Ischemic Exercise Pressor Test

With Special Reference to its Bearing on Neurogenic Mechanism of Essential Hypertension*

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The present investigation was undertaken to examine the individual difference of cardiovascular responses to exercise of ischemic muscle, with particular attention to the physiological mechanisms that mediate these responses. In addition, attempts were made to investigate the potential role of neurogenic factors in essential hypertension and an intermediate bridge mechanism between normotensive zone and essential hypertensive zone from an epidemiological view.

A. MAXIMAL ISCHEMIC EXERCISE PRESSOR TEST

METHOD

After resting in supine position with attachment of the experimental apparatus for 20 minutes in a quiet room, the left forearm blood flow was obstructed by inflating a sphygmomanometer cuff on the upper arm to about 280 mmHg. The subject was then asked to compress a rubber bulb at 5 second intervals to raise a mercury column to 200 mmHg within a period of 1 second. The timing was controlled by a bell signal.

(Figure 1). After a number of contractions, which varied with the subject, pain appeared in the forearm and increased gradually. The subject was encouraged to continue the exercise as long as possible. The pain disappeared on stopping the exercise and releasing the cuff inflation at the point of intolerable pain. The blood pressure and heart rate were measured in the right arm every 30 seconds before, during and after the exercise. This maximal exercise test represented an episode of acute emotional and maximal physical stresses of ordinary daily life.

RESULTS

The systolic and diastolic blood pressures increased with the onset of the exercise and reached

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ISCHEMIC EXERCISE PRESSOR TEST

Table 1. Results of maximal ischemic exercise pressor tests

<table>
<thead>
<tr>
<th></th>
<th>ΔB.P. (mm.Hg)</th>
<th>ΔH.R.</th>
<th>Recovery time (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>After 12X</td>
<td>After 24X</td>
<td>At Peak</td>
</tr>
<tr>
<td>Normotension</td>
<td>16/10</td>
<td>26/20</td>
<td>30/30</td>
</tr>
<tr>
<td>Early hypertension</td>
<td>50/30</td>
<td>60/36</td>
<td>80/46</td>
</tr>
<tr>
<td>Latent hypertension</td>
<td>50/30</td>
<td>70/50</td>
<td>70/60</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>24/20</td>
<td>50/30</td>
<td>70/50</td>
</tr>
<tr>
<td>Normotension with hypertensive response</td>
<td>30/30</td>
<td>45/50</td>
<td>76/50</td>
</tr>
<tr>
<td>Arteriosclerotic hypertension</td>
<td>40/20</td>
<td>75/30</td>
<td>80/30</td>
</tr>
</tbody>
</table>

![NORMOTENSION](image)

Figure 2. The pressor response to the maximal exercise of ischemic muscle in a normotensive subject. The systolic and diastolic pressures increased immediately after the onset of exercise and reached a peak when the pain became intolerable after 34 contractions. After stopping the exercise and releasing the vascular occlusion at the point of intolerable pain, the blood pressures fell toward the control levels within 2 minutes.

A peak when the pain became intolerable; upon release of the vascular occlusion which was associated with a relief of pain, the blood pressures fell toward the control levels (Figure 2).

The pressor response could be divided into two phases. An initial rise occurred almost immediately after the onset of exercise. Since this phase is associated with mental tension or concentration and the intensity of muscular work, this rapid and abrupt cardiovascular response at the beginning of exercise is almost certainly of cortical origin. The second rise began with the onset of pain and increased according to the severity of pain and work. These patterns of the pressor response were qualitatively similar but quantitatively different among subjects, while those in each individual were highly reproducible.

The pressor response (Δsyst. pr./Δdiast. pr.) of a normotensive subject was 16/10 mmHg after 12 contractions, 26/20 after 24 contractions, and 30/30 at the point of intolerable pain. The heart rate increased by 12 after 12 contractions, by 16 after 24 contractions, and by 26 at the point of intolerable pain. The recovery time was 2 minutes for both systolic and diastolic pressures and 3 minutes for the heart rate (Figure 2). On the other hand, in an early hypertensive subject, the corresponding pressor response was 50/30, 60/30, and 80/46 mmHg while the heart rate increased by 14, 22, and 22 respectively; the recovery time was 10 minutes for the systolic pressure, 7 minutes for the diastolic pressure, and 4 minutes for the heart rate (Figure 3).

In an uncomplicated established hypertensive subject treated with routine antihypertensive drugs for a year, the corresponding pressor response was 50/30, 70/50, and 70/60 mmHg while
the heart rate increased by 20, 26, and 24 respectively; the corresponding recovery time was 14, 14, and 4 minutes (Figure 4). As in these patients the corresponding response in a prehypertensive subject was 24/20, 50/50, and 70/50 mmHg while the heart rate increased by 16, 20, and 22 respectively; the corresponding recovery time was 7, 9, and 8 minutes (Figure 5). These typical pressor patterns of the hypertensives were not always obtained in all hypertensive subjects. Similarly, in a normotensive subject with hypertensive response, the corresponding pressor response was 30/30, 45/50, and 76/50 mmHg while the heart rate increased by 20, 24, and 28 respectively; the corresponding recovery time was 6, 7, and 6 minutes (Figure 6). Unlike in these patients, in a subject with arteriosclerotic hypertension, the corresponding pressor response was 40/20, 75/30, and 80/30 mmHg, while the heart rate increased by 20, 20, and 36 respectively; the corresponding recovery time was 4, 2, and 2 minutes (Figure 7). In other words, the pressor response of the systolic pressure in this group of patients was over twice as great as that of the diastolic pressure, which may be attributed to the reduced elasticity of the aortic tree associated with age. This finding may be used as a differential criterion between senile or arteriosclerotic and essential hypertension.

Above findings as summarized in Table 1 clearly indicate that patients with essential hypertension tend to exhibit a greater rise in blood pressure associated with a slower recovery than other groups. However, it should be borne in mind that the maximal exercise test may be accompanied by potential danger resulting from an
Figure 5. The pressor response to the maximal exercise of ischemic muscle in a prehypertensive subject. Pronounced diastolic and systolic pressor responses and a protracted recovery time were seen. The intolerable pain appeared after 35 contractions.

Figure 6. The pressor response to the maximal exercise of ischemic muscle in a normotensive subject with hypertensive response. Pronounced diastolic and systolic pressor responses and a protracted recovery time were similar with essential hypertensive subjects. The intolerable pain appeared after 35 contractions.

Figure 7. The pressor response to the maximal exercise of ischemic muscle in a subject with arteriosclerotic hypertension. The systolic pressure rise was markedly greater than that of normotensive subjects, while the diastolic within the limit of normotensive responses. The intolerable pain appeared after 32 contractions.

excessive pressure rise. Fortunately, analysis of the data indicated that the magnitude of initial pressure rise is parallel to that of the secondary, on the basis of which further attempts were made to develop a simplified test protocol.

B. SUBMAXIMAL ISCHEMIC EXERCISE PRESSOR TEST

METHOD

In this series, the ischemic exercise pressor test with 24 contractions was performed in accordance with the aforementioned protocol in 200 Korean healthy normotensive subjects (15 to 84 years of age) and in 100 Korean subjects with clinical diagnosis of essential hypertension (21 to 70 years of age). This group composed of 26 prehypertensives, 47 early hypertensives and 27 uncomplicated established hypertensives. Essential hypertensives accompanied by complication of the
cardiovascular system and the kidneys were excluded in this series. This submaximal exercise test represented an episode of acute emotional and moderate physical stresses of ordinary daily life. Simultaneously surveys on the personal characters of the hypertensive subjects were carried out: The subjects were asked to pick out three items which represented their characters most adequately from the thirty items of personal character list.

RESULTS

The average pressor response in normotensive subjects was 17/14 (4~36/10~30) mmHg after 12 contractions and 27/23 (10~38/10~34) after 24 contractions; the average recovery time was 3 minutes for the systolic pressure and 2 minutes for the diastolic pressure (Table 2). In subjects with essential hypertension, the corresponding pressor response was 34/23 (20~60/10~40) and 54/35 (30~100/20~50) mmHg while the recovery time was 5 and 4 minutes, respectively.

Among the normotensive subjects, about 22% showed a typical hypertensive response; at the end of 24 contractions, the pressor response was over 40/30 mmHg while the absolute blood pressure increased to over 160/95 or 150/100 mmHg. In this group with hypertensive response, the average pressor response was 25/23 (14~48/20~60) after 12 contractions and 44/36 (24~80/26~50) mmHg after 24 contractions, while the average recovery time was 4 and 3 minutes for systolic and diastolic pressures, respectively.

As in the previous series and a preliminary study (1), most of the patients with essential hypertension showed an excessive pressor response as well as a protracted recovery time.

In order to analyze the correlation between the rises in the systolic and the diastolic pressures, the former is plotted against the latter in Figure 8.

Figure 8. Distribution of the pressor responses to the submaximal exercise of ischemic muscle in normotensive and essential hypertensive subjects. Most of normotensives are shown in the left lower quadrant, while most of essential hypertensives are in the right upper quadrangle. About 22% of normotensive subjects belonged to the hypertensive area. About 15% of hypertensives belonged to the normotensive area.
In this graph, about 78% of normotensives were shown in the left lower quadrangle while about 85% of essential hypertensives in the right upper quadrangle. The dividing line between normotensive and hypertensive areas was drawn under the basis of 40/30 mm Hg in the pressor response and of 160/95 or 150/100 mm Hg in the absolute blood pressure. These values may be highly significant for the determination of hypertensive pressor response. About 22% of normotensives were shown in the hypertensive area. They may be regarded as possessing biological neurovascular predisposition susceptible to the development of essential hypertension. Accordingly, this technique may be adopted for differentiating subjects with hypertensive diathesis from normotensives. About 15% of essential hypertensives were shown in the normotensive area. They may be regarded as patients with essential hypertension who developed from persons with non-hyperreactive or normoreactive response to stress. The data indicate that the greater the activity of biological neurovascular pressor responsive, the incidence of essential hypertension increases. In addition, the above data suggest that there is not qualitative but quantitative difference in the activity of the vasomotor nerves between normotensive and hypertensive subjects.

The surveys of personal characters showed that out of 300 points of 100 patients with essential hypertension, the hypertension inducing characters took 217 points, noninducing characters 83 points, with the ratio of 2.5 to 1. The ranking of the points of hypertension inducing characters are as follows: 1) excitable temperament (70 points), 2) quick temper (45 points), 3) worrying temperament (30 points), 4) anxious & impatience temperament (20 points), 5) chivalrous temperament (18 points), 6) tenacious temperament (15 points), 7) timidity and fear (9 points) and 8) aggressive character (9 points). Approximately 97% of patients with essential hypertension had the above temperaments more or less.

**DISCUSSION**

A few hypotheses have been advanced on the physiological mechanisms of the pressor response to exercise of ischemic muscle which varied in the methods. Alam et al. suggested that the blood pressure raising reflex from ischemic muscle contraction depends upon the accumulation of metabolites produced in the contracting voluntary muscle, since the pressor response to exercise was remarkably greater under the arrest of circulation than without such arrest, and the rise of blood pressure in many subjects preceded the onset of pain. However, this concept can not explain the rapid and abrupt cardiovascular response at the beginning of exercise as well as the two step rises in pressure. Recently, Shapira et al. suggested that the pressor response to ischemic pain is mediated at least in part by a pathway (vasopressin or angiotensin II was suspected) other than the autonomic nervous system, since the ischemic pain stimulus caused a significantly greater pressor response than cold pressor test which is said to be mediated predo-

![Diagram](image-url)
Figure 10. Mental tension associated with mechanical compression by inflating a cuff prior to the beginning of exercise elicited pressor response in normotensive and hypertensive subjects. The greater the degree of compression, the greater was the pressor response. The pressor response to a given compression was greater in hypertensive subjects than that in normotensives.

minantly by the sympathetic nervous system. However, the concept that only the pain factor is a unique pressor component of the ischemic exercise or cold pressor test can not be agreed to by the author, since the pressor response to pain induced by ischemic exercise or cold (Figure 9) were greater than those to pain induced by subcutaneous injection or pinching skin (Figure 12). These findings indicate that pressor components of the ischemic exercise and cold pressor tests consist of other factors in addition to pain.

Biological reactions to stress have been stated to be mediated through the two pathways; first, the hemodynamic response through the hypothalamo-medullary-sympatho-adrenal axis by Cannon, and second, metabolic response through the pituitary-adrenocortical axis by Selye. In view of shortness of the time for the experimental procedure in the present test, it is likely that the former factor alone is related to the effects observed in the present investigation.

Physiological mechanisms of the pressor response to exercise of ischemic muscle can be clarified by analyzing the pressor components of the stimuli. The initial pressor rise is dependent upon the mental tension associated with the mechanical compression resulting from inflating cuff (Figure 10), mental concentration associated with accurately raising a mercury column to 200 mm Hg within 1 second, and then the intensity of muscular work (Figure 11). On the other hand, the second rise is dependent upon the pain sensation (Figure 12, 13) which is felt by local nociceptors due to stimulation of so-called Lewis' factor P accumulated in the contracting flexor muscles of the forearm at about one-half of the total number of contractions. Moreover, pressor responses to these components are considered to be mediated predominantly through the sympatho-adrenal system, and hence, the total pressure rise represents the summation of multiple reflex sympathetic activities.

Figure 14 shows a hypothesis on the mechanisms of the pressor response to exercise of ischemic muscle. The rapid and abrupt cardiovascular response at the beginning of exercise is almost certainly of cortical origin due to mental tension and concentration. During exercise, an activation of the sympathoadrenal system is elicited through the activity of the higher cephalic centers. Consequently, the peripheral vasoconstriction (especially in the splanchnic area) an increased venous return to the heart, a positive inotropic, chronotropic action of the heart, an increased cardiac output and the vasodilatation of the acting muscle may be induced. During the latter phase of the exercise, the pain sensation would also evoke an activation of the sympatho-adrenal system. Both the peripheral vasoc-
Figure 11. The pressor response to a continuous grasping of an air bulb of sphygmomanometer to various pressure levels. Both the systolic and the diastolic blood pressures increased in proportion to the intensity of muscular contraction.

Figure 12. Effects of pain sensation on the blood pressures in a normotensive subject. Intolerable pain sensation induced by continuous subcutaneous injection of saline and vitamine solutions or pinching the arm skin invariably raised the blood pressures to similar levels.

Constriction and the increased cardiac output due to the activation of the sympathoadrenal system would eventually elevate the blood pressure, as a result of which the blood flow to the active tissue would presumably increase.

The rise in diastolic pressure depends upon the peripheral vasoconstriction while the rise in systolic pressure upon the cardiac output as well as upon the response of the aortic tree. Since the sympathetic vasoconstrictor nerves are known to regulate the resistance vessels of the arterioles in the splanchic area, the rise in diastolic pressure may represent the activity of vasomotor nerves of the splanchnic area.

As described above, it was clearly noted that most patients with essential hypertension were significantly more pressor reactive than normotensive subjects to interoceptive as well as to exteroceptive noxious physiological stimuli such as emotional stress, muscular exercise, or pain sensation. Shapiro et al. reported that hypertensives were more pressor reactive than normo-
Figure 13. Effect of phantom pain on blood pressure in an essential hypertensive subject. During the recovery period of the ischemic exercise pressor test, adventitiously severe phantom pain appeared in the right lower leg. Simultaneously, the blood pressure began to rise, which increased with the severity of pain. Fifty minutes later, obtundation of the pain by subcutaneous injection of Meperidine hydrochloride (50 mg) began to lower the elevated blood pressure.

Figure 14. A hypothesis on the mechanism of the pressor response to the maximal exercise of ischemic muscle. During exercise, activation of the sympatho-adrenal system is elicited through the higher cephalic centers. The initial rise depends upon the mental tension, concentration and then the intensity of muscular work; the second rise depends on the pain sensation. The total rise thus represents a summation of the multiple reflexes mediated through the sympathetic activities. The hemodynamic responses consisting of peripheral vasoconstriction and an increase in the cardiac output, and a redistribution of blood from the viscera to acting muscles induce a circulatory readjustment.

tensives to angiotensin II as well as to cold pressor test and simple psychological stimuli.

Such excessive and protracted pressor responses as observed in essential hypertensive subjects may reflect an overaction of the vasomotor nerves, which may be a faulty regulation of the
biological hemodynamic responses through the higher cephalic centers as a neurovascular predisposition. Such an overaction of the vasomotor nerves may play an important role in initiating or triggering essential hypertension. An excessive impulse discharge of the sympathetic vasoconstrictor nerves to repeated stresses can produce a sustained, tonic constriction of the resistance vessel walls. Sokolow\(^{33}\) suggested that the hemodynamic data obtained in early hypertension had raised anew the question of the participation of the sympathetic nervous system early in the development of hypertension. Evelyn\(^{46}\) stated that 99% of patients with essential hypertension pass through a transitional phase of several years during which the blood pressure rises above normal level “at first only occasionally and then more frequently until the stage of established hypertension is reached”. His report is consistent with the author’s clinical experiences in which, in persons who develop hypertension, as defined by consistent diastolic pressure of above 90 mm Hg, their earlier history indicates a variability of blood pressure. Elevations in blood pressure are transient and fluctuate widely in response to emotional stress early in the course of the disease but eventually become permanent. These facts clearly suggest that there is an intermediate bridge pathway between normotensive zone and hypertensive zone. Presumably, it may be expected that persistent elevation in blood pressure forming the basis of essential hypertension, can be produced by fusion of the temporary excessive and protracted pressor rises to daily repeated mental, emotional or physical stresses.\(^{37,38,39}\)

Moreover, formation of facilitation (bahnung according to Exner) through the sympathetic vasomotor pathways elicited by repeated stresses evokes the pressor response more easily.

As noted above, about 22% of normotensives, who exhibited hypertensive response, may be considered as having neurovascular predisposition susceptible to the development of essential hypertension. Hines\(^{42}\) has claimed that some subjects with a normal pressure respond to a standard cold stimulus by an exaggerated and protracted blood pressure rise and that the incidence of later essential hypertension is much more frequent among these hyper-reactors than among normal subjects. Hines et al.\(^{41}\) restudied 27 years later and reported that of 300 subjects who had cold pressor tests in 1934, 18% were hyperreactors. Of those 207 subjects were restudied in 1961. Of 40 hyperreactors in 1934, 4 became hypertensives, whereas none of 167 normal reactors did so. Although far-reaching conclusion of Hines was later disproved by an other investigator,\(^{42}\) the relationship between normotensive subjects with hyper-reactor to pressor stimuli and essential hypertension can not be disregarded.

A number of investigators\(^{43,44}\) postulated that the etiology of essential hypertension lies in disharmony of interrelation of multiple factors. The author attaches importance to four factors—individual biological neurovascular pressor responsiveness, that is, activity of the vasomotor nerves, personal character, environmental emotional factors and excessive intake of salt—as initiating factors in essential hypertension.

The close relationship between biological neurovascular pressor responsiveness and occurrence of hypertension has been described by several investigators.\(^{1,45,47}\) They insisted that essential hypertension was much more frequent among hyper-reactors of the vasomotor nerves than among normal reactors. The individual responsiveness of vasomotor nerves to similar stress, which was highly reproducible, might result from hereditary constitutional traits. However, the data indicating that all of hyperreactors of the vasomotor nerves did not develop hypertension and that a number of normo-reactors developed hypertension suggest participation of other factors in addition to activity of the vasomotor nerves in the pathogenesis of essential hyper-
tension.

The author has clinically observed that there were common characteristic temperaments among patients with essential hypertension. In the past many investigators\textsuperscript{43,44,47} considered that personal characters or temperaments peculiar to patients with essential hypertension were one inducing factor of essential hypertension, but they showed no positive evidence. The author admitted that the aforementioned hypertensive characters were one of hypertension inducing factors and intensified the amplitude and length of pressure rise in the biological pressor response to emotional stress.

The author also has clinically observed that environmental emotional stresses might play an important role in the pathogenesis of essential hypertension. The emotional stresses involving mental tension, excitement, fear, anger, threatening, hostility, anxiety, impatience and worry etc. elicited more strongly individual biological pressor responsiveness to stress. Furthermore, such emotional stresses are inevitable in our human daily life. Whenever exposed to such stresses, blood pressure involuntarily rises in accordance with intensity and length of stresses. For instance, the high occurrence of elevated blood pressures among victims of explosion in Texas city (blast hypertension),\textsuperscript{48} the prolonged elevation of blood pressure of soldiers after battle,\textsuperscript{49} the elevation of blood pressure of over 60% of besieged citizens in Leningrad during World War II,\textsuperscript{50} experiment of causing hypertension by giving strong mental tension to cats,\textsuperscript{51} experiment of causing persistent hypertension by giving repeated strong auditory stimuli to rats\textsuperscript{52} and experiment of causing persistent hypertension by means of disturbing higher central nervous activity of monkeys\textsuperscript{53} etc. established the above fact.

Excessive intake of salt is also an important factor causing essential hypertension. For instance, high incidence of hypertension in the regions of excessive intake of salt such as the northeastern part of Japan\textsuperscript{44} and Nassau of Bahamas,\textsuperscript{45} low incidence of hypertension in the regions of intake of little salt such as among Eskimos in Alaska\textsuperscript{46} and Carajas in Brazil,\textsuperscript{47} Dahl's data\textsuperscript{54} indicating parallel between amount of salt intake and incidence of hypertension in his observations.

\begin{figure}[h]
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\includegraphics[width=\textwidth]{image.png}
\caption{Bridge mechanisms between normotensive zone and hypertensive zone. Essential hypertension is a product of the combination of intrinsic and extrinsic factors. The intrinsic factors consist of biological neurovascular pressor responsiveness and personal character. The extrinsic factors consist of emotional stress and excessive intake of salt. Other contributing factors help the development.}
\end{figure}
of Eskimos, Marshal archipelago, Brookhaven of New York State, Hiroshima city and Akita prefecture of Japan, animal experiments of salt hypertension in chickens by Selye, Lenel and Rodbard, in rats by Sapirstein and in rabbits by Fukuta etc. established the fact.

As for the causes of essential hypertension, although unknown, the present and past investigations lead to speculation that essential hypertension is a product of the combination of intrinsic or genetic and extrinsic or environmental factors (Figure 15). The intrinsic factors include 1) biological neurovascular pressor responsiveness and 2) personal character. The extrinsic factors include 1) emotional stress and 2) excessive intake of salt. 1) As the activity of vasomotor nerves becomes greater, 2) as traits of the aforementioned hypertension inducing characters are possessed more, 3) as the intensity, frequency and length of emotional stress become greater, 4) as intake of salt becomes excessive, so essential hypertension will develop more easily. In addition, other contributing factors such as gain of body weight, physical overexertion or alcohol drinking habit may help the development and progress of essential hypertension. Accordingly, essential hypertension is a by-product derived from disharmony of the biological hemodynamic response to life stress, resulting from interrelations among multiple factors.

In addition, the author presumes that the intrinsic factors are not of qualitative but of quantitative difference between normotensive and hypertensive subjects. Accordingly, the physiological fault of essential hypertensive subjects in view of qualitative difference from normotensives was by no means discovered.

SUMMARY

The pressor responses to exercise of an ischemic arm were studied in 200 normotensives and 100 hypertensives by means of the maximal ischemic exercise pressor test to examine the individual difference of cardiovascular responses, with special reference to the pressor components of the response. In addition, the submaximal ischemic exercise pressor tests were also applied to investigate the potential role of the vasomotor nerves. Simultaneously, surveys on the personal characters of hypertensive subjects were carried out. Thus an epidemiological approach to the pathogenesis of essential hypertension was investigated.

The results may be summarized as follows:

1) The pressor responses to similar ischemic exercise were qualitatively identical but quantitatively different among subjects while pressor response in each individual was quite reproducible.

2) The blood pressure increased in two phases. The initial rise was associated with mental tension and concentration at the beginning of exercise, and the second on the intensity of muscular work as well as on pain-sensation. Therefore the total pressure rise represents a summation of the multiple reflex sympathetic activities.

3) The ischemic exercise pressor test (submaximal) consisted of complex pressor components—mental tension, concentration, muscular work, muscular fatigue and muscular pain—represented an episode of moderate mental and physical stresses of ordinary daily life.

4) Diastolic pressure rise in this test may serve as an index to indicate the degree of peripheral vasoconstriction, that is, the activity of vasomotor nerves.

5) This test can be used as a clinical method foretelling an individual pressor response to moderate life stress.

6) Most of the patients with essential hypertension manifested an excessive and protracted rise in systolic as well as in diastolic pressure, which may reflect an overaction of the vasomotor nerves. Such an overaction of the vasomotor nerves may play an important role in the initiation of essential hypertension.

7) Among normotensive subjects, those who had over 40/30 mmHg (Δsyst.pr./Δdiast.pr.)
in the pressor response and simultaneously over 160/95 or 150/100 mmHg in the absolute blood pressure, to the submaximal exercise test were considered to have a hypertensive response. According to WHO criteria, about 22% of normotensives exhibited “hypertensive response”. They may be considered to have a neurovascular predisposition susceptible to the development of essential hypertension. Accordingly, this technique may be adopted for differentiating the subjects with hypertensive diathesis from the normotensives. In addition, these values may be used in clinical tests as criteria for the diagnosis of pre-, early, or latent essential hypertension.

8) Excitable or short temper, worrying, anxious & impatient, highly chivalrous, and tenacious temperaments, timidity and fear or aggressive character were considered as hypertension inducing characters. These characters, more or less, were found in about 97% of the patients with essential hypertension.

9) It is proposed that essential hypertension is a product of the combination of intrinsic or genetic factors, mainly biological neurovascular pressor responsiveness and personal character, and extrinsic or environmental factors, mainly emotional stresses and excessive intake of salt. In addition, other contributing factors such as gain of body weight, physical overexertion, or alcohol drinking habit may help the development and progress of essential hypertension. Accordingly, essential hypertension is a by-product derived from disharmony of the biological hemodynamic response to life stress, resulting from the interrelation among multiple factors.

10) The ischemic exercise pressor test (submaximal) developed by the author can be recommended as a simple technique for an epidemiological approach to the pathogenesis of essential hypertension.

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ISCHEMIC EXERCISE PRESSOR TEST

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