rate.

The second and last question stems conceptually from the previous one. Does constancy of blood pressure variation coefficient represent a generalized phenomenon that non-specifically characterizes any blood pressure rise? Does it take place for acute as well as for chronic elevations in blood pressure? To obtain information on this point, blood pressure variabilities were compared within single patients, taking advantage of the highly different average mean arterial pressure values that could be observed among the 48 half-hours. The results, shown in the upper panels of Figure 5, refer to the three half-hours that in each patient attained the lowest average mean arterial pressure value, the highest value, and a value intermediate between these two. From the lowest to the highest mean arterial pressure value, the SD for mean arterial pressure increased significantly and markedly. This increase was far beyond that accounted for by the blood pressure rise, so that the variation coefficient also showed a significant increase. There was concomitantly a marked and significant increase in the SD and the variation coefficient for heart rate. Thus, acute rises in blood pressure within patients are accompanied by much greater rises in blood pressure variability (and by rises in heart rate variabilities) than those that characterize the chronic blood pressure elevations of the essential hypertensive patients (Fig 5, lower panels). In the former condition a clear-cut increase in the variation coefficient for mean arterial pressure occurs, whereas in the latter this coefficient remains unchanged. It may be interesting to speculate whether this difference reflects a difference in the mechanisms that may be responsible for the production of the chronic compared with the acute and normally behaviorally induced blood pressure elevations or whether, in the transition from the acute to the chronic state, a readjustment of cardiovascular control mechanisms takes place which reduces the initial marked rise in blood pressure variability.

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Session 4

The Influence of Arterial Baroreceptors in Man on the Variability of Blood Pressure and Plasma Catecholamines in Man

Peter Sleight, M.D., D.M.*

There are several methods of expressing the variability of arterial pressure, but the most generally accepted method is to use the SD about the mean. Even within this definition there is room for differing interpretations. We define variability as the SD of all the individual pulses obtained during the period of recording.

The term "labile" blood pressure has been used to suggest greater variability than normal. Unfortunately, variability is seldom adequately quantified in studies purporting to be about labile hypertension.

We have been concerned over the last 15 years with measurement of intra-arterial blood pressure in subjects who were allowed to leave the hospital and carry out their normal daily routines at home and at work. When we examine such records, it is difficult to escape the conclusion that the blood pressure of all of us is extremely variable and much influenced by environmental factors, such as the state of activity, wakefulness, and sleep.

In this article I drew heavily on the work of one of my Ph.D. students, Dr. John Floras, a Rhodes Scholar now returned to Toronto.1

We set out to see how much the variability of arterial pressure was influenced by the arterial baroreceptors and also how much the changes in blood pressure reflected the activity of the sympathetic nervous system. Multivariate analysis showed that the pressure was most influenced by the baroreflexes and was not, contrary to popular belief, greatly related to age or to the level of resting arterial pressure. The plasma noradrenaline appeared to be a poor index of sympathetic nervous activity, except in the case of bicycling exercise.

METHODS

Arterial Pressure Measurement

This has been described in detail elsewhere.2 Briefly, a fine Teflon

*Field Marshal Alexander Professor of Cardiovascular Medicine, University of Oxford, John Radcliffe Hospital, Headington, Oxford, England.

Reprint requests: Dr Sleight, JR2 Hospital, Oxford, England
catheter is inserted into the brachial artery by the micro-Seldinger technique. The catheter is connected to a portable perfusion-manometer system which records the individual arterial pulses, together with the ECG and up to two other variables on an ordinary music audio cassette tape, slowed down to record over 24 hours.

The analysis is largely automated, using a Data General Eclipse S-200 minicomputer. An important step is the editing of artifact or damped pulses by a skilled observer. The tape replay is carried out in accelerated time, so that a 24-hour tape can be satisfactorily analyzed in one to two hours, depending on the amount of artifact. Means and SD of measured variables are readily obtained for hourly periods, the waking period, or the whole 24 hours (Fig I).

Variability here refers to the SD of all included beats over the waking period.

**Baroreflex Sensitivity**

This method is a refinement of the original method we developed using the relation between the pressure rise and reflex cardiac slowing produced by the intravenous (IV) injection of a pressor agent. Later we used phenylephrine rather than angiotensin and have recently automated the calculation (Fig 2). We regress the systolic pressure of successive pulses during the provoked pressure rise, to the pulse interval which follows each pressure pulse. The slope of the regression line (msec/mm Hg) gives an index of baroreflex control of heart rate. There is usually (but not invariably) a similar reflex change in blood pressure. We now carry out four or five injections at each steady state and use a weighted average of the slopes as the measure of baroreflex sensitivity (BRS).

**Plasma Noradrenaline Measurement**

Samples at rest were taken seated from an indwelling venous cannula after an interval of inactivity. Exercise samples were taken during the last minute of the differing forms of exercise. The samples were immediately centrifuged, the plasma frozen in liquid nitrogen and then stored at -40 °C. Noradrenaline values were estimated in Dr. P. Severs' laboratory (St. Mary's Hospital, London), with a radioenzymatic assay based on the method of Henry et al.

**Subjects**

We recruited 61 subjects (including 18 women) aged 16 to 69 years and thought to be hypertensive on the basis of at least three separate cuff measurements over one week apart (>140/90 mm Hg in those under 40 years and >160/95 in those over 40 years). Mean cuff pressures were 173.2 ± 19.6 systolic and 107.3 ± 9.6 mm Hg diastolic.
Satisfactory measurements for intra-arterial pressure and variability were obtained in 56 subjects and for catecholamines in 50 subjects. In the event, 20/59 subjects were found to have normal intra-arterial pressures (MAP < 108 = 140/90 mm Hg) during the waking hours.  

RESULTS

We found the waking mean arterial pressure ranged from 89.5 to 159.5 mm Hg. The variability (SD) of the waking pressures was positively correlated with the mean arterial pressure (r = 0.43, p < 0.005, n = 56).

When the data from a subgroup of eight subjects were more closely examined, we could not find any within-subject relationship between the level of arterial pressure at any particular time and the variability at that time. We examined this over two-minute means for 20 minutes during arousal from sleep (when blood pressure changes greatly) and also comparing hourly means and SD during the whole waking hours. We therefore saw no reason to use the coefficient of variation in subsequent analysis.

We related the variability found in any given subject to his age, mean blood pressure, and resting baroreflex sensitivity. All showed significant correlations, the first two positive (r = 0.32, p < 0.01, r = 0.43, p < 0.005 respectively) and the last negative (r = 0.47, p = <0.0002). When multiple regression analysis was carried out, baroreflex sensitivity was the only independent influence on variability of blood pressure. We also found a strong negative correlation between reflex sensitivity and the rise in MAP provoked by all forms of exercise.

These results fit well with animal data, which show a great increase in blood pressure variability when the baroreceptors are denervated either peripherally or centrally. Others have found a less strong relation in man.  

In our hands plasma noradrenaline appeared to be only a weak index of sympathetic nervous activity. There was no correlation between plasma NA at rest; a relation was seen during bicycle exercise, but not during isometric exercise, mental arithmetic, or a reaction time test. One problem is that although there is a good correlation between directly measured human sympathetic nerve activity and plasma NA, the relation between sympathetic nerve discharge and other variables, particularly blood pressure, is complex.

The complicating factors in relating sympathetic nerve activity to either plasma NA or blood pressure include: (1) The response to sympathetic nerve discharge may be strongly influenced by the amount of smooth muscle and the geometry of the arteriole; (2) The level of pressure rise achieved is subject to buffering by the arterial baroreflexes and the sensitivity of these declines with age and rise in blood pressure; (3) The response to noradrenaline may be influenced by receptor density on arterial smooth muscle. (4) The amount of noradrenaline released may be controlled by presynaptic β-receptors which are influenced by simultaneously released adrenaline.

SUMMARY

The variability of intra-arterial blood pressure, recorded over the waking hours in free-ranging subjects away from the hospital, was expressed as the SD of the mean of all recorded beats.

This variability was found to be related to age, the individual's level of arterial pressure, and his baroreflex sensitivity using the Oxford phenylephrine method.

Multiple regression analysis showed that baroreflex sensitivity was the only independent influence on variability. Baroreflex sensitivity also strongly determined the level of pressure rise in response to a number of different stimuli, including bicycling exercise, isometric exercise, mental arithmetic, a reaction time test, and the response to injected phenylephrine or noradrenaline.

Plasma noradrenaline proved a poor index of sympathetic nervous activity, except with bicycle exercise.

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The Pattern of Pressure Changes During Synchronized and Desynchronized (REM) Sleep as an Index of Baroreceptor Function*

Eduardo Moscýr Krieger, M.D., and
Luis Fernando Junqueira, Jr, M.D.

*Department of Physiology, Faculty of Medicine of Ribeirão Preto, Ribeirão Preto, Brazil.
Reprint requests: Dr. Krieger, Faculty of Medicine of Ribeirão Preto, Department of Physiology, Ribeirão Preto, S. R., Brazil 14.100