \( (H_a) \).

#### First Series of Experiments

| Energy type | Load ratio \((P/P_o)\) | 0.1  | 0.2  | 0.4  | 0.6  | 0.8  |
|-------------|-----------------|-----|-----|-----|-----|-----|
| \(H\)       |                 | 46.6| 61.4| 86.5| 109.2| 128.6|
| \(H_i\)     |                 | 28.6| 38.3| 61.1| 86.9 | 115.3|
| \(H_a\)     |                 | 34.5| 48.5| 76.0| 101.8| 125.7|

Means for 15 muscle preparations expressed in gram · centimeters per gram.

#### Analysis of variance

| Source of variation | DF | MS       | F    |
|---------------------|----|----------|------|
| Between muscle preparations (Blocks \(B\)) | 14 | 6,058.7 |      |
| Between energy types \((E)\) | 2  | 7,862.9  | 38.61*‡ |
| \(H\) vs. \(H_i\) | (1) | (15,669.3)| 117.03*‡ |
| \(H\) vs. \(H_a\) | (1) | (3,145.5) | 23.45*§ |
| Between loads \((L)\) | 4  | 56,609.7 | 421.98*‡ |
| \(E \times L\) | 8  | 194.2    | 9.50‡ |
| \(B \times E\) | 28 | 141.2    | 10.00‡ |
| \(B \times L\) | 56 | 446.6    | 31.62‡ |
| Residual            | 112| 14.12    |      |

* Compared with MS for \(E \times L\) interaction.
‡ \(P < 0.001\).
§ \(P < 0.01\).

for blocks and the block interactions contributed significantly to total variance. The isotonic heat, \(H_i\), was larger than either \(H\) or \(H_a\), particularly at lower loads \((E \times L\) interaction, \(P < 0.001)\). Separate analyses showed \(H\) to be larger than \(H_a\) at all loads \((P < 0.01 in all cases)\) whereas \(H\) was significantly \((P < 0.01)\) larger than \(H_a\) only when \(P/P_o = 0.1\) or 0.2.

#### Heat Production in Single Contractions

The above results show that both methods of analysis indicate that there is additional heat liberated when a muscle contracts isotonically. This additional
heat is more evident at light loads. We decided therefore that it would be useful to superimpose isotonic and isometric heat wave forms in a manner similar to that used by Hill (1949).

In 10 of the 23 experiments reported above the base line stability and signal to noise ratios were such that reasonable records could be made of the heat produced in a single twitch. Care was taken to standardize the prestimulus history of the muscles before each contraction. In none of these preparations did the rate of heat production in an isotonic contraction exceed the rate of heat production in an isometric twitch recorded at \( l_o \). A typical example is shown in Fig. 5 where the time course of the activation or tension-independent heat is also shown. The tension-independent heat is determined by shortening down the muscle until it can no longer develop any tension. The heat produced when the muscle is stimulated at this length is the activation or tension-independent heat. Note the very pronounced phase of relaxation heat shown
in the isotonic contraction. A series of isotonic contractions was normally recorded with gradually increasing afterloads and the deviation between the isotonic and isometric heat wave forms was found to be greatest at light loads and steadily to decrease with increasing afterload. This was true in all the

### Table II

| Load ratio (P/Po) | Energy type |
|------------------|-------------|
|                  | 0.1 | 0.2 | 0.4 | 0.6 | 0.8 |
| H                | 66.0 | 76.0 | 106.9 | 134.7 | 159.2 |
| Hs               | 33.1 | 44.7 | 72.4 | 106.7 | 142.5 |
| Ha               | 47.2 | 64.2 | 101.5 | 131.5 | 161.6 |

Means for eight muscle preparations expressed in gram. centimeters per gram.

### Analysis of variance

| Source of variation          | DF | MS       | F    |
|------------------------------|----|----------|------|
| Between muscle preparations  | 7  | 16,674.0 |      |
| (Blocks (B))                 |    |          |      |
| Between energy types (E)     | 2  | 9,087.5  | 43.46*† |
| H vs. Hs                     | (1) | (16,953.7) | 81.09*† |
| H vs. Hs                     | (1) | (1,213.7)    | 5.80*§  |
| Between loads (L)            | 4  | 45,783.9 | 218.98*‡ |
| E × L                        | 8  | 209.1    | 4.84*‡  |
| B × E                        | 14 | 553.6    | 12.82*‡ |
| B × L                        | 28 | 960.3    | 22.24‡  |
| Residual                     | 56 | 43.18    |      |

* Compared with MS for E × L interaction.
† P < 0.001.
§ P < 0.05.

preparations examined. It is apparent therefore that rabbit papillary muscles do not behave in the same way that frog and toad sartorius muscles do at 0°C.

### Contractile Element Work

In the second series of eight experiments the amount of internal work, $W_i$, was calculated by determining load-extension curves for the papillary muscles using the quick release technique of Wilkie (1956). The mean values so obtained are given in the legend to Fig. 6. With both the internal and external
work measured it is possible to calculate the contractile element work (C. E. W.) and to plot total energy against C.E.W. rather than against $P/P_o$. In Fig. 6(top) the C.E.W. has been plotted against the load $P$ and in Fig. 6 (bottom) the total energy $E_T$ has been plotted against C.E.W. The means of the

![Graph showing relationships among total energy (ET), isotonic heat (H), tension integral heat (H0), isometric heat (Hi), external work (We), and load. The results were obtained from eight muscles at a temperature of 23°C and the data are given in Table II.](image-url)
results shown in Table II have been used. The resultant plot is very similar to that obtained by Coleman (1968) in his oxygen consumption studies on cat papillary muscle. It may be possible to have an approximately linear correlation on the ascending portion of the C.E.W. plot (i.e., with loads up to 0.5 $P_o$) but as the afterloads increase past this point there is a complete breakdown of any simple linear correlation.

**Discussion**

In analyzing the total energy experiments the isotonic energy output was not compared with the isometric heat output at $l_o$ but with the isometric heat output for the same tension or same tension-time integral. Both methods of analysis make certain assumptions that can best be understood with reference to the schematic diagram (Fig. 7). In Fig. 7 $a$ two isometric tension records are shown; the larger is obtained at $l_o$ and the smaller with the muscle shortened down. In Fig. 7 $b$ the peak isometric record is shown together with an isotonic mechanical record, in which a load equivalent to the tension developed in the smaller contraction of Fig. 7 $a$ is being lifted. In Fig. 7 $c$ the actual isometric tension "seen" by the muscle during the isotonic contraction is shown, ignoring the complication of the passive resting tension. From Fig. 7 it is also apparent why in single contraction comparisons it may not be fair to
superimpose the isotonic heat wave form upon the isometric wave form recorded at a shortened length. Any change measured early or late in the contraction cycle could reflect an increase in $dP/dt$ (Fig. 7 a) or in the tension-time integral (Fig. 7 c) rather than an increase in a “shortening” heat component. We have somewhat overstated the case here in that it might be argued that for a considerable proportion of the isotonic contraction the muscle will in fact be at a length not too far distant from the shortened muscle length where the small isometric contraction was recorded.

The single contraction studies provide good evidence, insofar as the experimental technique will allow, that the rate of heat production in an isotonic contraction never exceeds the rate of heat production in an equivalent isometric contraction at $l_o$. This in itself does not provide evidence against additional heat being liberated when a muscle shortens. In the isometric contraction at $l_o$ the tension-dependent heat will be much greater and the large
series elasticity of cardiac muscle will allow sizeable internal shortening. In this situation it may be possible that during the onset phase of contraction the isotonic heat rate will never exceed the isometric heat rate.

Before examining the total energy results in some detail it is necessary to emphasize that in these cardiac experiments both the initial and recovery energies are being measured (Gibbs, 1969) and also the final heat measurements are being made 30-60 sec after the trains of contractions are completed. Thus if it is found that there is "additional" heat liberated in an isotonic contraction it is not possible to use the arguments put forward by Carlson, Hardy, and Wilkie (1963) or Davies, Kushmerick, and Larson (1967). These authors have suggested that in skeletal muscle mechanisms might exist such that in relaxation when the muscle lengthens, heat equal to the shortening heat is absorbed or a redistribution of heat occurs such that heat normally produced during relaxation occurs earlier during the contraction cycle in an isotonic response.

In the mechanochemical study of Pool et al. (1968) it can be seen in Fig. 1 that the relationship between the change in high energy phosphate and load is very similar to that seen in Figs. 3 and 4 of this paper. A multiple regression analysis with the form

\[ \Delta \sim P = k_0 + k_1A + k_2W_e + k_3W_e \]

was carried out, in which \( k_0 \), a constant representing the intercept of the regression equation, did not differ significantly from zero. The three remaining coefficients were highly significant and interestingly the regression coefficient associated with external work (\( k_3 \)) had a value of 0.0031 \( \mu \)mole/g·cm external.

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**Figure 7.** Schematic diagram of length (downwards) and tension (upwards) changes under various experimental conditions. Fig. 7a shows the typical changes that occur in tension myograms when a muscle is shortened. Fig. 7b shows that if a muscle lifts a load equal to the tension developed at the shortened length the isotonic contraction has a duration intermediate between that in the isometric "long" and "short" contractions. Fig. 7c shows the time course of the tension change during the isotonic contraction of Fig. 7b.
work, a value that compares favorably with that found in several skeletal muscle studies. The regression coefficient for internal work had a value about twice as high but this is difficult to interpret as it is well-known that internal work in cardiac muscle preparations correlates almost linearly with peak developed tension.

In order to determine whether a significant energy utilization could be associated with shortening per se a further regression analysis was performed such that:

$$\Delta \sim P = k_o + k_1A + k_2W_t + k_3S$$

The coefficient of regression for shortening had a large error and was not significant. In effect this is really an attempt to find a linear relationship between total isotonic energy minus equivalent isometric heat ($E_t - H_i$) (i.e. $\Delta \sim P - (k_o + k_1A + k_2W_t)$), and $S$ where $S$ is the distance shortened. Because the $\Delta \sim P$ term includes phosphate breakdown associated with the performance of external work the above analysis is necessarily rendered obscure and the assumption that the shortening heat coefficient is constant, may be incorrect as there seems to be experimental evidence that the shortening heat coefficient may be load-dependent (Hill [1964 a]).

We have already mentioned in the Introduction that certain isotonic cardiac experiments have been carried out and analyzed in a fashion similar to the myothermic experiments; i.e., isometric and isotonic afterloaded contractions at equal levels of tension development were compared and correlated with changes in $V_o_2$ (Coleman and Sonnenblick, 1967; Coleman et al., 1969). In the latter paper in Fig. 3 the increment in oxygen consumption was compared with external work; a linear correlation was found and the fact that the intercept of the regression equation describing this relationship was not significantly different from zero was taken to show that shortening per se had no effect on oxygen consumption. It should be emphasized that these authors are not dealing in any absolute units; i.e., they are plotting oxygen consumption vs. work. The comparison they are making is really total isotonic energy minus equivalent isometric heat ($E_t - H_i$) against $W_e$, whereas the plot which tells a good deal more is isotonic heat minus equivalent isometric heat ($H - H_i$) against $W_e$. Even so if the data presented in Fig. 4 of this study are replotted in a similar fashion (see Fig. 8), note that a similar good linear correlation would occur provided loads greater than 0.3 $P_e$ are considered. At lighter loads it is obvious that the curve would not extrapolate through zero. In the study of Coleman et al. (1969) it appears that the lowest loads used were about 0.25 $P_e$ and that there was no accurate estimate of $H_i$ or its oxygen equivalent for tension values less than about 0.5 $P_e$. For this reason we do not believe that these results can be considered as solid evidence against the idea of additional heat associated with muscle shortening.
It is important to note that in the cardiac experiments recovery heat is also being measured. Now Hill (1928) has shown that recovery heat production approximately equals initial heat production and that this relationship holds regardless of whether isometric or isotonic responses are being examined. Therefore if cardiac muscle behaves metabolically like skeletal muscle an argument can be advanced for subtracting out twice the external work from the total energy. Alternatively, it can be stated that the slope of the total isotonic energy minus equivalent isometric tension heat ($E_T - H_i$) vs. $W_e$ plot should be at least 2 and for medium to heavy loads this is approximately true (see Fig. 8) but at light loads there is still additional heat to be accounted for. It will also be noticed that this type of result would not occur if the heat vs. tension integral plot were used; i.e., the slope of total isotonic energy minus equivalent isometric tension integral heat ($E_T - H_i$) vs. $W_e$ is far less than 2. As this result is critically dependent upon (a) the calibration and (b) the ratio of recovery to initial energy output, it does not seem prudent to interpret this result too deeply. It could be taken as evidence against an additional heat associated with shortening or as evidence against the tension time integral as a major index of energy expenditure. It is obviously an important point, however, and should be thoroughly examined when the myothermic or other techniques are able to provide the necessary accuracy.
Britman and Levine (1964) originally proposed that contractile element work is a major determinant of myocardial oxygen consumption based on studies carried out on intact dog hearts and a high correlation coefficient (0.91) was reported. The formula they used to calculate C.E.W. has been criticized as giving a disproportionately large importance to fiber shortening rather than to tension development (McDonald et al., 1966). Recent studies by Coleman have shown that there is a lack of correlation between C.E.W. and myocardial oxygen consumption in cat papillary muscle and his results are supported by the present study. It must be remembered that in whole heart studies it is practically impossible to obtain the completed curves of stroke work vs. aortic pressure, left ventricular end-diastolic pressure, etc. Thus only half the classical bell-shaped external work curve obtained with papillary muscles is really measured (see Sonnenblick and Downing, 1963) and over this work range it would be quite possible to see a linear correlation between C.E.W. and myocardial oxygen consumption.

The present study supports our earlier results which showed that there is additional heat liberated in an isotonic contraction above that expected from an equivalent isometric contraction. The results are by no means unequivocal and to a certain extent our conclusions depend upon how one attempts to analyze the data. In terms of the data presented in this paper it would seem reasonable to suggest that an analysis of the isotonic results solely in terms of developed tension, would produce the maximum possible indication of additional heat associated with muscle shortening. Indeed because this analysis tends to minimize the cost of tension maintenance it probably produces an overestimate of such heat. On the other hand an analysis in terms of the tension integral still produces evidence of additional heat associated with shortening although reduced in magnitude. We would intuitively suggest that an analysis of the present results, based on the proposition that the time integral of the active state is the major mechanical index of energy expenditure, would give the most clear-cut answer. The problems of determining the active state in cardiac muscle are such as to make this approach unfeasible at present (see Brady [1968]).

In a recent and very timely review Mommaerts (1969) has discussed at some length the energies of muscular contraction and has attempted to correlate the biochemical and myothermic data from a wide range of different experiments. In attempting to set up a general balance sheet for energy expenditure in a twitch Mommaerts slightly modified Hill's (1964 c) equation so that:

\[ E_T = A + W_e + a(\Delta l) + f(P, t) \]

where \( A \) = activation heat, \( W_e \) = external work, \( a(\Delta l) \) represents the shortening heat, and \( f(P, t) \) is a term indicating that there is heat production linked in some way to the intensity and duration of a contraction.
The arguments for a separate activation heat component are well-documented in that review. The activation heat and the external work term can be measured with reasonable accuracy but in terms of balancing energy expenditure we are left with two terms that are both ill-defined and difficult to measure.

How are we to measure the tension-linked heat \( f(P,t) \)? Undeniably a certain amount of this heat represents in terms of the above equation degraded internal work and this will not be an insignificant fraction. It might be more logical, however, to do away with the distinction between internal and external work and add them together. As we have shown in this paper however, there is still heat unaccounted for. Should we regard this heat as being some index of the cost of tension maintenance or does it represent a shortening heat component? Mommaerts has made a critical summary of the shortening heat controversy and has argued with a good deal of justification that such a component should be regarded as a dissipational or waste heat accompanying the work process because this process cannot be conducted with unit enthalpy efficiency. This means that we are really looking at the efficiency of the transduction step at different contractile element velocities. Unfortunately until it is demonstrated that there is some mechanical index that determines the tension-linked heat \( f(P,t) \), it will not be possible to resolve the shortening heat controversy using the existing empirical equations. In the final analysis it is impossible in muscle to have either shortening, or the development and persistence of tension, without the continuous formation and disintegration of cross links between actin and myosin, and in this sense the distinction between a shortening heat component and a tension heat component may be highly artificial if indeed it even exists.

The authors would like to thank Mr. H. Vogelsanger for technical assistance and Miss D. Harrison and Miss S. Woolley for preparing the diagrams.
This work was supported by a Grant-in-aid from the National Heart Foundation of Australia.

Received for publication 2 February 1970.

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