Introduction

In 1896, Riva-Rocci developed the indirect arm-cuff method for the measurement of blood pressure (BP) (*1*), and in 1905 Korotkoff introduced the auscultation procedure into this indirect method (*2*). Since then, the indirect method for BP measurement has essentially remained unchanged for 100 years. However, in 1969 Posey *et al.* developed the cuff-oscillometric principle, which theoretically determines mean arterial BP, for the indirect measurement of BP (*3*). Thereafter, advances in theoretical analysis and technology led to a method for determining systolic and diastolic BP (SBP/DBP) on the basis of the cuff-oscillometric principle. As a result, recent electronic devices for self-measurement of BP at home (home BP) mainly use the cuff-oscillometric principle. Thus, although the Korotkoff sound method is the gold standard for clinical BP measurement, a different method is now generally used for home BP measurement.

Since the development of indirect BP measurement, hypertension research and treatment methodologies have been substantially advanced. The gold standard of BP measurement for practice and research has been the casual-clinic BP. However, an alternative to the casual-clinic BP was proposed 40 years after the introduction of indirect BP measurements. In 1940, Ayman and Goldshine reported the concept of "self-BP measurement" and demonstrated an apparent difference between the casual-clinic BP and the self-measured BP (*4*). Bevan *et al.* initially reported the concept of ambulatory BP monitoring (ABPM), which is based on the direct method, and demonstrated a marked and time-dependent variability of BP (*5*). It is apparent that the quality and quantity of BP information differ widely depending on the method of measurement. Therefore, the clinical significance of the casual-clinic BP has been a subject of much debate over the past 50 years. However, almost all data obtained from practice and research on hypertension, including epidemiological surveys, have been based on the casual-clinic BP or the BP obtained in a medical setting. This is the reason why the casual-clinic BP is the gold standard in clinical practice. However, data obtained from home BP measurements and ABPM have also been accumulating, and now it has been established that BP information obtained by these more recent methods has higher clinical significance than casual-clinic BP. The improved characteristics of home BP measurements and ABPM are essentially based on increased BP information obtained in relation to time. For example, ABPM measures BP every 15 to 30 min for 24 h or more, providing 50 to 100 BP measurements each day together with the clock time of each measurement. If home BP is measured once every morning and once every evening, this provides 60 measurements a month with information on the measurement time. Information on BP as a function of clock time, as well as an increased number of measurements, improves the quality of information. The implementation of the cuff-oscillometric principle in automated BP measuring devices, and the introduction of ABPM and home BP measurements into clinical practice, represent the major advances in the 100-year history of BP measurements.

ABPM provides BP in relation to time of measurement. To obtain such information, a special device for ABPM is necessary. Although the price of such devices has decreased recently, they still cost a few hundred thousand yen (a few thousand dollars), and such monitoring has not been covered by medical insurance in Japan. Therefore, ABPM represents a financial burden on individual patients as well as on medical institutes. For economic reasons, it is impractical to monitor ambulatory BP in the 35 million hypertensive patients in Japan. Furthermore, hypertension is a chronic disorder, and repetitive measurements for a long period are necessary to evaluate a patient's condition. ABPM also constitutes an excessive physical and mental load on patients. Therefore, it seems impossible to apply ABPM to all hypertensive patients. At present, ABPM is used for the diagnosis of particular conditions, such as intractable hypertension, white coat hypertension, episodic hypotension, or nocturnal hypertension. On the other hand, devices for home BP measurement are produced worldwide at a rate of more than 10 million a year, and 30 million such devices have already been distributed in Japan, with most being purchased by the general public or patients themselves (*6*). As a result, the availability of BP information for clinical practice in hypertension has increased extensively. Since the recent devices for home BP measurement can provide nocturnal BP during sleep, home measurements have improved the quality as well as the quantity of BP information (*7*). However, home BP measurement remains controversial as a result of questions related to the accuracy and reliability of the devices, and due to the use of unstandardized devices and unstandardized measurement procedures—as, for example, with respect to measurement frequency and schedule. The standardization of these factors is indispensable to maintain the quality and comparability of BP information, and the present lack of standardization affects the acceptance of home BP measurement as a tool for clinical decision-making.

The Sixth and Seventh Reports of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI and -7) (*8*, *9*), the 1999 World Health Organization-International Society of Hypertension (WHO-ISH) Guidelines for the Management of Hypertension (*10*), the 2003 European Society of Hypertension-European Society of Cardiology (ESH-ESC) Guidelines for the Management of Arterial Hypertension (*11*), and the Japanese Society of Hypertension (JSH) Guidelines for the Management of Hypertension (*12*) have all emphasized the importance of home BP measurements in clinical practice, clinical research, and clinical epidemiology, since home BP measurements reflect more accurately and reliably target organ damage and the prognosis of cardiovascular diseases (*13*, *14*). However, none of the guidelines have defined measurement procedures for home BP.

The Working Group for Establishment of Guidelines for Measurement Procedures of Self-Monitoring of Blood Pressure at Home of JSH has established standards for all techniques and procedures of home BP measurements. Home BP measurements based on these guidelines can be considered an appropriate tool for clinical decision-making, and these guidelines should serve to reduce confusion and confirm the place of home BP measurement in clinical practice. These guidelines have been established for adults.

1. Device for Self-BP Measurements at Home

Previously, mercury column manometers or aneroid manometers in conjunction with the auscultation method have been used for home BP measurement. However, these manometers, especially aneroid manometers, are sometimes unreliable and inaccurate. Mercury column manometers are cumbersome and cause environmental pollution. Furthermore, the auscultation method involves a subjective decision and a complex technique, and thus technical instruction and training are necessary to perform an accurate auscultation. For all of these reasons, previous devices for home BP measurements were not widely accepted and, consequently, not widely distributed.

In the 1960s, electrical devices based on the microphone method were introduced for home BP measurements. However, because of the mechanical properties of the microphone, these devices are costly and subject to frequent malfunctions. The microphone method also has an inherent shortcoming in determining the Korotkoff phase V, where an auscultation gap makes determination of the DBP inaccurate (*15*). Thus, microphone devices for home BP measurement were also not widely distributed.

During this period, theoretical analysis of the cuff-oscillometric principle advanced extensively. In 1969, Posey *et al.* discovered that the maximum oscillation of the intra-cuff pressure was nearly identical to the mean arterial BP (*3*), and the cuff-oscillometric principle was originally introduced as a method of determining mean arterial BP. Several experimental studies have revealed that SBP and DBP can be estimated from the pattern of the gradual increase and gradual decrease in cuff oscillation during cuff-pressure deflation. This basic algorithm has been improved by including procedures to correctly approximate the characteristic changes in cuff oscillation to the phase I and phase V Korotkoff sounds, and now almost all electrical devices for home BP measurement are based on the cuff-oscillometric principle.

However, the different properties of the Korotkoff sounds and cuff oscillation lead to an unavoidable difference in BP values between the two methods. Nevertheless, devices based on the cuff-oscillometric principle have become the norm for home BP measurement because of their simple mechanical properties, requiring only measurement of cuff-pressure change. Therefore, the device incorporates only a pressure sensor. Such a simple mechanism makes the device less troublesome and cheaper. The cuff-oscillometric device has another advantage when compared with the microphone device, in that surrounding noise does not interfere with BP measurements. More reasonable BP values in patients with atrial fibrillation or arrhythmia are also available by cuff-oscillometric devices when compared by Korotkoff sound method, since ectopically large or small pulse is averaged by the algorithm. Such factors encourage the production and distribution of cuff-oscillometric devices for home BP measurements. However, it is remarkable that sphygmomanometers used in the clinical setting have been changing from the Korotkoff sound method to cuff-oscillometric devices without causing much comment.

Although the mercury column sphygmomanometer with auscultation is becoming obsolete, we should remember that the gold standard for clinical practice is the Korotkoff sound method using a mercury column sphygmomanometer. Almost all epidemiological and clinical studies on hypertension have been based on casual-clinic BP measured by the Korotkoff sound technique. Therefore, clinical and epidemiological information obtained by the cuff-oscillometric method needs to be validated by accumulation of data. We must also be aware that the various manufacturers of devices using the cuff-oscillometric method may use different algorithms, leading to differences among devices in BP measurements from a single subject. In practice, the accuracy of the automatic devices is determined by comparison with the auscultation method, and no other standard method is currently available for this purpose. The issue here is the subjectivity and the possible inaccuracy of auscultation when the auscultation method is used as a standard. To exclude these shortcomings of the auscultation method, equipment based on objective methods should be developed for calibration of the automatic devices, in which the Korotkoff sound signal is treated with the established algorithm and the cuff-oscillometric devices are validated from this standard equipment. Objective and accurate evaluation of these automatic devices is a prerequisite for authorization of cuff-oscillometric devices for home BP measurement. The accumulation of clinical and epidemiological data obtained by authorized cuff-oscillometric devices may finally validate such devices as tools for clinical decision-making. Since BP measurements in a clinical setting are now mostly obtained by cuff-oscillometric devices, the data will be accumulated soon.

Recommendation 1

Arm-cuff devices based on the cuff-oscillometric method that have been validated officially, and of which the accuracy has been confirmed in each individual, should be used for home BP measurement.

2. Technical Instruction: Site for BP Measurement, Cuff Size, and Measurement Position

The cuff oscillometric principle is applicable to any site

where an arterial pulsation is available. However, the standard site for BP measurement is the upper arm, and several issues arise when BP is measured at sites other than the upper arm.

At present, 3 types of electrical devices for home BP measurement are commercially available: the arm-cuff device, the wrist-cuff device, and the finger-cuff device. In 1999, 7 million such electrical devices were produced in the far East (including Japan, Korea, and Taiwan), which represents 85% of the world production. Of those, 35% were wrist-cuff devices (*13*). Previously, finger-cuff devices commanded a considerable portion of the market share due to their convenience and ease-of-use. However, it is now apparent that finger BP is physiologically different from brachial BP, and issues of vasospasm in the winter season as well as hydrostatic pressure difference are inevitable. Therefore, manufacturers have now decreased production of finger-cuff devices and extensively increased production of wrist-cuff devices. In Japan, wrist-cuff devices possess 30% of the market share (*6*), and in Germany they possess almost half of the market share. Wrist-cuff devices are much easier to handle and more portable, but include several serious shortcomings. The most important issue is the necessity for correction of the hydrostatic pressure. The reference level for BP measurement is the right atrium. When the measurement site is 10 cm below the right atrium, SBP and DBP are measured 7 mmHg higher than those at the level of the right atrium, and *vice versa*. Therefore, the instructions for the wrist-cuff device indicate that the wrist must be kept at the heart level. However, it is uncertain whether general users can recognize the heart level accurately. For example, the apex of the heart is sometimes determined as the heart level, but is 5–10 cm lower than the right atrium, resulting in a 3.5–7 mmHg higher BP reading compared with measurement at the right atrium level. A 10 cm difference from the right atrium level easily and frequently occurs in the usual setting. This difference may have serious implications for public health policy as well as for clinical practice. This issue also applies to the arm-cuff device, and adequate instruction is necessary when home BP is measured by the arm-cuff device.

Even after appropriate correction of the hydrostatic pressure, another issue remains concerning the anatomy of the wrist. At the wrist, the radial and ulnar arteries are surrounded by the radial bone, the ulnar bone and several long tendons, including the long palmar tendon. Therefore, even a sufficient excess of cuff pressure over arterial pressure does not necessarily occlude these arteries completely (*16*). Measurements are also influenced by flexion and hyperextension of the wrist (*16*). As a result, wrist-cuff devices sometimes provide erroneous readings, especially for SBP. At present, the wrist-cuff device is inappropriate as a tool for clinical decision-making. Recently, a wrist-cuff device that does not work unless the device is at the heart level has been developed, but even such devices do not overcome the anatomical issue. However, the wrist-cuff device has a certain merit in terms of convenience. Arm-cuff devices also have some shortcomings, such as application to a thick arm, relation to clothes, and position of the arm-cuff in relation to the elbow joint. The wrist-cuff device can overcome these shortcomings. However, this Working Group recommends use of an arm-cuff device operated under the standard measurement procedure. Thus, instruction concerning the standard measurement method is indispensable. This should include matters such as keeping the arm-cuff at the heart level, extension of the lower arm, relaxation of the arm by means of a supporting pillow, cuff size, relationship between clothes and cuff, and relationship between the elbow joint and cuff.

At present, soft cuffs and hard plastic cuffs are available for automatic arm-cuff devices for home BP measurement. In individuals with thick arms, a hard plastic cuff does not necessarily fit to the arm, resulting in erroneous measurements. Thus, a soft cuff is most suitable, but in certain subjects a hard plastic cuff is convenient and measures BP accurately. Among the cuff-oscillometric devices, the width and length of the cuff bladder differ among producers. This is permitted by the American Association for Medical Instrumentation (AAMI) (*17*) and the American National Standard Institute Inc. (ANSI) (*18*) provided that the cuff pressure is transmitted to the artery and can occlude the brachial artery completely.

In individuals with excessively thick or thin arms, use of large cuffs and small cuffs, respectively, is recommended. In general practice, the BP difference between the arms must be evaluated. If a difference of BP between the arms is apparent, the BP should usually be measured with the arm that shows the higher BP. Self-measurement of BP at home, however, is usually performed using the non-dominant arm. When an apparent difference of BP is observed between the arms in a clinical setting, the arm showing the higher BP should be used for self-measurement. To provide consistent results, the same arm should always be used for self-measurement.

Recommendation 2

The BP should be measured at the upper arm. Finger-cuff devices and wrist-cuff devices should not be used for home BP measurements. The arm-cuff should be placed at the heart level. A soft arm-cuff is usually recommended. In subjects with standard proportions, a hard plastic cuff is also applicable. Instruction about standard measurement conditions is indispensable, and should include such points as keeping the arm-cuff at the heart level, extension of the lower arm, and relaxation of the arm by means of a supporting pillow. In subjects with excessively thick or thin arms, large cuffs and small cuffs, respectively, should be used. The non-dominant arm is usually used for home measurements, but when an apparent BP difference is observed between the arms, the arm showing the higher BP should always be used for home measurements.

3. Validation of the Device

The pressure sensors incorporated into recent devices for self-BP measurements are semiconductor sensors. The linearity, durability, and accuracy of these sensors are superior to those of the distortion sensors used previously. The older pressure sensors required validation with standard mercury column manometers, but this procedure is not necessary with semiconductor sensors. Indeed, there is no standard mercury column manometer available for the clinical setting. The mercury column manometers used in clinical practice are subject to several factors that may disturb their accuracy. Thus, validation of semiconductor pressure sensors with an inaccurate mercury column manometer sometimes leads to untoward results.

There are two reasons for validation of the device. The first is to confirm whether the type of device is clinically applicable for BP measurements in the general population, and the other is to confirm whether the device can accurately and properly measure BP in individuals.

Previously, validation of a device was performed by simultaneous measurement using a mercury column manometer and the device itself, both of which were connected to the arm-cuff of the device by a Y-tube, followed by determination of the difference between the two readings. However, this method has recently encountered a serious problem. Several guidelines have specified the deflation rate of the cuff pressure to be 2–3 mmHg/s or beat (*19*). However, recent cuff-oscillometric devices deflate by 5–7 mmHg/s or beat. In the cuff-oscillometric method it is possible to deflate rapidly, since SBP and DBP are determined by an algorithm that calculates BP from the increase and decrease in cuff pressure. Such rapid deflation is considered to be one of the advantages of the device, because of the lower physical burden for subjects. Therefore, simultaneous measurement using the auscultation method with a mercury manometer causes a large systematic error in the determination of SBP and DBP; the measured SBP is lower and the measured DBP is higher during rapid deflation than during standard deflation. Thus, it is difficult to measure BP effectively using the simultaneous method. To overcome this problem, the device should incorporate a calibration mode, wherein the deflation speed is limited to 2–3 mmHg/s or beat. However, the change in deflation speed makes it necessary to use a different algorithm to determine SBP and DBP. At present, therefore, it is impossible to apply the simultaneous method to validate these devices.

The currently recommended method is the sequential method. In this method, measurements with the standard auscultatory method and the device are performed sequentially on the same arm, and the difference of BP between the two methods is calculated. The International Protocol for the validation of BP measuring devices in adults proposed by the European Society of Hypertension recommends this method, with the preferred number of measurements being 4 by auscultation and 3 by the device (*20*). This guideline also recommends at least 2 measurements by auscultation and 2 measurements by the device for validation in the practical setting.

Simultaneous measurement using bilateral arms is superior from the viewpoint of simultaneity, but the BP difference between the right and the left arms affects the results of validation. To overcome this problem, a simultaneous measurement using both arms should be performed, where initially the auscultatory method is used on one side and the tested device on the other side. Then, each measurement is done using the contralateral arm. The differences in measurement by auscultation and by the device are averaged. At least two simultaneous measurements are necessary to cancel the BP difference between arms.

When a wrist-cuff device is used, validation by the simultaneous method using both arms or by the sequential method using one arm is indispensable.

Validation as to whether a type of device is clinically applicable for BP measurement in the general population is done in specialized institutes for that purpose, and should include a certain number of subjects with a wide range of BP and age. The auscultatory method may remain unchanged as the gold standard, although the issue of the subjectivity of auscultation will also remain. In the future, an international standard device will be developed, and validation will be performed by the difference between the standard device and the tested device. In general practice, however, validation of whether a device can accurately and properly measure BP in individuals will be done using the auscultatory method. In recent years, 10 million automatic devices for self-BP measurement have been produced annually in Japan, and a total of 30 million devices have already been distributed. Therefore, it is a serious clinical and epidemiological issue whether a home BP measurement device can provide an individual's BP accurately, and thus the validation of the device is very important for clinical practice as well as for public health. However, the validation of the device is not necessarily done properly in the medical setting because of an absence of proper information on the validation procedure and a lack of financial backing for validation from medical insurance. This Working Group emphasizes the need for financial support from medical insurance for the validation of automatic devices.

In the British Hypertension Society (BHS) guidelines for the validation of automated devices, devices for which a high proportion of BP measurements differ from auscultation by less than 5 mmHg are rated highly (*21*). Thus, a device that differs from auscultation by less than 5 mmHg is evaluated as accurate and suitable for a particular subject. However, it is uncertain whether this device is also suitable for other subjects unless a validation has been done. The AAMI states that a particular type of device is clinically applicable for self-BP measurements when the mean difference from

the auscultatory method is less than 5 mmHg and its SD is less than 8 mmHg (*17*). Thus, in each subject a maximal 13 mmHg (*mean+SD*) difference from the auscultatory method is approved on the basis of this standard, suggesting that devices conforming with the AAMI guidelines do not necessarily provide a proper BP value in individuals. It should be emphasized again that there are different purposes for validation: applicability to the general population and suitability of the device for an individual. In this guideline, we recommend a device for practical use when the difference in BP from the auscultatory method is less than 5 mmHg in a particular subject. It is a matter of course that the device should be adapted to the AAMI standards and BHS guidelines.

Home measurement devices should be validated before use, and at regular intervals during use.

Recommendation 3

Devices for home BP measurement should be adapted to the AAMI standards and the BHS guidelines. Furthermore, the difference between the auscultatory method and the device should be within 5 mmHg in each individual. The home measurement device should be validated before use, and at regular intervals during use.

4. Procedure

ABPM provides BP values measured every 15 to 30 min as a function of time and of daily activity on a particular day, and thus control of measurement conditions is not appropriate for ABPM. Conversely, home BP measurement characteristically provides BP values under controlled conditions that should remain as stable as possible for a long period. The JNC-VI and -7, the 1999 WHO-ISH Guidelines, the ESH-ESC Guidelines, and JSH Guidelines 2000 emphasized the clinical significance of self-measured BP at home. However, these guidelines do not refer to standardization of the measurement procedure for home BP. The most authorized guideline for self-BP monitoring, from the International Consensus Conference 2000, only stated very briefly that self-BP should be measured at the heart level after 5 min of rest (*22*). The clinician's manual on the self-monitoring of BP by Pickering, the only manual for home BP measurement, emphasizes that home BP values change markedly with alterations in measurement circumstances, but does not specify how, when, and where home BP should be measured (*23*). Other guidelines, including JNC-VI (*8*), JNC-7 (*9*), the WHO-ISH (*10*), the ESH-ESC (*11*), the American Heart Association (*24*), the American College of Physicians (*25*), the Canadian Coalition for High Blood Pressure Prevention and Control (*26*), the First International Consensus Conference on Self-Blood Pressure Measurement (*27*), and the European Society of Hypertension Recommendations for Conventional, Ambulatory and Home Blood Pressure Measurement (*20*), do not specify standards for the measurement procedure. All guidelines recommend measurement of home BP in the morning and in the evening. In the American Society of Hypertension *Ad Hoc* Panel, Pickering recommended measurement of BP at home on holidays as well as on working days, but he did not refer to the timing of the daily measurements (*28*).

This is an appropriate time to review the characteristics and the purpose of home BP measurement. All the guidelines and recommendations emphasize the good reproducibility and reliability of home BP. These characteristics arise from the ability to make multiple measurements over a long period: Home BP measurements are suitable for an assessment of the effect and duration of action of antihypertensive drugs and for the diagnosis of intractable hypertension and white coat hypertension. Furthermore, morning hypertension has recently been attracting attention as a risk factor for cardiovascular morbidity and mortality. Home BP measurement is the only practical method to obtain BP in the morning. Recently, white coat normotension (reversed white coat hypertension or masked hypertension) has also been attracting attention in relation to morning hypertension. This concept is defined as a normal clinic BP (<140/90 mmHg) with a home BP indicating hypertension (≥135/85 mmHg). This white coat normotension, determined by the home BP in the morning, is mediated at least in part by an insufficient duration of action of antihypertensive drugs.

From this viewpoint, if the reproducibility and reliability of home BP measurements could be increased, the clinical significance of these measurements would improve extensively. However, at present no standard exists for the measurement procedure of home BP.

As mentioned in the previous chapter, the most important feature of home BP measurement is long-term and repetitive measurement using arm-cuff devices under controlled conditions. In this respect, compliance or adherence with home BP measurement is a very important issue. Thus, the measurement of BP *per se* should be paramount. However, to increase the clinical significance and comparability of home BP measurement as a component of clinical decision-making, establishment of a standardized procedure for home BP measurement is essential.

The home BP should be measured at least twice daily, in the morning and in the evening. This is a requirement of almost all existing guidelines.

4-1. Morning-Measurement Procedure

In this guideline, the morning is defined as the time within a few hours after waking, *i.e.*, the time between waking and 10:00 AM. The Working Group, first of all, recommends that measurements should be performed within 1 h after waking. This condition is not necessarily strict enough. However, the most important point in home BP measurement is that subjects measure their own BP at home for a long period. Consequently, strict regulation of the timing of

measurements may disturb compliance or adherence with home BP measurements. The period within 1 h after waking includes several potential factors modifying BP, and thus the several conditions mentioned below must be considered. (In shift workers, 1 h after waking is not necessarily the morning. In this case, the timing of 1 h after waking may be kept as a condition, but the measurement time must be recorded.)

1) After Micturition

In general one urinates soon after waking. Before micturition, extension of the urinary bladder elevates BP, and after micturition BP decreases (*29*). The measurement condition of micturition in the morning after waking ensures a consistent physiological background.

2) Sitting Position with 1–2 min of Rest

A sitting position is the common position for BP measurement in all existing guidelines. In Japanese people, a sitting position includes cross-legged sitting or upright sitting, and in this guideline the sitting position depends on one's usual custom. When a sitting position is not available, measurement in a recumbent position is also permitted.

In general, many guidelines recommend 5 min of rest before measurement (*19*, *20*). However, this guideline proposes a more practical and generous condition to maintain compliance with home BP measurements, that is, that measurement be made after 1–2 min of rest.

3) Before Taking Antihypertensive Drugs

One of the most important purposes of home BP measurement is evaluation of the duration of the antihypertensive effect of drugs. Morning BP measurement before taking the next dose of an antihypertensive drug represents a "trough" measurement. Evaluation of the trough effect allows definition of the duration of action of drugs (*30*).

Recently, morning hypertension has been attracting attention, and some antihypertensive drugs are administered just after waking to control morning hypertension. In such cases, BP measurement before drug ingestion is recommended, although measurement 5–10 min after drug ingestion is also permitted.

4) Before Breakfast

Dietary routine affects BP most extensively among the daily habitual behaviors. BP generally increases during a meal and decreases after the meal. To exclude such variability, BP measurements before breakfast are recommended.

4-2. Evening-Measurement Procedure

Controlling the timing of the evening measurement is rather difficult when compared with that in the morning. Although clinical pharmacology studies to determine the effect or duration of the action of a drug often require that measurements take place before supper, before drinking alcohol, before taking a bath, or before taking a drug, in normal daily life in Japan it is practically impossible to request that such conditions be followed.

To improve compliance with measurement of home BP, only a single condition, that of measurement just before bedtime, is proposed. In general, Japanese men take an alcoholic beverage and a bath at about this time. These factors usually decrease BP. In the Ohasama study, where evening BP was measured under the above-mentioned condition, BP in the morning was a few mmHg higher than that in the evening. This was especially true in the hypertensive population of Ohasama, for whom the difference in SBP was 10–20 mmHg (*31*). When a long-acting antihypertensive drug is administered once in the morning, the BP in the evening corresponds to near the peak effect. Recently, the ratio of the morning effect to the evening effect has been used as an indicator of the duration of action of the antihypertensive effect, the morning *vs.* evening (*M/E*) ratio. This concept is derived from the trough *vs.* peak (*T/P*) ratio obtained from ABPM (*30*).

4-3. Measurement at Midnight

Recently, a new home BP device incorporating an integrated circuit memory and timer has been developed (HEM 747 IC-N, Omron, Kyoto, Japan) (*7*). This device is being used in a large-scale interventional study in Japan using home BP measurements and the Internet, known as the Hypertension Objective Treatment Based on Measurement by Electrical Device of Blood Pressure (HOMED-BP) study (*32*). In this study, the devices are preset to work automatically at 2:00 AM, since the nadir of the nocturnal BP was observed at around 2:00 AM in the population of the Ohasama study. Using this device set to work once at 2:00 AM, the subject can recall after waking the quality of sleep during the measurement. On the other hand, it is impossible to evaluate the quality of sleep during ABPM, since one cannot define the quality of sleep during measurements every 30 min. Although determination of nocturnal BP by home measurement devices is not yet widespread, this procedure is significant for determination of the circadian BP variation and the nocturnal BP level.

4-4. Measurement in the Workplace or during Daily Activities

Although portable devices allow self-measurement of BP in the workplace or during daily activities, in practice such measurements are difficult. In the future, development of accurate and reliable wrist-cuff devices may permit BP measurement under stressful circumstances. The importance of measurements in the workplace or under stressful circumstances was emphasized by Pickering (*13*). Elevation of BP in the workplace or under stressful conditions mediates white coat normotension or masked hypertension.

Recommendation 4

Home BP should be monitored under the following conditions:

a: In the morning within 1 h after waking, after micturition, sitting after 1–2 min of rest, before drug ingestion, and before breakfast.

b: In the evening just before going to bed, sitting after 1–2 min rest.

5. Frequency and Duration of Measurements

There is much difference of opinion concerning how many times home BP should be measured on each occasion and for how long home BP should be measured. The answers to these questions depend on the purpose of the home BP measurement. Thus, in this guideline, the most generalized method taking into account the convenience of subjects and the need to obtain useful information for clinical decision-making is proposed.

The guidelines of the International Consensus Conference for Self-Blood Pressure Monitoring (2000) recommended measurements of self-BP in the morning and in the evening, twice on each occasion, for 3 working days a week (a total of 12 measurements a week), but stated that the measurement frequency can vary depending on the indication and the objective for which the measurement is used (*22*). In practice, the measurement frequency can be modified depending on the severity of hypertension and the treatment situation—for example, treatment before prescription, during prescription, or during a change of medication. Pickering stated that a lower measurement frequency is permitted when the BP is stable and well-controlled (*23*). He preferred that in a newly diagnosed patient 3 consecutive readings should be obtained both in the morning and in the evening on 3 days a week for at least 2 weeks (36 measurements over 2 weeks) (*23*). He also stated that frequent readings are needed when a new medication is being prescribed or when the dosage is being changed.

As a tool for clinical pharmacology studies, Mengden *et al.* recommended that at the commencement of the home measurements there should be an initial 7-day measurement period with 2 measurements in the morning and 2 measurements in the evening, respectively, at pre-stipulated times (*27*). The measurements from the first day should be excluded from the statistical analysis. The average of these values (24 measurements over 6 days) is taken as the reference parameter in the dose-titration phase (*27*). Home BP measurements may be performed 1 day a week if hypertension is controlled. If the treatment is changed, the average of the home BP measured over 2 weeks should be used to assess the treatment effect.

Almost all guidelines or manuals recommend two consecutive measurements on each occasion. This recommendation is based on the evidence that regression to the mean during consecutive measurements on each occasion is frequently observed after long-term monitoring (*33*). de Gaudemaris *et al.* reported that even in normal subjects the first measurement was the highest and the third measurement was the lowest among consecutive measurements on a single occasion; the difference was 3/2 mmHg (*34*). In contrast, both the Ohasama study (*14*, *31*) and the HOMED-BP study of Japan (*35*) recommend at least one measurement in the morning and in the evening, respectively. The reasons for this recommendation are as follows.

1. Since home BP must be measured over a long period, a minimal demand on subjects, *i.e.*, at least once on each occasion, may improve compliance with measurement. A permanent requirement for multiple (2 or more) measurements of home BP on each occasion for a long period creates too large a burden for subjects, which lowers compliance.

2. Regression to the mean also appears during long-term measurement of the home BP. In the Ohasama study, it has been confirmed that the home BP level reaches the subject's inherent home BP level after 2 days of measurement in normotensive subjects, whereas it takes 5–7 days to reach the subject's inherent home BP level in hypertensive subjects (*36*).

3. If the measurement frequency is not regulated, subjects will measure their own BP with a voluntary measurement frequency—for example, 3 consecutive measurements on 1 morning and only 1 measurement on the following morning. Consequently, practitioners would be unsure of which measurements should be evaluated for clinical decision-making.

4. Consecutive and multiple measurements of home BP on each occasion provide different measurement results, which may cause confusion in some subjects. Generally, subjects tend to value the lowest BP obtained from multiple measurements. As a result, the lowest BP value may be reported to the practitioner, introducing selection bias.

5. Ideally, home BP in the morning or in the evening would be evaluated as a mean value averaged for a certain period. However, averaging procedures are very time-consuming, and neither subjects nor practitioners tend to work constructively at this procedure, such that there is often a selection bias in the values chosen for evaluation such that not all values can be evaluated.

6. Use of the first measurement on each occasion is a common procedure in many patients/subjects of many institutes or clinics, and thus averages of the first measurement of the home BP obtained in the morning and/or in the evening for a certain period are comparable among patients/subjects from many institutes or clinics. Furthermore, it has been confirmed that a single measurement of home BP in the morning has a higher predictive value for the prognosis of cardiovascular disease than the average of two clinic BPs, and that averaging the first measurement of home BP in the morning for 21 days has a much higher predictive value than clinic BP (*37*), suggesting that the clinical significance of home BP, even if obtained from one measurement on each occasion,

can be increased by averaging multiple measurements over a long period.

However, this guideline does not deny that multiple measurements on each occasion may be of value. The difference among home BPs measured consecutively on a single occasion includes information on BP variability or on the defense reaction to self-measurement (a kind of white coat effect). Such variability is also a characteristic of BP in individuals. Therefore, as mentioned in the next section, multiple home BPs measured on each occasion should all be recorded without selection. In the present situation, each practitioner instructs subjects differently as to the number of measurements on each occasion, and as a result the method of evaluating home BP may differ among practitioners. If we wish to record population levels of home BP, as well as individual levels for the purpose of clinical decision-making, the first measurement on each occasion might provide the most generalizable information. As a matter of fact, most epidemiological surveys based on self-measurement, including the Pressioni Arteriose Monitorate e Loro Associagiani (PAMELA) study (*38*), the Tecumseh study (*39*), and the Ohasama study (*37*), used one measurement on each occasion. However, as Stergiou *et al.* emphasized, regression to the mean on each occasion persists after long-term measurement (*33*). Therefore, the first measurement on each occasion may be higher than the average of multiple measurements on each occasion, even after long-term monitoring. Although it is important to recognize this fact, the Working Group recommends use of the first measurement on each occasion as a standard for evaluation of home BP, since it is convenient for subjects and results in good compliance and good equivalence for comparison (*13*). In addition, every measurement on each occasion, as well as the long-term average of the first measurement on each occasion, should also be evaluated as a matter of course.

It is not necessary to specify the duration of home BP measurements. Since home BP measurements characteristically provide long-term BP information, it is recommended that hypertensive subjects measure their BP once in the morning and once in the evening for a lifelong period, which may bring about improvements in drug compliance and self-management of health. In healthy normotensive subjects or in prehypertensive subjects, periodic measurements—for example, once a week or once every several weeks—are recommended. However, there is a concern that insisting on frequent self-measurement may sometimes disturb compliance with measurement.

On the other hand, regulation of the number and duration of measurements is indispensable for clinical pharmacology studies. The following recommendations for the number of measurements and the period of measurement needed for clinical pharmacology are based on data obtained from a total of 214 subjects from the general population of the town of Ohasama and in a hypertensive clinic in Japan (*36*). In that study, the reproducibility of home BP was examined. The difference between the home BP averaged over 5 days of an 8-day run-in period without placebo (the initial 3 days of measurement were excluded), and that averaged over 5 days between the 17th and 21st days of the placebo period, was $-1.9\pm7.0/-1.4\pm4.8$ mmHg (SBP/DBP), suggesting that there was good reproducibility and no placebo effect in the measurement of home BP.

Recommendation 5

1. Home BP should be measured at least once in the morning and once in the evening.
2. Home BP should be measured for as long as possible.
3. In clinical pharmacology studies, home BP should be measured over at least 5 days during a 7-day run-in period in subjects with mild-to-moderate hypertension (SBP$\leqq$179 and DBP$\leqq$109 mmHg in casual-clinic measurement). The run-in period may be 1 to 2 weeks depending on the patient's condition. In subjects with severe hypertension, treatment should generally be started without home BP measurements, although 1 to 3 days of measurement of home BP may be performed according to the judgment of the practitioner.
4. Home BP should be measured at least 3 days a week during periods when hypertension is well controlled.
5. Home BP should be measured at least 5 days a week when a medication is changed.

6. Documentation

All measurements of home BP should be documented without selection. This should help to prevent overestimation or underestimation of the home BP values. Mengden *et al.* reported that, among subjects who measured home BP, excess reports, insufficient reports, and even reports of phantom records were frequently observed (*40*). Therefore, the best way to rule out biases is to use equipment incorporating an integrated circuit memory. However, a personal computer is currently needed to read out the memory, and thus this function does not necessarily work efficiently in general practitioner. Furthermore, discrimination among the data from multiple users is not possible with the present form of the device, and thus a separate device is required for each user, and each user must be informed that the device is only for their personal use.

Among other methods to exclude selection bias, devices with a printer are sometimes useful, although selection bias cannot really by excluded using a printer, since subjects cannot be relied upon to consistently print all results. Therefore, subjects' documentation on worksheets still remains the most popular method to record home BP values. In this case, subjects must be instructed that all measurements, together with the pulse rate and the date and time of the measurement, should be documented.

Recently, many pharmaceutical companies have begun to distribute worksheets for the recording of home BP, although

the formats of these worksheets are inconsistent. For example, some of these forms ask subjects to record the trend of BP, and others ask for numerical information. Both types of information are useful for clinical practice, but recording of numerical information is more important. The worksheet should include spaces for the year, month, day, clock time, BP, and pulse rate. Spaces for morning values, daytime values, and evening values should also be included. A reference column is useful to record episodes of daily life. A duplication function is required on the worksheets so that the information can be available both at clinics/institutions and for subjects.

Recommendation 6
All home BP measurements should be documented without selection, together with the date, time, and pulse rate. Use of devices with a printer or an integrated circuit memory is sometimes useful to rule out selection bias.

7. Totaling

Before evaluation of home BP values, totaling of measured and documented values is necessary. As recommended in section 5, the home BP should be measured at least once in the morning and once in the evening for a long period. The home BP should be evaluated on the basis of the mean value and its SD, averaged for a certain period. The home BP in the morning and that in the evening may have different clinical significance because of the different measurement conditions, such as physical activity and environmental factors. Therefore, the home BP in the morning and that in the evening should be totaled and evaluated separately. In the process of totaling, the issue of how many times the home BP should be measured on each occasion arises again. The measurement frequency on each occasion may differ among clinics/institutes and individuals. The information common to all circumstances or individuals is the first measurement on each occasion. Thus, as a tool for clinical decision-making, clinical study, or clinical epidemiology, the mean of the first measurement on each occasion averaged over a certain period would be the most common value and the best for comparison among institutes or individuals. However, each BP value among multiple measurements on each occasion may also have clinical significance. Therefore, all of these measurements must be documented and evaluated by the practitioner. A regression to the mean during multiple measurements of home BP is generally observed in the usual measurement setting. From this viewpoint, the evaluation of all measurements is necessary, whereas for the evaluation of home BP level as a tool for clinical decision-making, a totaling of home BP under standardized measurement conditions is necessary—in other words, the mean of the first measurement on each occasion averaged over a certain period. Such totaling is applicable to clinical epidemiology as well as to daily practice, and as a result, data obtained in daily practice is comparable with data obtained in clinical epidemiology. The period over which the home BP should be averaged depends on the purpose of the measurement. Averaging measurements over 2 to 4 weeks is the most common and convenient method as a unit for evaluation of home BP, since patients usually visit the clinic every 2 to 4 weeks. In clinical pharmacology studies, averaging over at least 5 days is necessary (*36*). Day-by-day variability of home BP is believed to have a predictive value for cardiovascular disease risk, and thus SD should be calculated simultaneously. The home BP in the morning and in the evening must be evaluated separately.

Recommendation 7
The home BP in the morning and that in the evening should be averaged separately for a certain period. The first measurement on each occasion should be used for totaling. Day-by-day variability should be presented as SD.

8. Evaluation

The JNC-VI (*8*) and -7 (*9*), the WHO-ISH Guidelines (*10*), the ESH-ESC 2003 Guidelines (*11*), and the JSH 2000 Guidelines (*12*) all provide reference values for home BP. These reference values were introduced on the basis of the Ohasama study (*41*), the PAMELA study (*38*), and the International database (*42*). The Ohasama study is the only one to provide reference values based on a longitudinal prospective cohort study (*14*, *37*). On the basis of such studies or analyses, most guidelines propose that hypertension be defined as 135/85 mmHg and over, and normotension as less than 125/80 mmHg (*8–11*). The JSH 2000 guidelines define hypertension as 135/80 mmHg and over, and normotension as less than 125/75 (*12*). These values may be revised according to the results of future large-scale observational studies, although the values accepted at present are not expected to differ greatly from such future revised values. Therefore, the reference values of home BP are now considered to have reached a consensus.

Recommendation 8
Home BP values averaged for a certain period indicate hypertension when 135/80 mmHg and over (JSH 2000) and definite hypertension when 135/85 mmHg and over (JNC-VI and -7). Normotension is defined as less than 125/80 mmHg (WHO-ISH 1999) and definite normotension is defined as less than 125/75 mmHg (JSH 2000).

9. Conclusion

Home BP measurements are indispensable for the improvement of management of hypertension in medical practice as well as for the recognition of hypertension in the population. Therefore, establishment of self-measurement of BP is the first priority, and for this purpose it is not necessarily expect-

ed that strict measurement conditions will be set. However, the presence of a standard for home BP measurement may be convenient and useful for practitioners as well as for subjects. This guideline for home BP measurement is intended to instruct patients and subjects in the general population on how to measure BP at home. As a result, home BP measurements based on this guideline may provide a shared basis of information for clinical decision-making.

Fortunately, international reference values are now established. However, the treatment goal for home BP level has not yet been established. At present, the normotensive value of home BP is set at the level of 125/75–80 mmHg. This value is approximately equivalent to a casual-clinic BP level of 140/90 mmHg. Therefore, it seems that a value of less than 125/75–80 mmHg should be the goal for home BP. However, the setting of the goal for home BP must be based on the results of large-scale intervention studies. Among such studies, the Treatment of Hypertension according to Home or Office Blood Pressure (THOP) study (*43*) and the HOMED-BP study (*35*) are ongoing. Although such reference values have been proposed in several guidelines, standardization of measurement conditions has not yet been achieved. For example, in the Tecumseh study the measurement frequency was once in the morning and once in the evening, and the measurement duration was 7 days (14 measurements in total) (*39*). In the PAMELA study (*38*), the home BP was measured once in the morning and once in the evening on only 1 day (2 measurements in total). In the Ohasama study (*37*), the home BP was measured once in the morning and once in the evening for 21 days (42 measurements in total). In the THOP study, home BP was measured 3 times in the morning and 3 times in the evening for 7 days (*43*), while in the HOMED-BP study home BP was measured once in the morning and once in the evening for at least 5 days during the run-in period, and an average of these measurements was used as a reference value (*35*). In all studies except the HOMED-BP study, the measurement procedure was not controlled. In the HOMED-BP study, the home BP in the morning was measured within 1 h after waking, after urination, in the sitting position after a 1–2 min rest, before drug ingestion, and before breakfast, and in the evening before going to bed in the sitting position after a 1–2 min rest. Because of the great variety of measurement procedures among studies, it seems impossible to compare the results among them. In the future, internationally standardized measurement procedures will be established by consensus, and reference values on the basis of such standardized procedures will be proposed. However, common to all these measurements of home BP values, including those in past databases, is the use of the first measurement on each occasion. Therefore, the common information on home BP, which is available for retrospective analysis, prospective analysis, and even meta-analysis, is the mean of the first measurement on each occasion averaged over a certain period. For this reason, this Working Group recommends that home BP should be evaluated by the mean of the first measurement in the morning and in the evening, respectively, averaged for at least 5 days.

Standardization of the measurement procedure may elevate the position of home BP measurements in the practice of diagnosing and treating hypertension, and as a result, home BP measurements may bring an improvement of the accuracy of screening for hypertension, an improvement in drug compliance, and more accurate assessment of BP control during treatment. Home BP measurements under such controlled conditions are expected to have a beneficial effect on the economics of the diagnosis and management of hypertension.

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特集：早朝高血圧――重要性とその管理――

Q&A 早朝高血圧の臨床的意義とその具体的治療法

（回答）国立循環器病センター 高血圧腎臓内科部長 河野雄平（かわの ゆうへい）

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Q&A 早朝高血圧の臨床的意義とその具体的治療法

（回答）国立循環器病センター 高血圧腎臓内科部長 河野雄平（かわの ゆうへい）

――早朝高血圧は，なぜ悪いのでしょうか？

血圧が覚醒，起床とともに急に上昇することはよく知られています．朝の血圧上昇はモーニング・サージと呼ばれますが，これが著しい高血圧の患者さんは少なくありません．また，そのような例の多くは，朝が他の時間帯より明らかに高い早朝高血圧を呈します．

早朝高血圧が臨床的に問題となるのは，起床後の数時間は脳卒中や心筋梗塞が最も多い時間帯であり（図1），朝の血圧上昇がこれらの心血管事故の発症に重要な役割をもつと考えられるからです[1,2]．また，早朝高血圧を呈する患者さんの外来血圧は比較的低いことが多く，診察室での測定では日常の血圧を過小評価することになります．病院での血圧は正常で家庭血圧や24時間血圧は高い病態は，逆白衣高血圧や仮面高血圧と呼ばれますが，臓器障害が進行すると考えられます．

――早朝高血圧は，どのようにして診断すればよいでしょうか？

血圧のモーニング・サージの評価には，24時間血圧モニタリング（ABPM）が最も適しています．しかし，朝と夜の家庭血圧の測定によっても可能で，実用上はこちらが勧められます．家庭血圧は朝が夜より少し高い場合が多く，我々の検討では，降圧薬を服用していない高血圧患者の朝の家庭血圧は夜より平均で5/3 mmHgほど高値でした[3]．

早朝高血圧の診断には，朝の血圧が高いことと，またそれが他の時間帯より高いことを

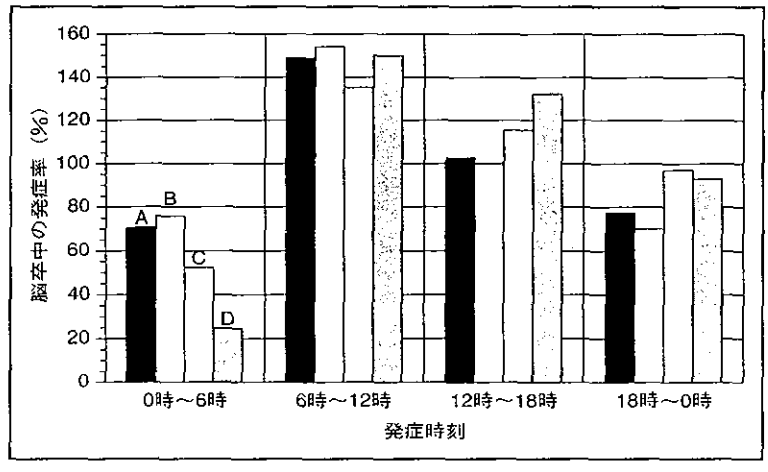

図1 脳卒中の時間帯による発症頻度のメタアナリシス（文献2：Elliott WJ, 1998による）
A：全脳卒中，B：虚血性脳卒中，C：出血性脳卒中，D：一過性脳虚血発作．

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確認することが重要と思います．まだ統一された診断基準はありませんが，家庭血圧による高血圧の基準が 135/80 mmHg ですので，朝の血圧がこれ以上で，しかも夜より高いことが目安になるでしょう．朝の家庭血圧が 140/90 mmHg 以上で夜より 10 mmHg 以上高ければ，明らかな早朝高血圧と考えられます．

――― 早朝高血圧の原因は，何でしょうか？

血圧の日内変動は種々の因子の影響を受けますが，交感神経系が最も重要と考えられます．覚醒，起床に伴う交感神経の活性化は生理的現象でもありますが，血圧上昇や心拍数増加，血液凝固能亢進をもたらします[1]．これらはプラーク剥離や動脈瘤破裂，心筋虚血や不整脈，血栓形成に働き，心血管事故発症の誘因になると考えられます．また，朝の急な血圧上昇には，夜間からの α 受容体の感受性亢進も関与しています．

生活習慣や環境因子によって早朝高血圧が生じることがあります．アルコールやストレス，寒冷などです．また，しばしば見られるのが，降圧治療の結果としての早朝高血圧です．すなわち，昼や夜は降圧薬により下がっているが朝のコントロールが不充分な場合です．しかし，早朝高血圧の原因を特定できない患者さんも少なくありません．

――― 早朝高血圧に対する生活上の注意は，何かありますか？

種々の生活習慣が血圧の値や変動に影響しますが，アルコールが早朝高血圧の原因となることがあります．アルコールは血圧を上げて高血圧の原因になると考えられていますが，実際には夜の血圧下降と朝の血圧上昇をもたらし，朝と夜の血圧差を増大させます[5,6]（図 2）．したがって，早朝高血圧を示す患者さんが飲酒者であれば，飲酒制限の指導が望まれます．ただし，アルコールによるモーニング・サージは朝の血圧上昇より飲酒後の血圧低下による部分が大きいので，アルコール制限だけで朝の血圧を正常化させるのは困難かもしれません．

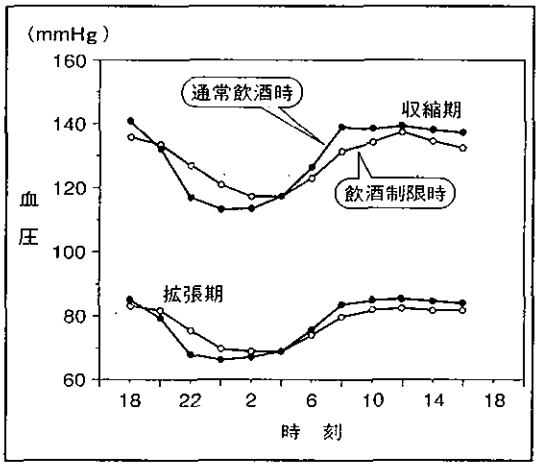

図 2　高血圧患者におけるアルコールの血圧日内変動への影響（文献 6：河野雄平，1998による）

ストレスや行動様式も血圧変動に関係します．患者さんが起床後の時間を慌ただしく過ごしていないか尋ねて，そうであれば余裕のある行動を勧めるのがよいでしょう．朝の血圧は，勤務日より休日のほうが低いことがしばしば観察されます．

また，早朝高血圧を呈する例では，朝の家庭血圧の測定状況にも注意を払うべきでしょう．例えば，寒い部屋での薄着や腕まくりしての測定や，排尿前で膀胱が充満した状態では，血圧が高くなります．家庭血圧では早朝高血圧なのに，ABPM ではモーニング・サージは明らかでないことがあります．朝の家庭血圧は，起床後なるべく早く，食事や服薬の前に測ることが勧められますが，排尿を済ませて少しゆっくりして測定するほうがよいでしょう．

――― 早朝高血圧に対する降圧薬の使い方を教えて下さい．

早朝高血圧に対する薬物治療においては，

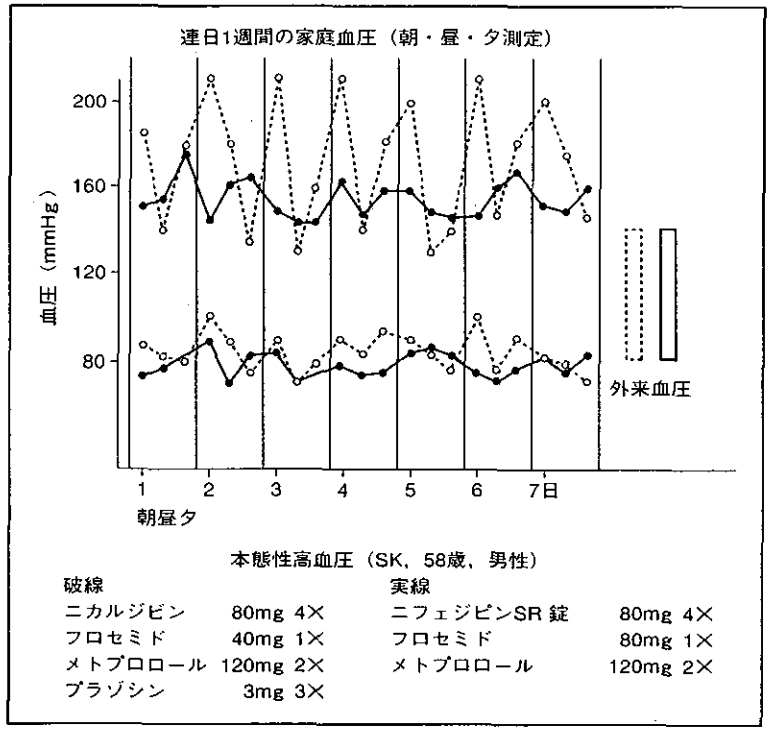

図3　短時間作用性降圧薬より長時間作用性薬剤への変更により早朝高血圧が改善した1例
（文献7：阿部　仁 他，1987による）

降圧薬の薬効持続時間と作用機序に注意する必要があります．日常診療においてしばしばみられるのが，使用した薬剤の持続時間が充分でないため，昼や夜は低いが朝は高い場合です．短時間作用性の降圧薬，とくにカルシウム拮抗薬は，1日3回食後に服用しても起床時には薬効が消失し，著しいモーニング・サージの原因になることがあります[7,8]（**図3**）．このような例では長時間作用性の薬剤に変更すべきであり，それによって朝の血圧はかなりコントロールできるでしょう．

しかし，長時間作用性の降圧薬でも，持続時間は薬剤によって異なります．1日1回朝の服薬では，翌朝には薬効が減弱してモーニング・サージの原因となることがあります．この可能性があれば，より長時間作用性の薬剤に変更する，現在の薬剤を朝と夜に分割投与する，現在の薬剤を夜に服用してもらう，などによって朝の血圧低下が期待できます．夜の降圧薬投与が予後を改善し，また危険性は少ないことは，ニトレンジピンを用いた大規模臨床試験で示されています[9]．

血圧のモーニング・サージには，交感神経系の活動亢進とα受容体の感受性亢進が関与しています．α遮断薬やαβ遮断薬，中枢性交感神経抑制薬は，モーニング・サージを抑制することが示されており，早朝高血圧の治療に有用です[10]．作用時間や副作用の面からは，夜の服薬，あるいは朝と夜の分割投与が効果的でしょう．**図4**に示す例では，α遮断薬ドキサゾシンを夜に追加することにより，早朝高血圧を効果的にコントロールできました．

これらの方法により，モーニング・サージや早朝高血圧の改善が得られると考えられます（**表1**）．しかし，降圧薬の変更や追加によっても早朝血圧のコントロールが困難な場合もあり，そのような例では早朝血圧を厳格

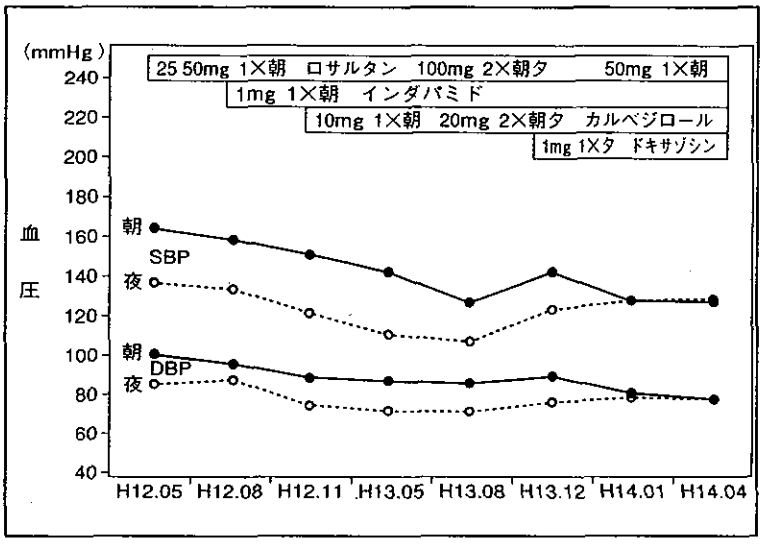

図4　夕食後のα遮断薬により早朝高血圧が改善した1例(文献10：河野雄平，2002による)

表1　早朝高血圧の治療

生活習慣に注意する（飲酒，ストレス）
長時間作用性の降圧薬を用いる
降圧薬を夜に服薬させる
交感神経系の抑制薬を用いる（α遮断薬，αβ遮断薬，中枢性交感神経抑制薬）

にコントロールすると昼や夜の血圧が下がり過ぎることがあります．患者さんの症状や朝と夜の家庭血圧，外来血圧などをみながら，早朝血圧を含めての適正な血圧コントロールができればよいと思います．

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特集　日本人のための降圧療法

総論
2．降圧療法における日本人のエビデンス

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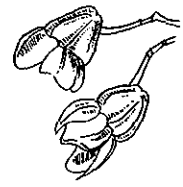
特集 日本人のための降圧療法



総論
2．降圧療法における日本人のエビデンス

又吉哲太郎*1)・河野雄平*2)

降圧療法が高血圧患者の予後を改善することは，大規模な臨床研究により確かめられているが，降圧治療のエビデンスのほとんどは欧米における研究によるものである。わが国では高血圧治療の臨床試験は少なく，エビデンスは乏しいが，NICS-EH(National Intervention Cooperative Study in Elderly Hypertensives)，GLANT (The evaluation Group of Long-term Antihypertensive Treatment)，JATE (Japanese Trial on the Efficacy of Antihypertensive Treatment in the Elderly)，PATE-Hypertension (Practitioner's Trial on the Efficacy of Antihypertensive Treatment in the Elderly Hypertension) などの研究が行われてきた。これらの研究は規模や方法にいくらか弱点があるが，高血圧患者の予後への効果は，Ca (カルシウム) 拮抗薬と利尿薬，ACE (アンジオテンシン変換酵素) 阻害薬の間にあまり差はないことが示唆されている。現在，JATOS (Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients)，CASE-J (Candesartan Antihypertensive Survival Evaluation in Japan)，HOMED-BP(Hypertension Objective Treatment based on Measurement by Electrical Devices of Blood Pressure Study)，HOSP (Hypertension Control Based on Home Systolic Pressure Study) などの無作為の大規模臨床試験が進行中であり，その成果が期待される。

1．はじめに

高血圧が種々の循環器病の主要な危険因子であり，降圧治療がそれらを予防し，予後を改善することはよく知られている。欧米では，1960年代後半から大規模な臨床試験が次々と実施され，多くの知見が得られてきた。一方，本邦では大規模な臨床試験はほとんど行われず，わが国の高血圧治療は欧米の，人種や生活習慣の異なるデータによるエビデンスに基づいてきた部分が大きい。循環器疾患の病態が異なるわが国において，欧米の成績がそのまま適用されるか否かは明らかではなく，日本人におけるエビデンスが求められている。

しかし，規模や方法などにやや弱点はあるものの，わが国でも降圧治療の臨床試験がいくつか行われてきた。また現在，いくつかの無作為の大規模臨床試験が進行中である。ここでは降圧療法における日本人のエビデンスとして，それらの臨床研究について解説する。

2．NICS-EH

NICS-EH (National Intervention Cooperative Study in Elderly Hypertensives)は，1989年に開

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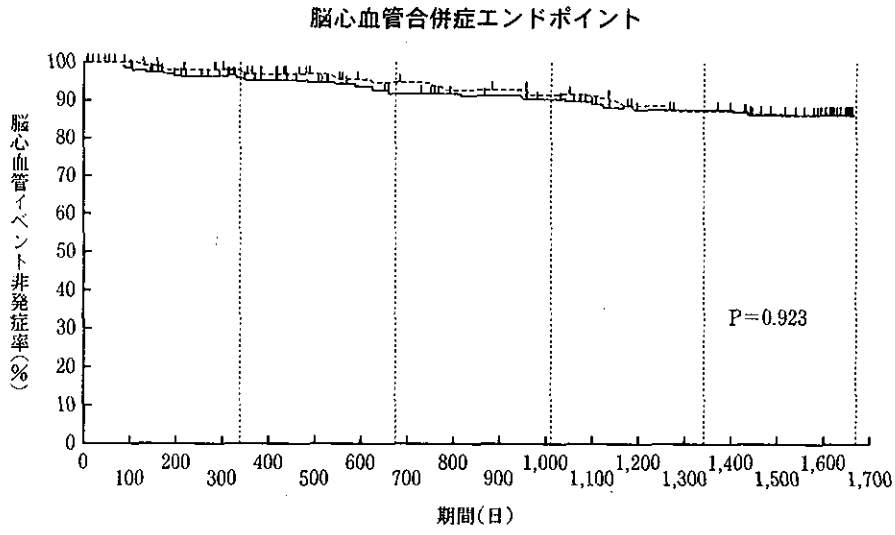

図1　NICS-EHにおけるNicardipine群（N群）とTrichlormethiazide群（T群）の心血管イベントの非発症率

全追跡期間を通して，両群のイベント発症率には差がない．

実線：N群，破線：T群

NICS-EH：National Intervention Cooperative Study in Elderly Hypertensives

（文献1より）

始された多施設二重盲検比較試験である[1]。この研究は，カルシウム(Ca)拮抗薬のnicardipineと，利尿薬のtrichlormethiazideの，老年者高血圧における脳心血管イベントに対する効果を比較したものである。対象は60歳以上で，収縮期血圧(SBP) 160～220mmHg，拡張期血圧（DBP）115mmHg未満の本態性高血圧患者414例で，無作為割付，二重盲検で5年間の追跡が行われた。Nicardipine群（N群）には，nicardipine徐放錠20mgを朝夕2回，trichlormethiazide群（T群）には，trichlormethiazideを2mg朝1回内服させた。効果不十分の場合は，倍量まで増量し，他剤の併用は禁止した。脳心血管イベントの発症をエンドポイントとした。

N群204例，T群210例が解析対象となった。両群とも25%の収縮期高血圧症例を含んでいる。両薬剤群で，ともに同程度に降圧された。（N群：172/94 → 152/85mmHg，T群：173/93 → 153/85 mmHg）。脳心血管イベントは，N群が21例，T群が18例で，発症率はそれぞれ27.8/1,000例/年と26.8/1,000例/年であった。（図1）。年齢，性別で調整したN群の相対危険度は0.973であり，有意差はなかった。脳卒中が両群とも8例ずつ，一過性脳虚血発作がN群のみ4例，心筋梗塞・狭心症は両群2例ずつ発症した。副作用では糖尿病の発症と，血清ナトリウムの低下，尿酸，尿素窒素の上昇がT群でN群に比べて有意に多かった。

この研究は，規模はあまり大きくないが，老年者高血圧の日本人において，Ca拮抗薬と利尿薬の心血管予後は同等であり，副作用は前者が少なかったことを示した点で評価される。

3．GLANT

GLANT（The evaluation Group of Long-term Antihypertensive Treatment）研究は，1990年に開始された臨床試験で，軽症から中等症の本態性高血圧患者を対象に，ACE（アンジオテンシン変換酵素）阻害薬であるdelaprilと，Ca拮抗薬の心血管イベントの予防効果を比較した試験である[2][3]。本試験はオープン試験ではあるが，大規模な多施設共同の臨床介入試験である。対象は，収縮期血