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16. Abstract

It is explained that the orthostasis test makes it possible to evaluate neurohumoral regulation and reaction of the circulatory system and to detect changes in the function of a number of internal organs (especially the kidney). Simultaneous recording of the ECG in an orthostatic position, despite nonspecificity, makes it possible to detect hidden damage (organic or metabolic) or increased sensitivity of the myocardium to stressor sympathetico-adrenal effects, stability of therapeutic effect and the action mechanism of a number of drugs.

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ORTHOSTASIS TEST IN THE PRACTICE OF THE CARDIOLOGIST

N. P. Moskalenko and M. G. Glezer[1]

Despite its simplicity, possibility of being done in any, even outpatient, conditions, and adequate information value, the orthostasis test is very rarely used by practicing physicians in the management of patients with various, especially cardiovascular, pathology. This is explained principally by insufficient knowledge of the nature of the shifts in the circulatory system and in the systems that regulate it during transition from a horizontal to a vertical position. /112*

In a healthy person the transition to a vertical position causes a slight migration of blood to the veins of the legs (its volume increases by 300-350 ml). As a response to hydrostatic pressure, part of the liquid fraction of the blood is filtered from the vascular bed to the tissues of the legs, which leads to an insignificant hemoconcentration, which, among other things, is manifested in a 3.1% increase in the hematocrit value. In these conditions deposition and reduction of the volume of circulating blood are expressed insignificantly (only by 7%). However, displacement of blood to the lower body regions defers and reduces its return to the heart, and the stroke volume is reduced by 20.8%. In connection with this, systolic arterial pressure is reduced by 2.5%. The lower degree of systolic arterial pressure reduction and the stability of average arterial pressure are effected by the marked gain in sympathetico-adrenal activity with a clear increase (by 17.0%) in the number of cardiac contractions, as a result of which the minute volume is reduced by 7.3%, and by the 10.3% rise in total peripheral resistance. The latter is brought about by an increase in the tension of the arterioles of the lower body regions, in connection with which the diastolic arterial pressure is increased by

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12.0% [1, 7, 14]. In healthy people in a vertical position the tension of the veins of the lower regions is also increased, which prevents gravitational migration of blood and also ensures a sufficient return of blood to the heart. The latter is effected by contraction of leg muscles in the connective elastic cover and by the presence of valves in the legs which permit blood to flow only in the direction toward the heart.

In a small number of healthy people in whom no pathology of the cardiovascular system is detected during examination in a horizontal position, the hemodynamic shifts in the vertical position differ from those described above. It should be stressed that these disturbances are characteristic for many diseases, and also develop as a result of drug therapy. Analysis of published classifications, personal observations with the use of clinical-hemodynamic correlations, and comparison of disturbances detected with pathologic conditions and the use of drugs with varied mechanism of action allowed us to separate these disturbances into 4 groups. This division was based on the expression of sympathetico-adrenal reactivity during the orthostasis test. As was shown, sympathetico-adrenal mechanisms are manifested in the stabilization of blood circulation, especially in the first minutes after the transition to the vertical position. One group with a "sympathetico-tonic" reaction type is characterized by a more marked increase in the /113 rate of cardiac contractions, diastolic arterial pressure and total peripheral resistance than in most healthy people. According to our observations, people with this type of reactions must be divided into two essentially differing types.

Noted in the first type is a sharper reduction of the stroke volume, and, in conjunction with this, also of the systolic arterial pressure, as a result, it may be proposed, of more marked migration of blood to the lower body regions and reduction of blood return to the heart, for example because of reduction of the volume of circulating blood, varicose dilation of the leg veins or reduction of their tension. The latter is noted during prolonged hypodynamia as a result of atrophy of the muscles of the extremities, after infectious, expecially viral,

diseases, and also as a result of dilation of the peripheral vessels under the effect of high temperature (hot bath, exposure to sun). The manifestation of increased sympathetic regulation in this type of orthostatic disturbances is a more significant than normal increase in the rate of cardiac contractions (by 20 beats per minute and more) and in total peripheral resistance (by 38.5%), which is expressed in a significant (by 18.9%) increase in diastolic arterial pressure; during this the average arterial pressure does not change substantially [1, 12, 17, 18]. When in a vertical position the patients complain of dizziness, weakness, spots before the eyes, palpitation and profuse perspiration. This type of orthostatic disturbances is encountered most frequently in the presence of aberrations in the orthostatic regulation of blood circulation and is commonly designated as "sympatheticotonic" [18], "hyperdiastolic" [16] or "statically labile" [15].

In the second type the increased sympathetico-adrenal reaction to an orthostatic position, along with increase in the cardiac contraction rate, diastolic arterial pressure and total peripheral resistance, is also accompanied by a marked increase in the systolic and average arterial pressure and the minute volume, and the stroke volume as well in some cases [6]. It is important that no disturbance of venous return of blood to the heart is noted in this [13]. It may be proposed that in these people there is a source of stimulation in the centers that regulate the sympathetic system or an increased release of catecholamines. As a rule these people are easily excited, suffer from insomnia and, undoubtedly, are in need of further observation for the solution of the question regarding their great inclination toward the development of hypertension. The described type of orthostatic disturbance of regulation is designated as "hypertonic," "hyperdynamic," "hypersympatheticotonic" [18] or "dynamically labile" [15].

The third type ("hypo- or asympatheticotonic," "postural hypotension" [16]) is characterized by a sharp reduction (up to absence) of the compensatory sympathetico-adrenal reaction to an orthostatic position. It is manifested as a smaller increase or absence of an increase in the rate of cardiac contractions, diastolic arterial pressure

and total peripheral resistance; in some people these indices can even be reduced. Systolic and average arterial pressure and the minute and stroke volume are reduced naturally. Usually lying at the base of this disturbance is a neurogenic disease, frequently with damage of the central nervous structures that take part in the synthesis of norepinephrine, or with damage of the spinal cord in the region of the preganglionic sympathetic neurons (tertiary syphilis, alcoholic neuro- and encephalopathy, syringomyelia, etc.). Clinically unlike the first type of people with sympatheticotonic orthostatic disturbance, in patients of this group in an orthostatic position pronounced weakness and dizziness (to fainting) are noted, unaccompanied by perspiration and palpitation.

The fourth type ("mixed" or "sympathetico-asthenic") is characterized by the appearance of a normal compensatory or hypersympathetico-tonic reaction with significant increase in the cardiac contraction rate, diastolic arterial pressure and total peripheral resistance immediately after transition to the vertical position. However, in 5-15 min, as a response to inducing factors (fear, pain, etc.) or spontaneously, the initial reaction to the orthostatic position is replaced by a marked reduction in systolic, diastolic and average arterial pressure and total peripheral resistance and by deceleration of the rate of cardiac contractions, frequently lower than its level in the horizontal position [1, 12]. These hemodynamic shifts develop as a result of exhaustion of the adaptive-compensatory sympatheticotonic reaction. Noted at the same time is a significant increase in the tension of the vagus nerve (vasovagal, vasodepressor hypotension, vasovagal crisis or syncope).

In addition to the indicated four types of marked deviation, the orthostatic reaction of healthy people can have several differences depending on age, constitution and a number of other factors. Thus, in younger people (to 35 years) in an orthostatic position a more marked increase in the rate of cardiac contractions, the absence of a clear change in average arterial pressure and less reduction in the stroke volume are noted; this is explained by a higher sympathetico-adrenal

activity. In the older-than-50-years age group the rate of cardiac contractions increases to a less degree, the stroke volume and average arterial pressure decrease more markedly and the total peripheral resistance and diastolic arterial pressure increase to a greater extent [14]. This may be caused by a reduction in sympathetico-adrenal activity or less sensitivity of the heart to sympathetic stimulation, by reduction of the tension of the veins of the lower regions with decrease in the return of blood to the heart and by alteration of the arterioles with thickening of their walls and in conjunction with this a more marked pressor reaction

The average arterial pressure and the minute and stroke volume are reduced to a greater extent, and the rate of cardiac contractions and /114
the total peripheral resistance are increased more significantly, in people of asthenic constitution in an orthostatic position than in people of normosthenic constitution. The sympatheticotonic type of orthostatic disregulation is frequently noted in them, which apparently is caused by a reduction of venous tension and more marked migration of blood to the lower extremities. In people of hypersthenic constitution, on the other hand, orthostatic hypotension rarely develops. In an orthostatic position fluctuations of arterial pressure in them are insignificant, and the increase in the cardiac contraction rate is less marked in them than in people with a normosthenic constitution. It is possible that this is due to a well developed muscular system, thanks to which the "pumps" of the legs provide adequate return of blood to the heart.

Thus, to evaluate the nature of hemodynamic shifts in an orthostatic position and to form an approximate idea of the condition of the regulating adaptative systems (especially the sympathetico-adrenal), it is sufficient for a practicing physician to record the cardiac contraction rate and the arterial pressure with the patient in a horizontal position and after transition to a vertical position. The results of our examinations of patients with arterial hypertension [3, 5] may serve as an illustration of this. Thus, in early stage hypertension

on transition to a vertical position the systolic arterial pressure does not change and the diastolic and average pressure increase more significantly than in healthy people. The stroke volume decreases, and the cardiac contraction rate and the total peripheral resistance grow to a greater extent than in healthy people. Sharply expressed shifts of the last indices in response to the orthostasis test reflect the presence of sympathetic excitability in stage I hypertension. In stages IIA and IIB of the disease the systolic arterial pressure in the vertical position is reduced more clearly, and the diastolic is increased to a less extent, than in healthy people; the average arterial pressure does not change in stage IIA and is reduced reliably in stage IIB. As the disease progresses, a more significant reduction of the stroke and minute volume is noted in the orthostatic position, which is caused by reduction in the tension of the veins and more significant migration of blood with reduction of venous return of blood to the heart. The cardiac contraction rate in the orthostatic position grows less in stage IIB hypertension than in healthy people. The total peripheral resistance in the orthostatic position also grows as the disease progresses, in conjunction both with neuroreflex mechanisms and with thickening of the walls of the arterioles and, consequently, more marked narrowing of the lumen of the vessels even during normal contraction of their smooth musculature. Thus, the reaction of the cardiovascular system to the orthostasis test in patients with hypertension differs from the reaction of healthy people and depends on the stage of the disease [3, 4, 6, 8].

In patients with the hypertonic form of chronic diffuse glomerulonephritis, with sufficient kidney function the reaction of the cardiovascular system to the orthostasis test is characterized by a slightly larger reduction in systolic arterial pressure and stroke and minute volume than in healthy people. A significantly greater increase in the cardiac contraction rate and the total peripheral resistance indicates increased reaction of the sympathetic system in response to change in body position [5]. The growth of total peripheral resistance is also caused by thickening of the vascular walls in connection with disruption of water-electrolyte metabolism. With development of chronic re-

nal insufficiency, the compensatory adaptative reaction of the circulatory system in response to change in pody position is reduced. In azotemia the toxic effect on the walls of the veins and on the nervous system causes reduction of venous tension, as a result of which the return of blood to the heart, the stroke and minute volume and the systolic arterial pressure are decreased [5]. A lower degree of increase of the cardiac contraction rate in the orthostatic position is also apparently related to the toxic effect on the nerve centers in these pstients.

Still another aspect of the use of the orthostasis test is important--appraisal of the function of a number of internal organs. Thus, we studied the nature of the change in kidney function on transition from a horizontal to a vertical position [1]. The homeostatic reaction of the kidneys of healthy people to the necessity of maintaining adequate blood supply and circulation of the brain, lungs and right auricle ("centralization of circulation") is expressed in a spasm of the arterioles with increase in the resistance to blood flow in the kidneys by 23.6% and decrease in renal blood flow by 16.7%; in comparison with the latter the glomerular filtration is reduced to a lesser extent (by 11.3%), which indicates primary narrowing of the afferent vessels, in connection with which the filtration fraction grows by 10.8%. Diuresis is also reduced (by 19.7%); this reduction is seen to a greater extent than the decrease in glomerular filtration, which indicates the role of increased reabsorption in the tubules. In some cases in practically healthy people, as was indicated above, the reaction to the orthostasis test differed from the normal. Irrespective of the nature (type) of changes of the indices of general hemodynamics, in all the patients there was a sharper reduction in renal blood flow (by 35.5%), glomerular filtration (by 22%) and diuresis (by 29%). However, in the first and second (hypersympatheticotonic) types the resistance to blood flow in the kidney vessels grew significantly more (by 49.5%) than in healthy people, whereas in the third (hyposympathetico-tonic) type the resistance to blood flow in the kidney vessels in an orthostatic position did not change significantly [1, 12]. Therefore, in people with orthostatic disregulation the sharp reduction in renal

blood flow is brought about primarily by either a more marked narrowing of the renal vessels or by a sharper fall in cardiac ejection [1, 12]. In patients with hypertension, especially in the late stages, and with /11 glomerulonephritis, the resistance to blood flow in the kidney vessels grows significantly more (by 34.6%) and renal blood flow and glomerular filtration are reduced significantly more (by 27.6% and 23.4%, respectively) in an orthostatic position as compared to healthy people [3, 5]. These results may explain the decrease in diurnal diuresis when patients are in a vertical position and the presence of nocturia in many such patients.

Recording of the ECG not only in the generally accepted horizontal, but also in an orthostatic, position gives additional information. In healthy people the ECG recorded in an orthostatic position does not differ practically from that taken in a horizontal position; a slight reduction of the T wave in the $V_{5,6}$ lead, displacement of the electrical axis of the heart to the right, insignificant reduction in the height of the P wave and increase in the P wave in the chest leads can sometimes be seen [10, 11, 13]. It is thought that the cause of the development of these shifts is a change in the anatomic position of the heart in the chest cage, since in an orthostatic position the heart is more vertical and can rotate to a small extent clockwise around its axis. With recording of the ECG in a vertical position, reduction of the S-T interval and inversion of the T wave were noted in 1/5 of the patients with ischemic heart disease, in whom negative dynamics of the ECG signs were noted during exercise on a bicycle ergometer [13]. In some patients who have had a myocardial infarct the Q wave is deepened and the P wave is reduced in the region of the postinfarct wave [10, 11, 13] in an orthostatic position. With ischemic heart disease atrial or ventricular extrasystoles and sinoatrial blockades are recorded on the ECG in an orthostatic position in a number of cases [13]. Thus, recording the ECG in an orthostatic position in ischemic heart disease does not replace the bicycle ergometer test, but can be used to detect hidden myocardial changes that are not recorded during examination in a horizontal position in cases in which it is difficult or impossible to conduct bicycle ergometry. In addition, the mechanisms of the ECG

change are probably not the same in the two tests. Thus, negative dynamics of the ECG signs were noted in 1/3 of the patients with early stage hypertension and only in 10-15% of patients with a late stage [13]. With this, in patients with early stage hypertension a physical load on the bicycle ergometer did not cause negative shifts in the ECG, but with the presence of changes on the ECG at rest, the load led to their decrease or disappearance. It has been proposed that this may be explained by the fact that with a physical load the venous return of blood and the systolic volume are increased, and the blood supply to the myocardium is therefore also increased. In the absence of coronary stenosis the latter is also caused by the accumulation of the products of metabolism in the myocardium during a physical load.

The appearance or intensification of ECG changes in an orthostatic position is nonspecific; they can be noted in patients with various changes of the myocardium. The mechanism of these ECG changes in the orthostatic position includes a number of factors; among the basic ones are the action of the extremely increased sympathetico-adrenal effects on the myocardium and the reduction of its tolerance to these actions because of metabolic disturbances. This is confirmed by the results obtained by us and other authors: the orthostatic changes on the ECG often disappeared or decreased after treatment with propranolol, potassium salts and pyridoxilate.

In connection with the latter it is important to stress the importance of the use of the orthostasis test with the recording of shifts of hemodynamic parameters and the ECG in the appraisal of the effectiveness and stability and the effect of drugs. Thus, according to our data, in patients treated with potassium salts, pyridoxilate or propranolol, with a clear improvement of the signs of the ECG recorded in a horizontal position, in an orthostatic position in some of the patients this improvement could be maintained, and in some, negative dynamics arose; at the same time in a number of patients without marked positive dynamics on the ECG in a horizontal position, the orthostasis test caused a marked reduction or disappearance of negative shifts.

The use of the orthostasis test for the detection of differences in the action of drugs is of considerable interest. Thus, for example, in treatment with several hypotensive agents (guanethidine, alpha-methyldopa, propanolol) that reduce sympathetic activity, with the examination of patients in a horizontal position in a number of cases it is possible to obtain hemodynamic shifts that are close in character in the form of decrease in the cardiac contraction rate and reduction of the minute volume in the absence of marked changes in the total peripheral resistance to blood flow. However, in the orthostatic position the direction and expression of the hemodynamic shifts can be extremely varied [2, 4, 7-9].

In an orthostatic position during treatment with alpha-methyldopa and especially with guanethidine there was a marked reduction in systolic arterial pressure, and the diastolic pressure, which was increased before treatment, began to decrease; treatment with propranolol did not affect the nature of the change of arterial pressure on transition from a horizontal to a vertical position. The minute volume in the orthostatic position was reduced more sharply during treatment with alpha-methyldopa and especially with guanethidine; during treatment with propranolol the extent of its reduction was unchanged. The nature of the changes of the minute volume in the orthostatic position was partially causes by the reduced growth in the cardiac contraction rate during treatment with all three drugs, partially--by the nature of the change of the systolic volume. The systolic volume in the orthostatic position decreased less during treatment with propranolol and more during treatment with guanethidine than before treatment. The latter is caused by a greater reduction of the tone of the smooth musculature of the capacity vessels and decrease in the return of blood to the heart. The degree of constriction of the arterioles and the expression of the increase in peripheral resistance to blood flow in an orthostatic position during treatment with propranolol were not changed /116 substantially, and during treatment with alpha-methyldopa and especially with guanethidine they were significantly less. Therefore, marked orthostatic hypotension during treatment with drugs that reduce sympathetico-adrenal activity is caused primarily by reduction in the tone

of the smooth musculature of the veins with decrease in the return of blood to the heart and of the arterioles with less marked increase in total peripheral resistance, and also by less growth in the cardiac contraction rate in the vertical position.

Thus, the orthostasis test makes it possible to appraise the adequacy of neurohumoral regulation and reaction of the circulatory system and to detect the nature of the changes of function of a number of internal organs (in particular, the kidneys), which is important for the basis of work and medical recommendations. Simultaneous recording of the ECG in an orthostatic position, despite nonspecificity, makes it possible to detect hidden damage (organic or metabolic) or increased sensitivity of the myocardium to stressor sympathetico-adrenal effects, stability of therapeutic effect and the action mechanism of a number of drugs.

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