Beat-to-beat estimation of windkessel model parameters in conscious rats

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Molino, Paola, Catherine Cerutti, Claude Julien, Guy Cuisinaud, Marie-Paule Gustin, and Christian Paultre. Beat-to-beat estimation of windkessel model parameters in conscious rats. Am. J. Physiol. 274 (Heart Circ. Physiol. 43): H171–H177, 1998.—A windkessel model was applied on a beat-to-beat basis to evaluate the arterial mechanical characteristics in seven conscious rats. Ascending aortic arterial pressure (AP) and blood flow were recorded during steady-state in basal conditions, during infusions of isoprenaline, sodium nitroprusside, and phenylephrine, and after intravenous atenolol injection. For each cardiac cycle the exponential decay time constant (τ) was estimated from the aortic AP curve, peripheral resistances (R) were taken as the ratio of mean AP to cardiac output, and systemic arterial compliance (C) was calculated as τ/R. In all conditions, mean correlation coefficients of the exponential regression and ~70% of values in each rat were > 0.99, demonstrating the model validity. In all conditions τ and C exhibited a large spontaneous variability over time, and beat-to-beat correlations were high between τ and C (0.83 ± 0.03). C was increased by sodium nitroprusside, decreased by isoprenaline, but not significantly decreased by phenylephrine [5.1 ± 0.2, 3.2 ± 0.3, and 3.9 ± 0.2 μl/min/mHg, respectively, vs. 4.2 ± 0.3 μl/min/mHg (baseline)]. In conclusion, the windkessel model enables τ and C to be reliably estimated in conscious rats during spontaneous and drug-induced hemodynamic variations.

exponential decay time; aortic blood pressure; cardiac output

THE ARTERIAL TREE is a complex system not only because of its geometry but also because of its nonlinear mechanical properties. Thus biophysicists and physiologists have been trying to develop simplified representations of this system to describe some of its functional aspects. Some characteristics of the mechanical properties of the whole arterial tree can be derived from the continuous measurements of aortic arterial pressure (AP) and blood flow. Among the parameters that can be estimated in the most straightforward way for each cardiac cycle, the vascular resistance (R), computed as the ratio of mean AP (MAP) to mean aortic flow, and the time constant of the diastolic AP decrease according to a monoexponential model (τ) are the simplest and the most interesting ones. According to Poiseuille’s law with the assumptions of a Newtonian fluid and a laminar flow in a cylindrical tube, R contributes to the dissipation of the circulatory energy in the arterial tree during each cardiac cycle. The time constant signals the restoration of energy stored by the arterial wall during the elastic distension due to ventricular ejection. The determination of this time constant depends on the accuracy of the exponential fit of the diastolic part of the AP curve. Such a model based on the windkessel effect has been widely used (13, 21, 24, 30) since Frank (6), and numerous studies have been performed to improve it and to better estimate and interpret the model parameters (3, 10, 15, 18, 20, 25, 27, 32).

In the simplest windkessel model made up of two elements, τ can be considered as the product of R, as previously defined, and the overall compliance of the arterial tree, the so-called systemic arterial compliance (C). Numerous works dealing with this topic and aiming at improving the quality of the models by increasing their complexity (4, 5) never approached the study of these models over long periods of time, probably because of the lack of computing resources, problems with signal acquisition, and interpretation difficulties. Therefore, the interpretations of the model parameters are essentially physical and do not sufficiently take into account physiological regulations.

Many investigators are now interested in the study of local compliance obtained from the direct measurement of distensibility of a single arterial section. Several techniques for local estimation of arterial distensibility have been developed using ultrasonic techniques in humans (8, 26) and in anesthetized (7, 9, 17) or awake but restrained (28) animals. However, local compliance may differ from systemic compliance, which expresses the properties of the whole arterial tree, and the relationships between these two parameters are poorly documented (14).

The purposes of the present study were 1) to assess the quality of the beat-to-beat estimation of τ using a two-element windkessel model applied to the ascending aorta pressure curve in conscious unrestrained rats over long periods in basal conditions and in various hemodynamic situations induced pharmacologically, and 2) to study the spontaneous variability over time of the classical hemodynamic parameters and of the windkessel parameters τ, R, and C.

METHODS

Animals. Experiments were performed in seven male Sprague-Dawley rats (Iffa Credo, L’Arbresle, France) weighing 300–400 g and housed in controlled conditions (21 ± 1°C, 12:12-h light-dark cycle). The animals received standard rat chow (Usine d’Alimentation Rationnelle A03, Villemoisson-sur-Orge, France) containing < 0.3% of sodium, and water ad libitum.

Chronic instrumentation. Rats were anesthetized with pentobarbital sodium (60 mg/kg ip) and were intubated. Body temperature was maintained at 37°C using an electric heat-
ing pad during and after surgery until rats awakened. A lateral thoracotomy was performed through the right third intercostal space (22), and the proximal aortic root was exposed by blunt dissection of the surrounding adipose and connective tissue. An ultrasonic transit-time flow probe (model 2.5 SB, Transonic Systems, Ithaca, NY) was then placed around the ascending aorta as proximal to the aortic valve as possible. The cable was passed through the thoracotomy and led subcutaneously to exit at the back of the neck and was left under the skin. The connector of the flow probe was exteriorized at the time of catheter implantation (see below). Rats were given penicillin G (100,000 IU i.p.) 3 days postoperatively. They were given 10–15 days to recover and to allow for fibrosis to develop around the probe. Two days before the study, rats were reanesthetized with halothane (2% in oxygen) for implantation of catheters. Polyethylene catheters were inserted via the left femoral vein into the inferior vena cava and via the right common carotid artery into the ascending aorta. The position of the ascending aortic catheter was verified by recording the waveform during the operation: the catheter was first inserted into the left ventricle and then withdrawn a few millimeters into the ascending aorta. Catheters were sutured to the vessels, filled with heparinized saline (50 IU/ml), and led subcutaneously to emerge between the ribs (apex of the lung). The connector end of the flow probe was protected in a small cap sewn to the skin. Antibiotic (neomycin sulfate) was applied topically. The anatomic location of the carotid arterial catheter tip was checked by postmortem dissection of the aortic wall.

Signal recording. After cannulation, rats were placed in large cylindrical recording cages with food and water ad libitum. After 48 h, animals had regained their initial body weight. The aortic catheter was connected to a pressure transducer (Spectramed, Oxnard, CA) and was flushed (0.5 ml/h) with heparinized glucose (25 IU/ml) throughout the experiment to avoid blood diffusion and signal dampening. The cardiac flow probe cable was connected via a spring-guarded cable to an ultrasonic transit-time flowmeter (model T106, Transonic Systems). AP was amplified (model 13–4615–52, Gould, Cleveland, OH) and fed, simultaneously to aortic flow, to a chart recorder (model 8802, Gould). The analysis of the frequency response of the whole AP measurement system showed a slight underdamping and a resonance frequency of 36 ± 0.7 Hz, which did not affect the AP signal. Analog-to-digital conversions of both signals were simultaneously performed on-line at the sampling rate of 2,000 Hz with a PC 486 DX2/66 equipped with an acquisition board (AT-MIO16H-9, National Instruments, Austin, TX) and with software developed with LabVIEW 3.1.1 (National Instruments).

Experimental protocol. The recording session began after a stabilization period of 15–30 min, when the animals were quiet and displayed normal activity. A baseline recording was taken over a period of 2.5 h. Animals then received intravenous administrations of four vasoactive drugs to produce various important hemodynamic changes. Infusion of isoproterenol (0.5 µg·kg⁻¹·min⁻¹) was performed to induce an increase in cardiac output (CO) and raises in pulse pressure of ~15 mmHg and in heart rate (HR) of ~15% through β-adrenoceptor stimulation. Infusions of sodium nitroprusside (6.5 µg·kg⁻¹·min⁻¹) and of phenylephrine (13 µg·kg⁻¹·min⁻¹) were used to produce direct vasodilatation (reducing AP by 15 mmHg) and vasoconstriction (increasing AP by 20 mmHg), respectively. For each infusion of a vasoactive agent, the steady state was reached in 5–10 min and the recording started at that time for a 15-min duration. The administrations were separated by 45 min of recovery. Finally, a bolus of atenolol (1 mg/kg iv) was used to induce a bradycardia of >40 beats/min. The recording lasted 1 h after reaching steady-state HR values.

Drugs. Isoprenaline HCl, sodium nitroprusside, and phenylephrine HCl were obtained from Sigma Chemical (St. Louis, MO), and atenolol was obtained from ICI Pharma (Cergy, France).

Beat-to-beat computation of hemodynamic parameters. Offline data processing was performed on a workstation (SPARC Station I, Sun Microsystems, Mountain View, CA). For each cardiac cycle, MAP, HR, CO corresponding to mean aortic flow, and R, defined as MAP/CO, were computed. The time constant τ was estimated beat to beat using the exponential decay time method previously described (13, 21, 25), with model AP(t) = AP₀e⁻ʳt, where t is time and AP₀ is the AP value at time 0, the initial time for application of the model. The model was applied to the last one-third of the AP curve, the end points of which were computed after determination of the cardiac cycle end points. When each cardiac beat was considered, it was verified that aortic flow was null during the selected period, and a linear regression was performed after logarithmic transformation of AP values, which yielded a correlation coefficient (r) that expressed the quality of the exponential fit. The slope of the regression line was −1/τ, and systemic arterial compliance was calculated using the windkessel relationship, C = τ/R. The exponential fit and the estimation of τ were performed during the baseline period, which contained about 40,000 cardiac cycles, and during each of the pharmacological situations, which each contained 4,000–7,000 cardiac cycles.

Statistics. For all parameters, the overall variability was defined as the variation coefficient of all values recorded during each experimental condition. Relationships between hemodynamic parameters (r, R, and C) were tested in each rat using linear regression analysis applied to beat-to-beat values. These analyses yielded one correlation coefficient for each rat in each experimental condition.

Results are expressed as means ± SE. For comparisons of paired data obtained in the different pharmacological conditions, a nonparametric analysis of variance (Friedman test) was used, followed by the Wilcoxon rank test in case of significance. Differences were considered significant at P < 0.05. All calculations were made using Systat 5.0 software (Systat, Evanston, IL).

RESULTS

Figure 1 shows three ascending aortic AP curves and the corresponding aortic flow curves obtained in baseline conditions and in two pharmacological situations. The segment of the AP curve from which the monoexponential fit was calculated is shown. In all three cases, the aortic flow was null during this period. The first part of the diastole, where reflected waves contribute to the AP waveform, was excluded from the computations. The accuracy of the linear fit after logarithmic transformation is demonstrated in each condition by r, which was between 0.993 and 0.995. These values slightly differ from mean r values given in Table 1 because of the beat-to-beat variability of r. The distribution of r values obtained for all recorded beats gives the quality of the model used. An example of a histogram of r values obtained in basal conditions in one rat is given in Fig. 2. Mean r values and percentages of r values > 0.99 obtained in each experimental condition are given in Table 1. In all conditions, mean r was > 0.99. About
70% of cardiac beats had an \( r_t \) value > 0.99 in baseline conditions, and this percentage was higher during isoprenaline or phenylephrine infusions and after atenolol administration.

The steady state was tested by the differences in aortic pressure at the start and at the end of each beat, which were evaluated in each rat and at each experimental condition. Mean differences were 1.4 ± 0.1 mmHg in baseline conditions, 1.5 ± 0.2, 1.2 ± 0.1, and 1.9 ± 0.2 mmHg during isoprenaline, sodium nitroprusside, and phenylephrine infusions, respectively, and 1.4 ± 0.2 mmHg after atenolol administration. In addition ~80% of the beats exhibited pressure variation < 2 mmHg in all conditions, except with phenylephrine (65–70%). When beats with a pressure variation > 2 mmHg were eliminated, mean values of MAP, HR, \( r_t \), and C were only slightly modified. Differences in mean values obtained with all the beats and after elimination only reached 0.6% as a maximum for HR and C. The analysis was thus performed on all cardiac beats as steady state was verified.

Mean values of hemodynamic parameters obtained in all experimental conditions are summarized in Table 2. During infusions of vasoactive drugs, hemodynamic parameters varied in the expected way. MAP varied moderately, from −13% with sodium nitroprusside to +24% with phenylephrine. Variations of CO ranged from −14% with phenylephrine to +31% with isoprenaline, and those of HR ranged from −22% with phenylephrine to +23% with isoprenaline. Vascular resistances were modified from −29% with isoprenaline to +44% with phenylephrine. The time constant \( \tau \) was decreased by isoprenaline (−47%) and increased by phenylephrine (+32%). C was significantly decreased (−24%) during isoprenaline and increased (+21%) during sodium nitroprusside infusions. During phenylephrine infusion, C tended to be reduced, but this did not reach statistical significance (\( P = 0.063 \)). Atenolol did not induce any significant change of the windkessel parameters \( \tau \), R, and C.

### Table 1. Correlation coefficients \( r_t \) of the monoexponential decay fit of the ascending aortic pressure curve and percentages of cardiac beats with \( r_t \) values > 0.99 in basal and pharmacological conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>( r_t ) ± SE</th>
<th>Percentage of Beats With ( r_t ) &gt; 0.99</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>0.990 ± 0.002</td>
<td>68.7 ± 10.9</td>
</tr>
<tr>
<td>Isoprenaline</td>
<td>0.996 ± 0.001</td>
<td>96.0 ± 1.7*</td>
</tr>
<tr>
<td>Sodium nitroprusside</td>
<td>0.990 ± 0.004</td>
<td>75.7 ± 12.6*</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>0.994 ± 0.001</td>
<td>89.8 ± 2.9*</td>
</tr>
<tr>
<td>Atenolol</td>
<td>0.992 ± 0.002</td>
<td>83.8 ± 5.4*</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SE; \( n = 7 \) rats. \( *P < 0.05 \) vs. basal value.
An example of spontaneous evolution with time of cardiovascular parameters over a period of 80 s in basal conditions is presented in Fig. 3. All parameters, including τ and C, show a marked variability due to fast oscillations, obvious for CO and R, and due to slower patterns lasting up to 10 s. In addition, chronograms of τ and C exhibit a close visual correspondence. Figure 4 shows variation coefficients of hemodynamic parameters obtained in all conditions. They were, 10% for MAP, HR, CO, and R, whereas τ and C exhibited higher values, between 10 and 18%, in basal and pharmacological conditions.

Correlations between beat-to-beat values of τ and C or R are presented in Fig. 5. A strong linear correlation was found between τ and C with mean correlation coefficients of ~0.8 in basal conditions. On the contrary, correlation coefficients between τ and R were <0.5 in all experimental conditions.

Figure 6 presents an example of a scatterplot of beat-to-beat values of MAP and C obtained in one rat during the baseline period. The strong dispersion of C values makes it difficult to outline a specific relationship between the two parameters. When each rat was considered, no significant linear correlation between MAP and C could be evidenced, either in basal or in pharmacological conditions (−0.3 < r < 0.2).

### DISCUSSION

The major finding of this study is the excellent accuracy of the exponential AP decay time model in conscious unrestrained rats, applied over long periods of baseline recording, as well as during various pharmacological interventions. The results evidence spontaneous variations over time of the windkessel parameters and their changes after different pharmacological stimuli. The time constant τ and the systemic arterial compliance C appear as hemodynamic variables spontaneously varying with time and with the hemodynamic state. In addition, our results show that spontaneous variations of τ and C are linearly related, therefore suggesting that τ may constitute an index of C in basal conditions.

The diastolic AP decay reflects the mechanical behavior of the arterial tree, and its analysis enables parameters to be numerically estimated. The two-element windkessel model, including one resistive element and one capacitive element, has long been used by many

<table>
<thead>
<tr>
<th>Condition</th>
<th>MAP, mmHg</th>
<th>HR, beats/min</th>
<th>CO, ml/min</th>
<th>R, mmHg·s·ml⁻¹</th>
<th>τ, ms</th>
<th>C, µl/mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>122 ± 4</td>
<td>378 ± 13</td>
<td>70 ± 6</td>
<td>109 ± 8</td>
<td>460 ± 52</td>
<td>4.2 ± 0.3</td>
</tr>
<tr>
<td>Isoprenaline</td>
<td>113 ± 4*</td>
<td>466 ± 13*</td>
<td>92 ± 7*</td>
<td>77 ± 7*</td>
<td>246 ± 26*</td>
<td>3.2 ± 0.3*</td>
</tr>
<tr>
<td>Sodium nitroprusside</td>
<td>106 ± 3*</td>
<td>416 ± 12*</td>
<td>83 ± 7*</td>
<td>80 ± 6*</td>
<td>407 ± 34*</td>
<td>5.1 ± 0.2*</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>151 ± 5*</td>
<td>296 ± 13*</td>
<td>60 ± 5*</td>
<td>157 ± 11*</td>
<td>607 ± 51*</td>
<td>3.9 ± 0.2</td>
</tr>
<tr>
<td>Atenolol</td>
<td>113 ± 4*</td>
<td>331 ± 7*</td>
<td>66 ± 6</td>
<td>108 ± 9</td>
<td>513 ± 35</td>
<td>4.8 ± 0.3</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SE; n = 7 rats. MAP, mean arterial pressure; HR, heart rate; CO, cardiac output; R, total peripheral resistance; τ, aortic time constant; C, systemic arterial compliance. *P < 0.05 vs. basal value.

![Fig. 3. Example of spontaneous evolution, over an 80-s period, of mean arterial pressure (MAP), HR, cardiac output (CO), total peripheral resistances (R), τ, and systemic arterial compliance (C) obtained in 1 rat during baseline period.](http://ajpheart.physiology.org/)
authors (13, 15, 21, 24). The estimation of the model parameters relies on the classical decay time method. Arterial system modeling widely uses the three-element windkessel model (3, 20, 21, 27, 32) and more complex ones (4) that better depict AP and blood flow dynamics. In these models, the aortic characteristic impedance and the systemic vascular resistance are estimated from the aortic impedance spectrum (18), and C is often obtained from the decay time method (2, 5, 10, 20, 27, 32). Stergiopulos et al. (25) compared classical and recently proposed compliance estimation methods and showed that the classical exponential decay method was more accurate than new three-element windkessel-based methods and yielded errors of usually <10%. In this work, the decay time method was applied to the last one-third of the AP curve, and the relaxation time constant came from the terminal stretch of the diastolic curve. For each cardiac cycle, compliance was thus determined at end-diastolic pressures. The different pharmacological administrations enabled the study of the cardiovascular system in different hemodynamic states to evaluate the power of the method in different conditions of steady state. In all experimental situations, this part of the curve corresponded to null flow, and the first part of the diastolic curve, where reflected waves constrain the AP curve to deviate from exponential model (2, 25), was excluded. In that way, the presence of wave reflections did not seem to affect the accuracy of the model in most of the cardiac cycles. The validity of the model was proven by the correlation coefficient \( r \) of the linear regression after logarithmic transformation of the data. This coefficient was computed on a beat-to-beat basis, which is for \( >40,000 \) cardiac cycles in basal conditions, and mean values were >0.99 in all experimental conditions. Other studies using the same method (10, 21, 25) reported similar \( r \) values, but they were obtained in anesthetized animals or from a few selected cardiac beats in the case of human studies or still from numerical simulation models. In the present study \( r \) was slightly lower for some rats, in which for a large number of cardiac beats the part of the AP curve used for calculations might still contain reflected waves, causing a deviation from exponential model. However, in all the rats, \( r \) was >0.99 for more than 50% of the cardiac beats.

Because \( R \) could also be estimated using beat-to-beat CO measurement, \( C \) was computed. However, we must keep in mind the limitations for using these parameters, due to the assumption of Poiseuille’s law for the estimation of \( R \) and due to the two-element windkessel model for \( r \). In addition, as already stressed by some authors (27), beat-to-beat estimation of \( R \) with the ratio MAP/CO should not be applied during non-steady-state conditions because of the varying amounts of blood stored in the compliant vessels. In this study we verified that steady-state conditions were almost reached over the whole selected recording sessions. In addition, mean values of all parameters, including windkessel parameters, were almost unchanged after a drastic selection of beats.

It was shown in rats (17) that an increase in HR resulted in a larger inaccuracy of the method, but our data do not confirm this result. In fact, during isoprenaline infusion, the correlation coefficients remained elevated, even showing a trend to increase, despite the

![Fig. 4. Variation coefficients of MAP, HR, CO, R, r, and C obtained in 7 rats in basal (BASE) and pharmacological conditions (ISO, isoprenaline; SNP, sodium nitroprusside; PHE, phenylephrine; ATE, atenolol).](http://ajpheart.physiology.org/)

![Fig. 5. Correlation coefficients between beat-to-beat values of \( r \) and \( C \) \( [r(C)] \) and between \( r \) and \( R \) \( [r(R)] \) obtained in 7 rats in basal and pharmacological conditions.](http://ajpheart.physiology.org/)
tachycardia. In basal conditions and during sodium nitroprusside infusion, the mean \( r \) values were the lowest. This may be explained by the fact that during large systemic vasodilations, the pulse wave moves slowly and the wave reflections may be superimposed on the diastolic part of the AP curve considered for the estimation of \( \tau \).

As classically observed, spontaneous variability of MAP, HR, CO, and R was evidenced by the representation of their time course. The existence of a large variability over time of \( \tau \) and C also appeared on the chronograms and moreover with the variation coefficients, which were much higher for these parameters than for the classical ones. Although these variation coefficients were computed over periods of different durations in basal and pharmacological conditions, the differences between \( \tau \) and C and the other parameters were maintained in all experimental conditions. When these differences in data dispersion and the windkessel equality \( \tau = R \times C \) are considered, it clearly appears that the variations of \( \tau \) mainly reflect those of C, and this is quantified by the correlation coefficient between \( \tau \) and C. The visual correspondence of \( \tau \) and C chronograms corroborates this result. Therefore, this correlation seems to be related to the difference between variation coefficients of \( \tau \) and R, which is particularly great in basal conditions and during isoprenaline or sodium nitroprusside infusions. In addition, it appears logical that \( \tau \) beat-to-beat variations were better related to C than to R, inasmuch as vascular resistance is smooth muscle dependent and varies more slowly. Indeed, vascular smooth muscle responses to sympathetic nerve stimulation in conscious rats were found to be significant up to 1 Hz (23), therefore eliminating fast beat-to-beat variations of R. Our beat-to-beat results do not confirm previous observations in humans and in anesthetized dogs (31), which showed that 1-min averages of the time constant were well correlated with R. When one considers the relationship \( \tau = R \times C \), the high linear correlation between \( \tau \) and C indicates that relationships between \( \tau \) and R and between R and C should also exist, but in a nonlinear way. However, the strong linear relationship between beat-to-beat values of R and 1/C, which was expected, was not found (data not shown). In addition, looking at R and C mean values during pharmacological administrations, we cannot suggest any clear association of their variations. Systemic arterial compliance is the result of complex physiological adjustments involving all vascular beds and its variations cannot be interpreted in so simplistic a way. A single R value may be associated with various C values, and because of various regional distributions of blood flows, inverse variations of R and compliance at the single-vessel level cannot be evidenced at the systemic level. The high correlation between \( \tau \) and C in all the rats in basal conditions suggests that \( \tau \) may constitute an index of C. However, although the regression lines between \( \tau \) and C nearly cross the ordinate axis at the zero point in basal conditions, \( \tau \) cannot be considered as a true measure of C because slopes of the linear regression exhibited large interindividual variability and changes with the hemodynamic state (data not shown).

Recently, arterial compliance has often been determined at regional levels by measuring variations of arterial diameter in the course of the cardiac cycle as a function of AP changes (11, 17, 29) or from the pulse wave velocity along the aortic pathway with noninvasive Doppler ultrasonic technique (12). The role of vascular smooth muscle tone in the arterial stiffness (9) and the importance of pressure pulsatility (7) were demonstrated in rats. In humans, specific arterial alterations with aging and hypertension were found (11, 19, 29). However, relationships between regional compliance and C are poorly documented (14), and it is not known whether C better reflects carotid, aortic, or large-artery compliance.

It is now accepted that arterial compliance changes are due to 1) the mechanical effect of AP variations, 2) functional modifications of vascular tone (7, 14), and 3) structural changes of the arterial wall (9, 11, 16). In the present study the first two mechanisms were taken into account in the conscious rat by studying compliance variations induced by different pharmacological stimuli. No clear relationship appeared between beat-to-beat C and MAP values although the lowest MAP observed under sodium nitroprusside and the highest MAP observed under phentolamine were associated with the highest and the lowest C values, respectively. It was demonstrated in isolated vessels that graded increases in AP produced corresponding reductions of arterial compliance, following a nonlinear curve (3, 15, 16). As already suggested by other authors (7, 14), some variations of C may be independent of MAP variations but may be related to modifications of the vascular smooth muscle tone. A drastic decrease of \( \tau \) was found during isoprenaline infusion, associated with a decrease of C, which may be surprising according to the vasodilating properties of isoprenaline. Previous observations made on the isolated carotid artery (1) showed that the compliance was unchanged after local administration of isoprenaline. The lack of effect was explained by the absence of \( \beta \)-adrenergic-mediated modulation of the carotid arterial compliance. As already described for the carotid compliance calculated from the arterial diameter measurement (7), C was increased by sodium nitroprusside, whereas no significant variation of \( \tau \) was noted. The differences between isoprenaline and sodium nitroprusside may be due to the different vasodilating mechanisms: vascular \( \beta \)-adrenoceptor stimulation with isoprenaline, inducing vasodilatation preferentially in the skeletal muscle, and NO release with sodium nitroprusside, inducing systemic vasodilatation. Phenylephrine induced a large increase in \( \tau \), which was associated with a slightly lower C value, but the statistical test of difference did not allow us to conclude that there was a significant decrease, although the probability was close to the significance threshold. Previous observations made on carotid compliance showed a decrease with similar phenylephrine doses (7).

In conclusion, this work shows the validity of the two-element windkessel model for beat-to-beat application in basal as well as in pharmacological conditions. It
appears that the relaxation time constant $\tau$ presents an important spontaneous variability over time, and it may constitute a valuable index of C. The spontaneous variations over time of $\tau$ probably signal variations of the hemodynamic state that remain to be specified.

Perspectives. This study opens several areas of research. It would be first of interest to compare C with local compliances to clearly establish whether these two parameters are related and to specify the conditions in which they are linked. The determination of arterial compliance in regional circulations with simultaneous local measurements of AP and blood flow should then be examined to improve the physiological aspects of the study. Some hypotheses concerning C variations as a function of regional resistances and compliances, due to regional variations of blood flow, should be verified. In addition, one could compare young to aged normotensive rats, in which C is known to be lower for a similar AP level. Thus it would be possible to better explain the respective effects of AP and vascular muscle tone on C.

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