Analysis of Left Ventricular Pressure
During Isovolumic Relaxation
in Coronary Artery Disease

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SUMMARY When a decrease in left ventricular isovolumic pressure is considered as an exponential, the rate of relaxation can be defined by a time constant (T). Previously, T has been calculated from the slope of ln (pressure) against time, but this method is valid only when the asymptote of the exponential is zero. In this study two estimates of T were made: T_in from the slope of ln (pressure) against time, and T_exp by a method of exponential analysis that also estimated the asymptote. These techniques were applied to measurements of left ventricular pressure made at increasing pacing rates in three groups of patients catheterized for chest pain: group 1 (n = 9) — normal coronary arteriograms; group 2 (n = 9) — coronary artery disease (CAD) but no angina or lactate production during pacing; and group 3 (n = 9) — CAD and angina during pacing. T_in was always shorter than T_exp, and in groups 1 and 2 T_exp was dependent on heart rate, whereas T_in was not. The asymptote was negative, and increased toward zero during pacing in groups 1 and 2. The difference between T_exp and T_in could be related to the value of the asymptote. In 18 of 20 beats tested, pressures calculated from T_exp and the asymptote were in closer agreement with measured pressures than were the pressures predicted by T_in. Despite these different values, T_exp and T_in each distinguished between the three groups. Although the choice of an exponential model is arbitrary, isovolumic pressure decrease approximates to a single exponential; but this study suggests that both T and the asymptote are variable.

THE STUDY of the decrease in left ventricular pressure during isovolumic relaxation is hindered by the lack of a method of quantifying pressure decrease that can be used to compare individual subjects. The maximal rate of pressure decrease (dP/dt min) can decrease during ischemia, but dependence on end-systolic pressure and fiber length limits its value. More recently, a pressure decrease from the point of dP/dt min has been treated as a single exponential, which allows derivation of a time constant that describes relaxation. The time constant is calculated as the negative reciprocal of the slope of ln (pressure) against time, and the correlation coefficient is used to test the validity of the monoexponential model. The time constant so derived is relatively insensitive to heart rate, ventricular volume and the level from which pressure decreases, but is prolonged during ischemia.

This semilogarithmic method of estimating the time constant of an exponential is valid only when the asymptote of the exponential is zero. The zero reference for pressure measurement is an external point; one cannot assume that it corresponds to the asymptote of ventricular pressure decrease or that the asymptote remains constant under different conditions. In this study, we estimated the time constant of isovolumic pressure decrease both from the plot of ln (pressure) against time and by a method of exponential analysis that also estimates the asymptote. We used these techniques to analyze pressure measured during pacing in patients who were evaluated for chest pain.

Patients and Methods

Twenty-seven patients (ages 34–59 years) limited by chest pain were studied during diagnostic cardiac catheterization for suspected coronary artery disease. The protocol was approved by the hospital ethical committee, and each patient gave written consent.

Cardiac Catheterization

The catheterization procedure has been described in detail elsewhere. Briefly, after routine pressure measurements and coronary arteriography, a catheter-tip micromanometer (Telco MM52 or #5 Millar) was positioned in the left ventricle through a long sheath. A Ganz pacing and thermistor catheter was advanced into the coronary sinus from a left antecubital vein. No measurements were made for at least 20 minutes after coronary arteriography. Left ventricular pressure was measured and blood samples were drawn from the left ventricle and coronary sinus at the basal heart rate and at increasing paced rates. Left ventricular cineangiography was performed at the end of the study.

Computer Analysis of Pressure Signals

The sternal angle was used as zero reference for all pressure measurements. Left ventricular pressure was measured simultaneously by the catheter-tip micromanometer and by the lumen of the Telco (or the long-sheath when the Millar catheter was used). The signals were displayed on a Cambridge 12-channel recorder and stored on tape (Phillips seven-channel FM recorder) and analyzed off line with a Varian computer (620/L-100).
The computer analyzed pressure signals in 9-second periods, each of which was accompanied by a zero and calibration signal for the fluid-filled pressure channel. The record was broken into individual beats by computer recognition of the R wave of the ECG. The micromanometer signal was digitized every 5 msec and the fluid-filled pressure every 10 msec. After an appropriate correction for time delay, the two signals were matched; the correct zero and calibration for the micromanometer were calculated by least-squares regression and used in the analysis of that record.

Ideally, pressure should be analyzed from the point of dP/dt min to mitral valve opening. As the latter cannot be identified confidently from the left ventricular pressure signal, we used the period from the point of dP/dt min to the time at which pressure decreased to the level of end-diastolic pressure of the preceding beat. For each beat, the digitized micromanometer signal during this period was analyzed in two ways.

**Semilogarithmic Method**

The semilogarithmic method assumes the asymptote of pressure fall is zero. Thus, \( P(t) = ae^{bt} \), and \( \ln P(t) = A + bt \). The value of b was estimated from the slope of \( \ln \) (pressure) against time by least-squares regression. The time constant \( (T_{in}) = -1/b \).

**Exponential Method**

The exponential method does not assume the asymptote to be zero. Thus, \( P(t) = ae^{bt} + c \). The parameters a, b and c can be determined by considering three points equally spaced in time on a pressure-time curve. For three values of pressure at times o, m and 2m, it can be shown that

\[
b = -\frac{1}{m} \ln \left( \frac{P(o) - P(m)}{P(m) - P(o)} \right)
\]

and the asymptote (c) is given by \( c = P(o) - a \), where \( a = (P(o) - P(0))/(e^{-b\cdot m} - 1) \).

These equations were applied to the digitized pressure signal as follows: The parameters were calculated using sets of three points \( P(o), P(20), \) and \( P(40) \), where 0, 20 and 40 refer to time in msec after dP/dt min — then \( P(o), P(20), \) and \( P(40) \),... until all the points were used. The mean values of b and c were calculated for each beat. The time constant \( (T_{exp}) = -1/b \). The computer also calculated KVMax (from developed pressure), dP/dt max and dP/dt min for each beat. The values that appear in the results are the mean of all the beats in a 9-second record. The beats were displayed during analysis, so that ectopic, postectopic and technically unsatisfactory beats could be excluded. The digitized pressure record could be retrieved from the computer to test the predictions of the time constants with measured pressure.

**Measurement of Lactate Concentration**

Left ventricular and coronary sinus blood were sampled simultaneously. Samples were added to an aliquot of perchloric acid, put on ice and stored at \(-20^\circ C\). Lactate concentration was estimated by a fluorometric method. The extraction ratio is defined as the difference in concentration between arterial and coronary sinus blood expressed as a percentage of arterial concentration.

**Statistical Methods**

For individual beats, pressures at 5-msec intervals were calculated for the period of isovolumic pressure decrease from the parameters of the two models of pressure decrease and compared with the digitized micromanometer signal. The chi-square test was used to test the hypothesis that predicted and observed pressures were identical. The ratio of the residual to the total sums of squares (RSS/TSS) was used to estimate the proportion of the total variance in the observed pressure-time curve that could not be accounted for by the predictions of the model. Thus, the smaller the ratio the better the agreement between predicted and observed pressure. Elsewhere, the t test and linear regression were used. Values are expressed as mean ± SEM and \( p < 0.05 \) is considered significant.

**Results**

The 27 patients were divided into three groups on the results of coronary arteriography and effects of pacing. Group 1 included nine patients with normal coronary arteries who did not have pain or produce lactate on pacing. Group 2 included nine patients with coronary artery disease in whom pacing did not provoke angina or lactate production. Group 3 included nine patients with coronary artery disease who had angina during pacing. The details of the three groups are listed in tables 1–3.

Twenty heart beats from eight patients, including at least two patients from each group, were used to test the goodness of fit of the pressure decrease predicted by the two models with measured pressure (fig. 1). Exponential analysis estimated the time constant \( (T_{exp}) \) to be 66 msec and the asymptote of pressure decrease to be \(-32 \text{ mm Hg}\); the semilogarithmic method gave an estimate of 32 msec for the time constant \( (T_{in}) \). When predicted and observed pressures are compared, \( \chi^2 = 0.52, p > 0.9995 \) and RSS/TSS = 0.03% for the exponential model, and \( \chi^2 = 7.54, 0.95 < p < 0.99 \) and RSS/TSS = 4.5% for the semilogarithmic method. Figure 1C shows the plot of ln (pressure) against time from which \( T_{in} \) was derived. The points do not form a straight line, the slope becoming steeper at low values of ln (pressure); despite this, \( r = -0.97 \). In figure 1D, this departure from the linear has been abolished by plotting ln (pressure — asymptote) against time. Linear regression now yields a time constant of 67 msec instead of 32 msec, and \( r = -0.99 \). Large differences were found between \( T_{exp} \) and \( T_{in} \) in all three groups, particularly when the estimate of the asymptote was low (fig. 2). The fit of pressure predicted by the exponential model to measured pressure was superior to the predictions of the semilogarithmic model in 18 of 20 beats tested. For the exponential model, the range of values was \( \chi^2 = 0.33, p > 0.9995, \) RSS/TSS = 0.1%, to \( \chi^2 = 5.4, 0.95 < p < 0.99, \) RSS/TSS = 2.6%; for the semilogarithmic model,
χ² = 0.5, p > 0.9995, RSS/TSS = 0.5%, to χ² = 23.5, 0.3 < p < 0.4, RSS/TSS = 9%.

Group 1

The patients in group 1 had good left ventricular function and normal myocardial lactate extraction (table 1). With pacing, dP/dt max increased and left ventricular end-diastolic pressure decreased between the highest and lowest pacing rates, and lactate extraction ratio did not change significantly (table 2).

The estimates of TEXP and the asymptote are shown in figures 3A and 3D. Between the lowest and highest heart rates, TEXP decreased from 55 ± 4 msec to 34 ± 2 msec (p < 0.001), and the asymptote increased from −25 ± 3 mm Hg to −9 ± 2 mm Hg (p < 0.01). There was a significant inverse relation between TEXP and heart rate (r = −0.75, p < 0.01) and a positive correlation between the asymptote and heart rate (r = 0.68, p < 0.01). In all instances, TEXP was greater than TIN. Between the lowest and highest heart rates, TIN decreased from 32 ± 3 msec to 24 ± 3 msec (p < 0.05), but when all pacing rates were considered together, TIN was not related significantly to heart rate. The ratio of the time available for relaxation (the interval between dP/dt min and end-diastole) to TEXP decreased as heart rate increased (r = −0.8, p < 0.01), but never fell below 3 (fig. 4A).

Group 2

The basal hemodynamic results of the patients in group 2 did not differ significantly from those in group 1, although ejection fraction, cardiac index and myocardial lactate extraction ratio tended to be lower and end-diastolic volume index higher. With pacing, KVmax increased, but dP/dt max, end-diastolic pressure and lactate extraction ratio did not change significantly.

The estimates of TEXP and the asymptote are shown in figures 3B and 3E. Between the lowest and highest heart rates, TEXP decreased from 57 ± 2 msec to 46 ± 3 msec (p < 0.01), and when all pacing rates were considered, TEXP related inversely to heart rate (r = −0.61, p < 0.01). The asymptote increased from −24 ± 4 mm Hg to −15 ± 4 mm Hg (NS), and there was a weak correlation between the asymptote and heart rate (r = 0.44, p < 0.05). TIN decreased from 35 ± 3 msec to 32 ± 3 msec (NS). The ratio of the time available for relaxation to TEXP decreased as pacing

### Table 1. Angiographic and Basal Hemodynamic and Metabolic Results

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 9)</th>
<th>Group 2 (n = 9)</th>
<th>Group 3 (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary arteriograms</td>
<td>Normal</td>
<td>5 one-vessel</td>
<td>3 two-vessel</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 two-vessel</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 three-vessel</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.66 ± 0.016</td>
<td>0.56 ± 0.055</td>
<td>0.58 ± 0.03</td>
</tr>
<tr>
<td>End-diastolic volume index (ml/m²)</td>
<td>59 ± 4</td>
<td>69 ± 7</td>
<td>95 ± 14*</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>3.07 ± 0.32</td>
<td>2.54 ± 0.23</td>
<td>2.34 ± 0.15*</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>6.3 ± 2.0</td>
<td>6.2 ± 1</td>
<td>12.6 ± 1.3</td>
</tr>
<tr>
<td>dP/dt max (mm Hg/sec)</td>
<td>1527 ± 58</td>
<td>1745 ± 110</td>
<td>1282 ± 49†§</td>
</tr>
<tr>
<td>KVmax (sec⁻¹)</td>
<td>91.8 ± 5</td>
<td>95 ± 8</td>
<td>82 ± 5</td>
</tr>
<tr>
<td>dP/dt min (mm Hg/sec)</td>
<td>−1825 ± 87</td>
<td>−1844 ± 104</td>
<td>−1451 ± 80†‡</td>
</tr>
<tr>
<td>Lactate extraction ratio (%)</td>
<td>25.7 ± 3.4</td>
<td>18.5 ± 4.8</td>
<td>11.5 ± 3.5†</td>
</tr>
</tbody>
</table>

* p < 0.05, group 1 vs group 3.
† p < 0.01, group 1 vs group 3.
‡ p < 0.025, group 2 vs group 3.
§ p < 0.005, group 2 vs group 3.

Abbreviations: LVEDP = left ventricular end-diastolic pressure.

### Table 2. Hemodynamic and Metabolic Changes Induced by Pacing

<table>
<thead>
<tr>
<th></th>
<th>Group 1 Heart rate</th>
<th>Group 2 Heart rate</th>
<th>Group 3 Heart rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimum</td>
<td>Maximum</td>
<td>Minimum</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>6.3 ± 2</td>
<td>p &lt; 0.05</td>
<td>6.2 ± 1.1</td>
</tr>
<tr>
<td>dP/dt max (mm Hg/sec)</td>
<td>1527 ± 58</td>
<td>p &lt; 0.001</td>
<td>2083 ± 8.2</td>
</tr>
<tr>
<td>KVmax</td>
<td>91.8 ± 5.1</td>
<td>NS</td>
<td>100.4 ± 82</td>
</tr>
<tr>
<td>dP/dt min (mm Hg/sec)</td>
<td>−1825 ± 87</td>
<td>NS</td>
<td>−1823 ± 138</td>
</tr>
<tr>
<td>Lactate extraction ratio (%)</td>
<td>27.5 ± 3.6</td>
<td>NS</td>
<td>22.7 ± 4.3</td>
</tr>
</tbody>
</table>

Abbreviations: LVEDP = left ventricular end-diastolic pressure.
Table 3. Mean Values of $T_{EXP}$, the Asymptote and $T_{In}$ in the Three Groups of Patients

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal heart rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate</td>
<td>86 ± 6</td>
<td>85 ± 7</td>
<td>77 ± 6</td>
</tr>
<tr>
<td>$T_{EXP}$ (msec)</td>
<td>55 ± 4</td>
<td>57 ± 2</td>
<td>80 ± 6*</td>
</tr>
<tr>
<td>Asymptote (mm Hg)</td>
<td>-25 ± 3</td>
<td>-24 ± 4</td>
<td>-38 ± 41</td>
</tr>
<tr>
<td>$T_{In}$ (msec)</td>
<td>31 ± 3</td>
<td>35 ± 3</td>
<td>49 ± 38*</td>
</tr>
<tr>
<td>Highest pacing rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate</td>
<td>132 ± 5</td>
<td>129 ± 5</td>
<td>127 ± 7</td>
</tr>
<tr>
<td>$T_{EXP}$ (msec)</td>
<td>34 ± 2</td>
<td>47 ± 3†</td>
<td>84 ± 10**</td>
</tr>
<tr>
<td>Asymptote (mm Hg)</td>
<td>-9 ± 2</td>
<td>-15 ± 4</td>
<td>-35 ± 81</td>
</tr>
<tr>
<td>$T_{In}$ (msec)</td>
<td>24 ± 2</td>
<td>32 ± 3*</td>
<td>50 ± 68*</td>
</tr>
</tbody>
</table>

Group 1 vs group 2:  
* $p < 0.05$.  
† $p < 0.01$.  
Group 1 vs group 3:  
‡ $p < 0.05$.  
§ $p < 0.01$.  
Group 2 vs group 3:  
¶ $p < 0.05$.  
** $p < 0.01$.  

Discussion

Treating the decrease in left ventricular pressure from the point of dP/dt min as a monoexponential rate increased ($r = -0.83, p < 0.01$), and the lowest value was 3.0 (fig. 4B).

Group 3

Basal cardiac index, dP/dt max, dP/dt min and myocardial lactate extraction ratio were significantly lower and end-diastolic volume index higher in group 3 than in group 1, and dP/dt max and dP/dt min were lower than in group 2. At the highest pacing rate, all nine patients experienced angina, which was associated with a significant reduction of myocardial lactate extraction from resting levels. Despite angina, dP/dt max increased significantly between lowest and highest pacing rates; dP/dt min did not change significantly, and in only one patient was a large reduction observed during angina (from $-2041$ to $-900$ mm Hg/sec).

There was considerable individual variation in $T_{EXP}$ both at rest and during pacing (figs. 3C and 3F), and $T_{EXP}$ failed to decrease as heart rate increased. The mean values at the lowest and highest pacing rates (80 ± 6 msec and 84 ± 10 msec) did not differ significantly. At the highest heart rate, during angina, several patients had very high values of $T_{EXP}$ (range 63–131 msec). Similarly, the asymptote did not change significantly with pacing, and the values showed considerable individual variation. $T_{In}$ was similar at the lowest (49 ± 3 msec) and highest (50 ± 6 msec) pacing rate. The ratio of time available for relaxation to $T_{EXP}$ decreased as heart rate increased ($r = -0.53, p < 0.02$), and was 3 or less in each patient during angina (fig. 4C).

Comparison of Groups

The mean values of $T_{EXP}$, the asymptote and $T_{In}$ are listed in table 3. To allow comparison of the three groups to be made at similar heart rates, the means for group 1 were calculated using the results at the second highest pacing rate for three of the nine patients. At the basal heart rate, the mean values of $T_{EXP}$, the asymptote and $T_{In}$ were similar in groups 1 and 2, but $T_{EXP}$ and $T_{In}$ were longer and the asymptote lower in group 3 than in groups 1 and 2. At the highest pacing rate, $T_{EXP}$ and $T_{In}$ were longer in group 2 than in group 1, and greater in group 3 than in groups 1 and 2. The asymptote was similar in groups 1 and 2, but lower in group 3 than in groups 1 and 2.

![Figure 1](https://example.com/figure1.png)

**Figure 1.** Analysis of the decrease in left ventricular pressure from the point of dP/dt min (time 0) until it reaches the level of end-diastolic pressure of the preceding beat. (A) Dots represent measured left ventricular pressure digitized at 5-msec intervals. The solid line indicates the course of the pressure decrease predicted by exponential analysis. For this beat, $T_{EXP} = 66$ msec and the asymptote $= -32$ mm Hg. (B) The same beat as in panel A. Dots represent measured pressure digitized at 5-msec intervals. The solid line indicates the course of the pressure decrease predicted by semilogarithmic analysis. For this beat, $T_{In} = 32$ msec. (C) The plot of $\ln$ (pressure) against time for the same beat. $T_{In}$ was derived by linear regression of this plot. The plot deviates from linearity at low values of ln (pressure), but $r = -0.97$. (D) The plot of $\ln$ (pressure - asymptote) against time for the same beat. The plot is linear, $r = -0.999$, and the slope gives a time constant of 67 msec, which is in close agreement with $T_{EXP}$ (66 msec). In this and subsequent figures, $T_{EXP} = time$ constant estimated exponentially; $T_{In} = time$ constant estimated semilogarithmically.
allows the derivation of a time constant that describes isovolumic relaxation.\textsuperscript{4, 5, 6} As the time between dP/dt min and mitral valve opening is short, any model predicting rapid pressure decrease will show some success. The choice of an exponential model is arbitrary, and statistical analysis cannot confirm that pressure decrease is exponential, but merely tests how closely the predictions of the model approximate measured pressure.

In previous studies, the time constant has been calculated as the negative reciprocal of the slope of ln (pressure) against time.\textsuperscript{4, 5, 6} This method is valid only when the asymptote of pressure fall is zero. Our results suggest the asymptote is lower than zero reference pressure and dependent on heart rate.

In figure 5A, all three hypothetical pressure-time curves are monoexponential and have the same time constant but different asymptotes. The slope of ln (pressure) against time (fig. 5B) differs for each value of asymptote, and \( T_{\text{exp}} \) is correct only when the asymptote is zero. In addition, when the asymptote is not zero, the relation between ln (pressure) and time is a curve, so the slope determined by linear regression depends upon the part of the curve analyzed, and hence the level to which pressure decreases (fig. 6).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Relationship between \( T_{\text{exp}}/T_{\ln} \) and the asymptote for the patients in group 1. The ratio increases as the asymptote decreases further below zero.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Individual values of \( T_{\text{exp}} \) and the asymptote in the three groups. (A) Group 1. Relation between \( T_{\text{exp}} \) and heart rate \((r = -0.80, p < 0.01)\). (B) Group 2. Relation between \( T_{\text{exp}} \) and heart rate \((r = 0.61, p < 0.01)\). (C) Group 3. Values before (dots) and during angina (triangles) are shown. \( T_{\text{exp}} \) and heart rate were not related significantly. (D) Group 1. Relation between asymptote and heart rate \((r = 0.68, p < 0.01)\). (E) Group 2. Relation between asymptote and heart rate \((r = 0.44, p < 0.02)\). (F) Group 3. Values before (dots) and during angina (triangles) are shown. The asymptote and heart rate were not related significantly.}
\end{figure}
These factors have a large effect on the slope, but little effect on the correlation coefficient. Therefore, $T_{in}$ is an unreliable estimate of the time constant, and the correlation coefficient does not test its validity.

$T_{in}$ is correct only where the asymptote and zero reference pressure coincide, and the greater the difference between them, the greater the inaccuracy of $T_{in}$. Thus, $T_{in}$ for a given beat will depend upon the choice of zero reference. Had our reference pressure been at the midchest level rather than at the sternal angle, the values of $T_{in}$ would have been slightly longer.

The exponentially derived time constant ($T_{EXP}$) is independent of the asymptote. As it is calculated from differences in pressure between successive points in time, $T_{EXP}$ is also independent of absolute pressure. Thus, $T_{EXP}$ for a given beat will be the same whether pressure is measured with respect to the sternal angle, midchest, or intrathoracic pressure. The estimate of the asymptote depends on absolute pressure; a given change in reference pressure produces an equal but opposite change in the asymptote.

Although the exponential model has these advantages, it is based on a more complicated model. The asymptote cannot be measured, and the only statistical test that can be applied is the comparison of the predictions of the whole model with measured pressure. In all examples tested, predicted and observed pressures agreed closely, and in 18 of 20 beats the exponential model was superior to the semilogarithmic model. The $T_{EXP}$ was always longer than $T_{in}$ and, as would be expected, the ratio of $T_{EXP}$ to $T_{in}$ decreased as the asymptote increased toward zero. The relation between $T_{EXP}$ and asymptote was not precise, because $T_{in}$ depends upon both the asymptote and the level to which pressure decreases. This discrepancy between $T_{EXP}$ and $T_{in}$ should be eliminated by calculating $T_{in}$ from the plot of $\ln$ (pressure - asymptote) against time (fig. 1D).

The independence of $T_{in}$ and heart rate can be explained by changes in the asymptote. At low heart rates, when the asymptote was negative, $T_{in}$ underestimated markedly the time constant, but at high heart rates, when the asymptote increased toward zero, $T_{in}$ was in closer agreement with the shorter time.
Incoordinate relaxation has been studied by analyzing the early and late parts of isovolumic pressure decrease separately, and in patients with coronary disease, $T_{in}$ derived from the first 40 msec is longer than $T_{in}$ derived from the later points; but this does not provide evidence of incoordination or allow its quantification, because when the asymptote is negative, as is usually the case, the ln (pressure)-time relation is a curve, and linear regression of its early and late parts inevitably yields two different values of $T_{in}$ (fig. 6).

Ventricular volume and contractility have little effect on $T_{in}$ but one cannot assume that $T_{exp}$ is similarly independent. Prolongation of $T_{exp}$ might therefore be caused by ventricular dilatation or depressed contractility rather than by a specific effect of ischemia on relaxation. Within the three groups, $T_{exp}$ could not be related to indexes of contractility or ventricular volume. There was considerable overlap between groups 2 and 3 in values of $K_{Vmax}$, ejection fraction and end-diastolic volume, but $T_{exp}$ was significantly longer in group 3. Our observations suggest that prolongation of $T_{exp}$ is due to ischemia, and may precede angina and lactate production.

The asymptote is the level to which pressure would decline if isovolumic pressure decrease continued indefinitely, rather than the pressure to which the ventricle would relax if it did not fill; for it cannot be assumed that the process underlying isovolumic relaxation continues into diastole. Indeed, the low values of the asymptote during angina are contrary to what would be expected if it represented pressure at complete relaxation. The asymptote is a mathematical term that, in conjunction with $T_{exp}$, describes isovolumic pressure decrease and is applicable only to this part of the cardiac cycle.

Weisfeldt et al. considered that the process described by $T_{in}$ continues throughout diastole, so that the ratio of the interval between $dP/dt$ min and end-diastole to $T_{in}$ measures how completely the ventricle relaxes (fig. 4). Ratios less than 3.5 are associated with an upward shift of the pressure-dimension curve of the canine ventricle, suggesting that incomplete relaxation alters diastolic properties. Because $T_{in}$ depends upon the level to which pressure decreases, the association of low value of this ratio and high end-diastolic pressure may not be causal. We used $T_{exp}$ to calculate the ratio, which was always 3 or less during angina; but end-diastolic pressure did not increase with pain in all patients, suggesting that the ratio is a poor predictor of diastolic properties. If this is the case, calculating the ratio adds no information, as the differences in its value between the groups are due solely to differences in $T_{exp}$.

We conclude that although the choice of an exponential model is arbitrary, the isovolumic pressure decrease closely approximates a single exponential. Our results suggest that in the human heart, an exponential model requires both the time constant and

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**Figure 6.** (upper left) The two pressure-time curves are monoexponentials, having the same time constant (50 msec) and asymptote (-20 mm Hg). (upper right) The plot of ln (pressure) against time of the curves A and B shown in the left-hand panel. Linear regression of A yields $r = -0.97$ and $T_{in} = 23$ msec, and of B yields $r = -0.99$ and $T_{in} = 29$ msec. Thus, when the asymptote is negative, an upward shift of the pressure-time curve results in prolongation of $T_{in}$, even though the time constant has not really changed. (below) The plot of ln (pressure) against time for a monoexponential of which the time constant is 50 msec and the asymptote -20 mm Hg. Pressure decreases from 0-40 msec and from 45-75 msec have been analyzed separately. For 0-40 msec, $r = -0.999$ and $T_{in} = 36$ msec; for 45-75 msec, $r = -0.99$ and $T_{in} = 18$ msec. Thus, the early and late parts of the plot yield different values of $T_{in}$. 

constant. A similar explanation for the load-independence of $T_{in}$ cannot be excluded.

Isolated cardiac muscle relaxes slowly during hypoxia. In human coronary disease, ventricular relaxation is incoordinate, and this, rather than slow relaxation of myocardial fibers, might be responsible for prolongation of $T_{exp}$. Isovolumic pressure decrease is the net result of relaxation of the different regions of ventricular myocardium and, although it approximates to a monoexponential, can be determined by several exponentials with different time constants, asymptotes and times of onset. If pressure decrease is determined by several identical exponentials, each starting at a slightly different time, exponential analysis of measured pressure will yield the time constant and asymptote of the constituent exponentials. Thus, in an exponential model, incoor-
the asymptote to be variable. Although $T_{\text{EXP}}$ and $T_{\text{IN}}$ each discriminated between the three groups of patients, $T_{\text{IN}}$ measures the time constant only when the asymptote coincides with zero reference pressure.

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