●原 著

低圧環境下での自律神経反応

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健常人10名に対して360 mmHg，3時間の低圧下負荷を行い自律神経の反応を深呼吸下及び安静時で観察した。自律神経反応は心電図記録を行い，不整脈の出現様式及び深呼吸時の瞬時最大心拍および瞬時最小心拍を測定することにより判定した。低圧時の深呼吸時に限って2例に上室性期外収縮が出現し，1例に房室ブロックが認められた。低圧になると平均心拍が66.7±10.1(bpm)より85.5±18.6(bpm)と有意に($P<0.01$)増加し，収縮期血圧は117.0±8.4(mmHg)より104.4±8.4 (mmHg) と有意の低下を示した。深呼吸時の最大心拍と最小心拍の差は有意の変化を示さなかった。以上の結果より，低圧下では，交感神経系の機能亢進と副交感神経系の反射の亢進があることが推測された。

キーワード：低圧，深呼吸負荷，自律神経

Autonomic Nervous System Under Hypobaric Pressure

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We studied autonomic nervous function during hypobaric pressure in ten volunteers by using a controlled-climate-room. The pressure was set at 360 mmHg, and the subjects were resided for three hours. The autonomic function was assessed by deep breathing testing (DB-test). Second degree AV-block was observed in one subject and SVPCs were observed in two subjects only during the DB-test under hypobaric pressure. Mean heart rates increased during hypobaric pressure. The systolic blood pressure decreased significantly. However the heart rate variability as assessed by maximum heart rate minus minimum heart rate during DB-test did not change statistically. These findings suggest that hypobaric pressure of 360 mmHg provokes an increase in mean heart rate not due to withdrawal of parasympathetic tone. And the vagal reflex was suspected to be augmented, under hypobaric pressure.

Keywords :
Hypobaric pressure
Deep-breathing testing
Autonomic nervous system

Introduction

A hypobaric pressure decreases the oxygen content of the blood to induce tissue hypoxia. Various factors are involved to adjust the circulation to adapt adequately to hypobaric pressure or hypoxia. The se include endocrine systems, metabolic system and nervous system. Nervous control mechanisms are ideally suited to short term circulatory control because they respond quickly to environmental stresses. The brain controls the circulation primarily via the efferent nerves of the sympathetic and parasympathetic nervous systems. Immediately after arrival at a high altitude, bradycardia is reported to

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appear as a first phase, with reduction of the pulse pressure and reduction in cardiac output, after one or two hours the first parasympathicotonia gives way to second phase "amphotonus". In an experimental study, rapidly produced hypoxemia often results in bradycardia and conduction disturbances, terminating with cardiac arrest because of an increased vagal tone (3). On the other hand, Korner (4) reported that acute exposure to hypoxia in man results in an increase in cardiac output and heart rate. Eckberg et al. undertook a study to determine whether bradycardia develops during systemic hypoxia and to get a conclusion that the hypoxic stress reduced the cardiac vagal motoneuron output (5). And they concluded that in conscious human volunteers systemic hypoxia lead to cardioaccerelation. Thus, the neural cardiovascular control under hypobaric pressure may be affected through a complex interaction of both sympathetic and parasympathetic feedback reflex mechanisms. So it is likely that information about this interaction can be extracted from the heart rate variability signal and electrocardiogram. Accordingly the present investigation was designed to assess the autonomic nervous function under hypobaric pressure by heart rate variability signal and electrocardiogram.

Methods

Subjects : Volunteers who intended to climb a high mountain, were ten healthy men whose average age was 31.9 ± 9.6 (SD) year.

Methods : Theexperinents were conducted in a controlled-climate-room in our laboratory with the subjects in the sitting position. Four cases were examined per one day. It took for 3 days to examine the test for ten subjects. The test was performed at 13 : 00 o'clock each day. The pressures were decreased from ambient pressure of about 760 mmHg to 360 mmHg at a decompressing speed of 12 mmHg/min. The subjects resided in the hypobaric chamber for 3 hours under the pressure of 360 mmHg. After that the pressures were increased to ambient pressure at a compressing speed of 12 mmHg/min. Ink writing recorder was used to monitor the electrocardiogram during the test. The electrocardiogram and pneumogram were recorded simultaneously by using 2-channel Holter ECG recorder. The blood pressure were measured by using sphygmomanometer before hypobaric pressure and 3 hours after hypobaric pressure. Autonomic nervous function was assessed by deep breathing testing (DB-test) originally described by Wheeler and Watkins (6). The maximum and minimum instantaneous heart rates were measured during a period of slow, steady, deep breathing at six breaths per minute to assess the parasympathetic activity. The mean heart rates before the DB-test, maximum and minimum heart rates during the DB-test were measured before the hypobaric pressure, 1-, 2- and 3 hours after the start of the hypobaric pressure.

Statistical Analysis : Statistical comparisons were made with the paired and unpaired t -test.

Results

An example of sequential histogram of instantaneous heart rate during DB-test in one subject is shown in Fig. 1. Mean heart rate during quiet breathing was 64 beats/min. During deep breathing instantaneous heart rate ranged between maximum of 65 and minimum of 45 beats/min. An example of electrocardiographic changes for 4 subjects during DB-test is shown in Fig. 2. During the control period, each subject showed an decrease in R-R intervals during expiration phase and increase of R-R intervals during inspiration phase. In subject A, supraventricular extrasystole (SVPC) was found

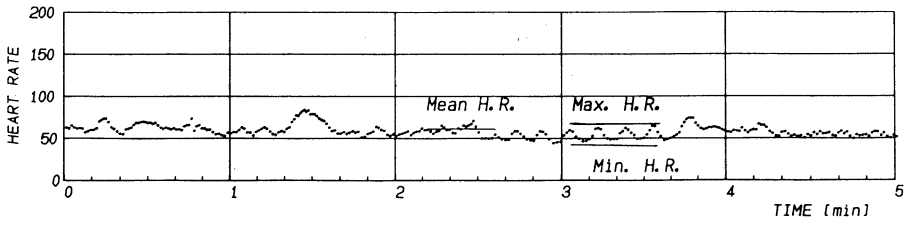

Fig. 1. Sequential histogram of instantaneous heart rate during the DB-test.

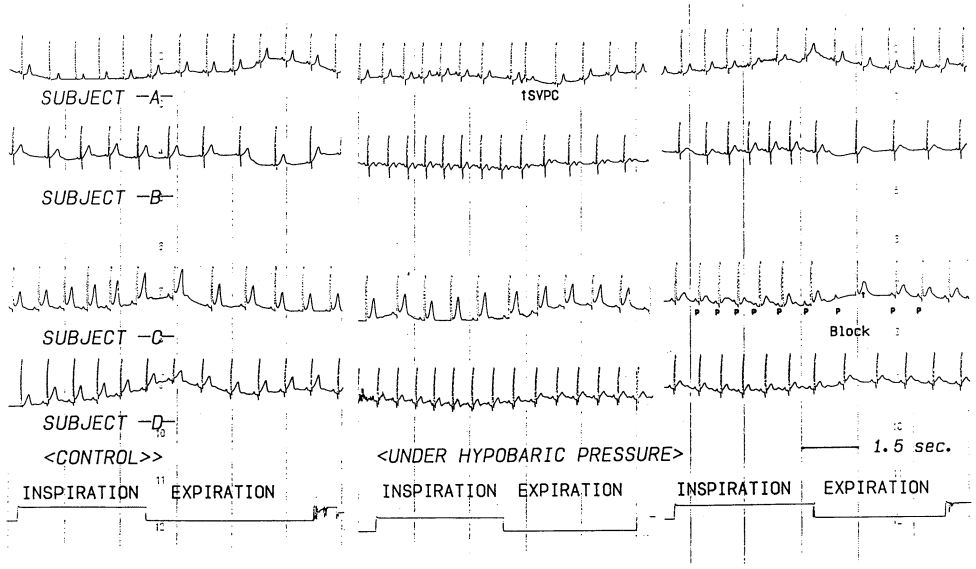

Fig. 2. Electrocardiograms of four subjects during the DB-test under control period and under hypobaric pressure. SVPC was observed in subject -A- during the expiration phase of deep breathing. Second degree of AV -block was observed in subject -C- during the expiration phase of deep breathing.

during the expiration phase of the deep breathing. In this subject, SVPC was not found before the hypobaric pressure and during hypobaric pressure except during the DB -test. The appearance of SVPC was reproducible only during the DB-test under hypobaric pressure. In subject C, second degree AV block (Wenckebach-type) was observed as shown in Fig. 2. In this case, the AV block was also observed only during the DB-test. Mean and standard deviation of the mean heart rates before hypobaric pressure, 1 -, 2-, and 3-hours after the start of hypobaric pressure were 66.7 ± 10.1, 83.2 ± 19.6 ($p<0.05$), 87.9 ± 8.0 ($p<0.01$) and 85.5 ± 18.6 ($p<0.01$) respectively (Fig. 3). The increase in heart rate during hypobaric pressure were statistically significant. Mean and standard deviation of the maximum heart rate before the DB-test before the hypobaric pressure (control period), 1-, 2-, and 3-hours after the hypobaric pressure were 77.5 ± 10.8, 88.2 ± 16.1 ($p<0.05$), 83.1 ± 11.9 ($p>0.05$), 85.2 ± 15.9 ($p>0.05$) respectively (Fig. 4). The increase

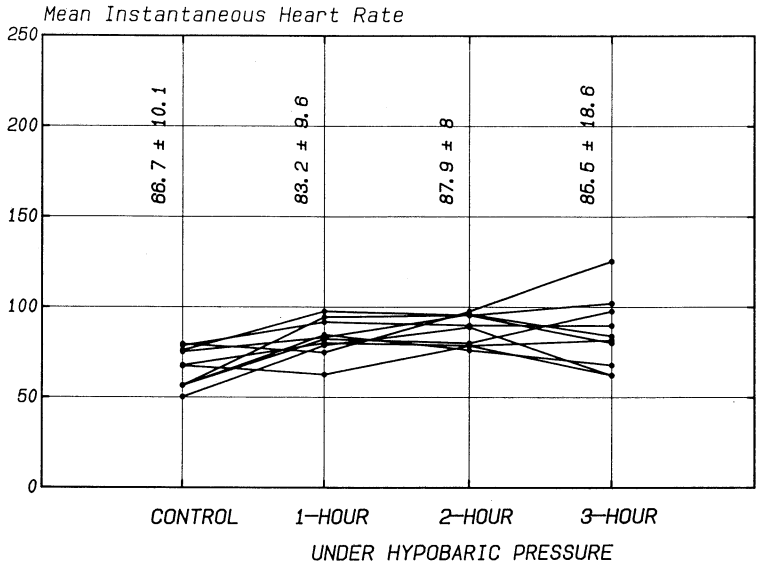

Fig. 3. Mean instantaneous heart rate in the control period, and 1-, 2-, and 3-hours after start of hypobaric pressure.

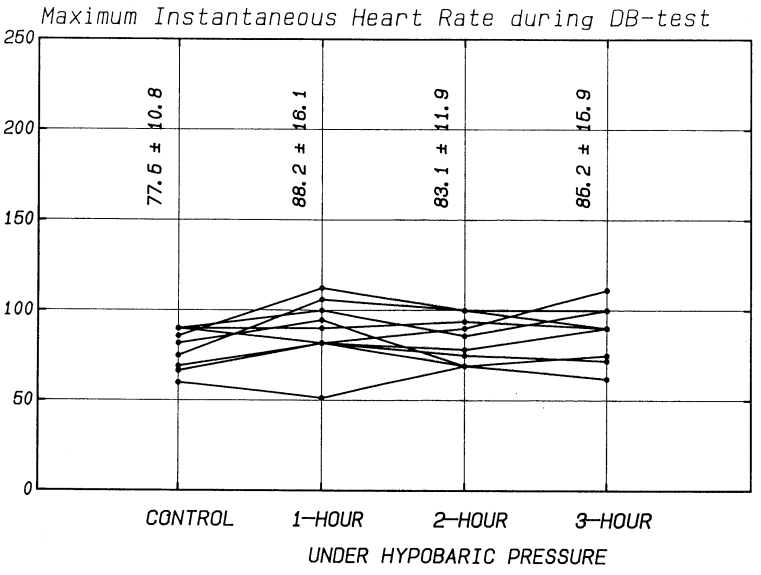

Fig. 4. Maximum instantaneous heart rate during the DB-test in the control period and during the hypobaric pressure.

in maximum heart rate were statistically significant in one hour after the start of hypobaric pressure. Mean and standard deviation of the minimum heart rate during DB -test before, 1-, 2-, and 3-hours after the hypobaric pressure were 57.6 ± 11.3, 61.9 ± 14. 3 ($p>0.05$), 62.1 ± 13.9 ($p>0.05$), and 60.1 ± 8. 9 ($p>0.05$) respectively (Fig. 5). Not significant changes in minimum heart rate were observed during DB-test between the hypobaric

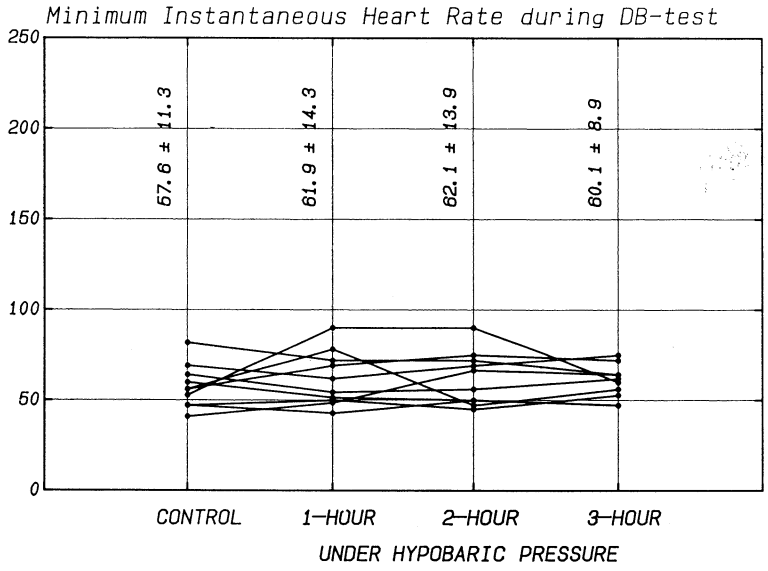

Fig. 5. Minimum instantaneous heart rate during the DB-test in the control period and during the hypobaric pressure.

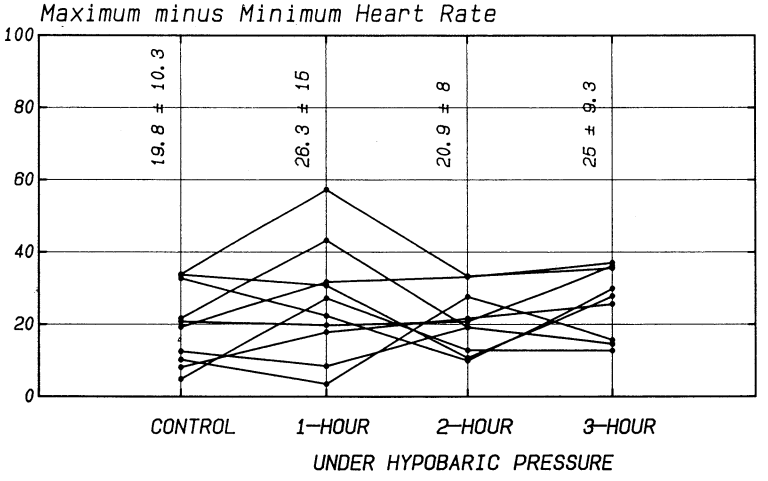

Fig. 6. Maximum minus minimum heart rate during the DB-test in the control period and during the hypobaric pressure.

pressure and ambient pressure (sealevel). Mean and standard deviation of the heart rate variation (maximum instantaneous heart rate minus minimum instantaneous heart rate) during the DB-test at ambient pressure (sea level), and 1-, 2-, and 3-hours after the hypobaric pressure showed mean ualues of 19.8 ± 10.3, 26.3 ± 15.0 ($p>0.05$), 20.9 ± 8.0 ($p>0.05$), and 25.0 ± 9.3 ($p>0.05$) respectively (Fig. 6). The values at ambient pressure and during the hypobaric pressure were statistically not significant. The systolic blood pressure was 117.0 ± 8.4 mmHg. before the hypobaric pressure and 104.4 ± 11.4 mmHg. during the

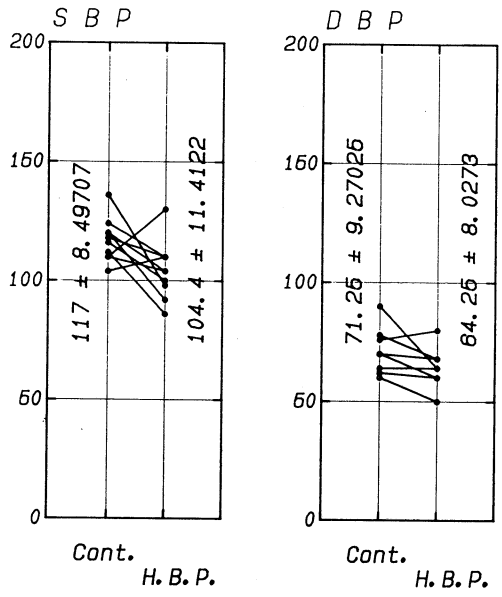

Fig. 7. Systolic blood pressure and diastolic blood pressure in control period (Cont.) and during the hypobaric pressure (H.B.P.).

hypobaric pressure ($p<0.05$). During the hypobaric pressure the systolic blood pressure was significantly lower than in the control period (ambient pressure). But the diastolic blood pressure during hypobaric pressure were unchanged from control value.

Discussion

In the present study, indirect indices of heart rate variability, and electrocardiogram were utilized to assess the autonomic nervous response during hypobaric stress. During the DB-test, AV-block was observed in one case and SVPCs were observed in two cases. Strasberg et al.(7) reported two cases with deep inspiration caused paroxysmal AV block in apparently healthy subjects due to hyperresponsiveness of the AV node to vagotonic reflex(7, 8). Deep inspiration also induce sinus arrest due to hyperresponsiveness of the sinus node to vagotonic reflex (9). Acute hypoxia often increase vagal tone mediated by hypoxic stimulation of chemoreceptors (3). Hypoxic stimulation of chemoreceptors and hyperresponsiveness of AV node to vagotonic reflex were considered as possible causes of the DB-test induced AV block in a subject in our study. The mechanisms of DB-test induced SVPCs were unclear. As in the case with DB-test induced AV block, vagotonic reflex might induced this arrhythmia, because the arrhythmia was solely presented during the phase of deep breathing at a breathing frequency of 6 per minute. The sinus arrhythmia is a breathing frequency dependent phenomenon, and the breathing frequencies about 5-6 breaths/min. swings the amplitude of sinus arrhythmia (10), and this sinus arrhythmia is decreased in patients with cardiac parasympathetic nervous dysfunction (6). The fact that the DB-test induced SVPCs had been occurred only in the phase of maximum amplitude of sinus arrhythmia might indicate that the SVPCs were vagally mediated phenomenon. It is suspected that the AV-block and the SVPC might be vagally mediated through the vagal reflex arc.

Sayers et al.(11) analysed the frequency contents of heart rate by measuring the power spectrum. Thermoregulatory factor, muscle flow factor and respiratory factor were responsible for heart rate fluctuation. This frequency domain analysis could also afford the parameters about autonomic nervous activity on the heart(12). However, frequency domain heart rate analysis is complex and needs sophisticated computer system. On the other hand, measurement of maximum and minimum heart rate during slow, steady, deep inspiration at six breath per minute to know parasympathetic activity is reproducible and the heart rate variation can easily be recorded even in an outpatient situation(13). Normal subjects almost invariably have differences in heart rate of more than 15 beats/min., whereas patients with diabetes mellitus with auto-

nomic neuropathy have differences of 10 beats/min. or less (14). It is suspected that parasympathicotonia increase this heart rate variability. In our study, the mean values of the difference of maximum and minium heart rate were slightly increased during the hypobaric pressure, but were statistically not significant. Mean values of the difference of maximum and minimum heart rate were more than 15 beats/min. during the study. This indicates that the vagal tone did not decrease under hypobaric pressure.

The mean values of the mean heart rate before the DB-test increased significantly during the hypobaric pressure. The hypoxic initial parasympathicotonia (1, 2) was not observed in our study. The initial bradycardia was reported to appear at altitudes between 1,900 and 2,300 (2). The hypobaric pressure of 360 mmHg, which is produced in our study, is consistent with a height of 5,500 m. In this simulated altitude, signs and symptoms of central nervous system and circulatory system appears. This condition, the hypoxic stress is stronger than that at an altitude of 2,000 m. And, somewhat different circulatory adjustment of acute acclimatization might be appeared. It is suspected that the initial parasympathicotonia was too short or diminished, and gives way to the second phase with tachycardia in this extreme condition. Recent study shows that the heart rate is surprisingly normal on acute exposure to high altitude. At Cerro de Pasco (4330 m), the heart rate was in the range of 68 to 84. However with a slight exercise the pulse rate increase significantly. This tachycardia probably has a role as an early acclimatization to high altitude. As mechanisms of tachycardia under systemic hypoxia, decrease of cardiac vagal motoneuron output, or increase of sympathetic nervous tone might be considered. The blood pressures were decreased significantly during acute exposure to hypobaric pressure. The arterial baroreflex sensitivity was not altered by mild hypoxia (15). Thus, the decreased systolic blood pressure might cause the parasympathetic withdrawal to induce tachycardia. However the vagal tone as assessed by maximum and minimum changes of heart rate did not change significantly during hypoxic stress. It is suspected, therefore, that the increase in mean heart rate might be due to augmented activity of sympathetic nervous activity.

In conclusion, our finding suggest that the hypobaric pressure of 360 mmHg provoked a slight increase in mean heart rate perhaps due to the augmented sympathetic activity, because the heart rate variability did not change significantly between the control phase and hypobaric pressure. However in some subject, the vagal reflex as shown by DB-test induced AV-block and SVPC was increased in the hypobaric pressure. These types of cardiac bradycardia, especially the AV-block, reduce the cardiac output and sometimes induce syncopal attack. It is suspected that a syncopal attack, when it occurs on a glacier or on a slippery rock or snow at an high altitude, might be one of the high risk factor at a high altitude.

It is warned that act or behavior which induce vagal reflex should not be done in a high altitude.

References

1) Berk, J.L., and Levy M.N.: Profound reflex bradycardia produced by transient hypoxia or hypercapnia in man. Surg. Res. 9: 75–84, 1977.
2) Jungmann H., and Halhuber, M.J.: The physiology of Altitude. in Medical Climatology (ed. by Licht, S.) pp 257–279, Elizabeth Licht Publisher, Connecticut, 1964.
3) Ayres, S.M., and Mueller, H.: Hypoxemia, hypercapnia, and cardiac arrhythmias: The importance regional abnormalities of vascular distensibility. Chest, 63: 981–985, 1973.
4) Korner P.I.: Circulatory adaptations in

hypoxia. Physiol. Rev. 39 : 687–730, 1959.
5) Eckberg D.L., Bostow H., and Scruby, A.E. : Modulation of human sinus node function by systemic hypoxia. J. Appl. Physiol., 52 : 570–577, 1982.
6) Wheeler, T., and Watkins, P.J. : Cardiac denervation in diabetes. Br. Med. J., 8 : 584–586, 1973.
7) Strasberg, B., Lam W., Swiryn S., Bauerfeined, R., Scaglotti D., Palileo E., and Rosen. K. : Symptomatic spontaneous paroxysmal AV nodal block due to localized hyperresponsiveness of the AV node to vagotonic reflexes. Am. Heart J., 103 : 795–801, 1982.
8) James T.N., Urthaler F., and Hageman, G.R. : Reflex heart block. Baroreflex, chemoreflex and bronchopulmonary reflex causes. Am. J. Cardiol, 45 : 1182–1188, 1980.
9) Strasberg B., Svclarovsky S., Arditti A., Lewin R.F., and Agmon J. : Deep inspiration induced sinus arrest. An unusual manifestation in a patient with the sick sinus syndrome. J. Electrocardiol., 19 : 91–92, 1986.
10) Coulter N.A., and Angelone A. : Respiratory sinus arrhythmia : a frequency dependent phenomenon. J. Appl. Physiol. 19 : 479–482, 1964.
11) Sayers, B.M. : Analysis of heart rate variability. Ergonomics, 1 : 17–32,1973.
12) Pomerantz, B., Macaulay R.J.B., Caudill, M. A., Kutz, I., et al. : Assessment of autonomic function in humans by heart rate spectral analysis. Am. J. Rhysiol. 248 : 151–153, 1985.
13) Hilstead J., and Jensen, S.B. : A simple test for autonomic neuropathy juvenile diabetics. Acta. med. Scand. 205 : 385–387, 1979.
14) Mackay J.D., Page M.M., Cambridge J., and Watkins P.J. : Diabetic autonomic neuropathy. The diagnostic value of heart rate monitoring. Diabetologia 18 : 471–478, 1980
15) Bristow J.D., Brown E.B., Cunningham D.J.C., et.al : The effects of hypercapnia, hypoxia and ventilation on the baroreflex regulation of the pulse interval. J. Physiol. London. 216 : 281–302, 1971.