

AMBULATORY BLOOD PRESSURE MONITORING IN THE MANAGEMENT OF HYPERTENSION

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Ambulatory blood pressure measurement (ABPM) is being used increasingly in clinical practice. In recognition of this the British Hypertension Society has published recommendations for the use and interpretation of ABPM in clinical practice,¹ and the European Society of Hypertension has published recommendations on blood pressure measuring devices, including devices for ABPM.² Importantly, the technique has finally been approved for reimbursement in the USA.³ So with worldwide acceptance of the technique, it is timely to reappraise the reasons why ABPM has at last become an indispensable technique for the management of hypertension, and to summarise current recommendations for its use in clinical practice.

WHY IS ABPM SUPERIOR TO CONVENTIONAL BP MEASUREMENT?

The evidence that ABPM gives information over and above conventional blood pressure measurement (CBPM) has been growing steadily over the past 25 years.^{w1} There are a number of obvious advantages: the technique simply gives more measurements than CBPM, and the real blood pressure is reflected more accurately by repeated measurements⁴; ABPM provides a profile of blood pressure away from the medical environment, thereby allowing identification of individuals with a white coat response⁵; ABPM shows blood pressure behaviour over a 24 hour period rather than giving a snapshot of blood pressure; ABPM can demonstrate the efficacy of antihypertensive medication over a 24 hour period rather than making a decision based on one or a few CBPMs confined to a short period of the diurnal cycle⁴; ABPM can identify patients whose blood pressure does not reduce at night-time—the non-dippers—who are probably at high risk⁶; and finally, the technique can demonstrate a number of patterns of blood pressure behaviour that may be relevant to clinical management—isolated systolic hypertension, hypotension, dipping and non-dipping, etc.^{w2} These advantages should have brought ABPM into much wider clinical use many years ago. However, this eventuality was delayed because despite a large body of work showing that ABPM predicted outcome based on surrogate markers of outcome, such as left ventricular hypertrophy and microalbuminuria,⁴ there was insufficient prospective evidence to show that ABPM was superior to CBPM in predicting cardiovascular mortality. There was also concern, particularly in the USA, that the technique, once approved for reimbursement, would be over used in practice.

Evidence is now available from longitudinal studies that ABPM is a much stronger predictor of cardiovascular morbidity and mortality than CBPM,^{7–9 w3 w4} and in the USA, the Centers for Medicare and Medicaid Services (CMS) have recently approved ABPM for reimbursement.³ It would seem, therefore, that there is now international acceptance that ABPM is an indispensable investigation in patients with established and suspected hypertension, and that it should therefore be available to all hypertensive patients. This recommendation none-the-less has important implications for clinical practice. Among the questions that need to be answered are:

- ▶ which ABPM devices should be used?
- ▶ how should the data be presented?
- ▶ how best can doctors and nurses unfamiliar with the technique be educated in its use and interpretation of the data?
- ▶ how can the technique be best used to yield the maximum of information without subjecting patients to unnecessary investigation?
- ▶ what are the financial implications?

CHOOSING AN ABPM DEVICE

The first step in adopting the technique of ABPM is selecting a device, and the first consideration is to ensure the device selected is accurate.^{1 2} It is acknowledged that the accuracy of blood pressure measuring devices should not be based on claims from manufacturers, which can at times be somewhat extravagant, and independent validation with the results published in peer reviewed journals should be demanded.² However, manufacturers often ignore this recommendation and potential purchasers are generally unaware of this requirement, assuming—not unreasonably—that if a product reaches the market place, it will measure blood pressure accurately. Aware of this

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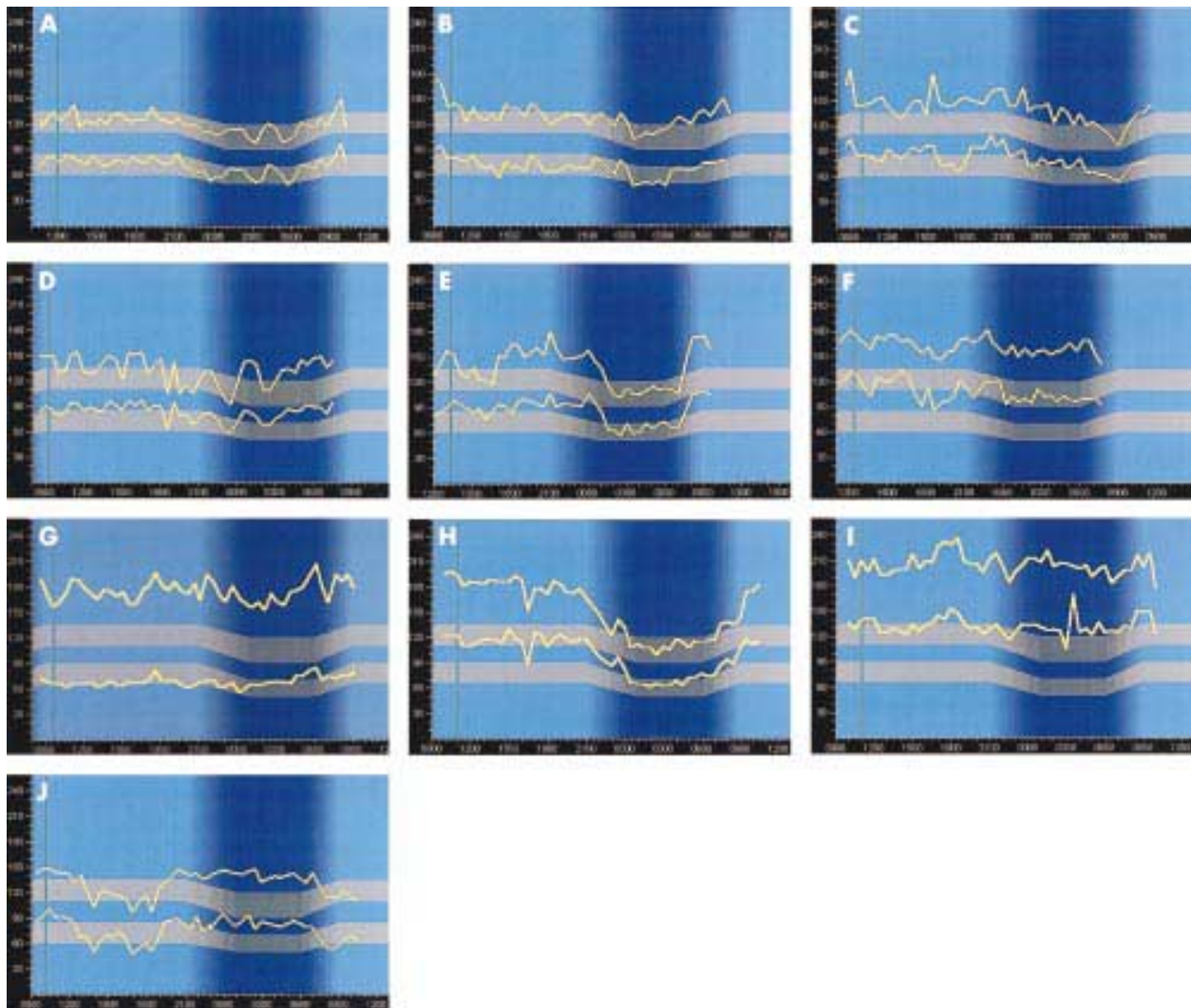


Figure 1 (A) Normal ABPM pattern. On the basis of the data recorded and the available literature (which is the case for all the patterns shown here), the ABPM suggests normal 24 hour systolic and diastolic blood pressure (128/78 mm Hg daytime, 110/62 mm Hg night time). (B) White coat hypertension. The ABPM suggests white coat hypertension (175/95 mm Hg) with otherwise normal 24 hour systolic and diastolic blood pressure (133/71 mm Hg daytime, 119/59 mm Hg night time). (C) White coat effect. The ABPM suggests mild daytime systolic hypertension (149 mm Hg), borderline daytime diastolic hypertension (87 mm Hg), borderline night time systolic hypertension (121 mm Hg), and normal night time diastolic blood pressure (67 mm Hg) with white coat effect (187/104 mm Hg). (D) Borderline systo-diastolic hypertension. The ABPM suggests borderline daytime systolic and diastolic hypertension (135/87 mm Hg) and mild night time systolic and diastolic hypertension (132/81 mm Hg). (E) Moderate systo-diastolic hypertension. The ABPM suggests mild daytime systolic and diastolic hypertension (147/93 mm Hg) and normal night time systolic and diastolic blood pressure (111/66 mm Hg). (F) Severe systo-diastolic hypertension. The ABPM suggests moderate daytime systolic and diastolic hypertension (164/112 mm Hg), severe night time systolic hypertension (157 mm Hg), and moderate night time diastolic hypertension (101 mm Hg) with white coat effect (181/134 mm Hg). (G) Isolated systolic hypertension. The ABPM suggests severe 24 hour isolated systolic hypertension (176/68 mm Hg daytime, 169/70 mm Hg night time). (H) Hypertensive dipper. The ABPM suggests severe daytime systolic hypertension (181 mm Hg), moderate daytime diastolic hypertension (117 mm Hg), and normal night time systolic and diastolic blood pressure (111/68 mm Hg). (I) Hypertensive non-dipper. The ABPM suggests severe 24 hour systolic and diastolic hypertension (210/134 mm Hg daytime, 205/130 mm Hg night time). (J) Autonomic failure. The ABPM suggests normal daytime systolic and diastolic blood pressure (125/72 mm Hg), moderate night time systolic hypertension (140 mm Hg), and mild night time diastolic hypertension (84 mm Hg) with mild white coat effect (148/91 mm Hg).

problem, the Association for the Advancement of Medical Instrumentation published a standard for electronic or aneroid sphygmomanometers in 1987, which included a protocol for the evaluation of the accuracy of devices, and this was followed in 1990 by the protocol of the British Hypertension Society; both protocols were revised in 1993.^{55 56} These protocols, which differed in detail, had a common objective—namely, the standardisation of validation procedures to establish minimum standards of accuracy and performance, and to facilitate comparison of one device with another. A large

number of blood pressure measuring devices, including many ABPM devices, have been evaluated according to one or both protocols.² However, experience has demonstrated that the conditions demanded by the protocols are difficult to fulfill. The working group on blood pressure monitoring of the European Society of Hypertension recently published a simplified protocol to facilitate manufacturers to submit their products for validation so as to obtain the minimum approval necessary for a device to be used in clinical medicine, in the hope that in time most devices on the market will be assessed for basic accuracy according to this protocol.¹⁰

Table 1 Recommended levels of normality for ambulatory blood pressure monitoring

	Blood pressure levels (mm Hg)		
	Optimal	Normal	Abnormal
Daytime	<130/80	<135/85	>140/90
Night time	<115/75	<120/70	>125/75

The evidence supporting the normal and abnormal demarcation levels are based on firm evidence from a number of studies; the evidence is not yet available to make recommendations for the intermediate pressure ranges between the "normal" and "abnormal" levels, nor for recommendations lower than those given. It must be emphasised that these levels are only a guide to "normality" and that lower "optimal" levels may be more appropriate in patients whose total risk factor profile is high, and in whom there is concomitant disease, such as diabetes mellitus.

CHOOSING ABPM SOFTWARE

Though the British Hypertension Society protocol does make certain recommendations in relation to the software programs in ABPM devices, too little consideration has been given to this important aspect of the technique. All ABPM devices are sold with individual software packages, which present data in a variety of ways; in some instances the software programs are neither "user friendly" nor inexpensive. It is important, therefore, to be sure that the software program with the ABPM device selected is suitable for the use for which the device has been chosen. For example, in a busy general practice, perhaps only basic data giving average day and night time values and a visual plot are all that will be required. For research purposes, however, statistical detail on the windows of the 24 hour profile and indices such as pulse pressure, blood pressure load, coefficient of variation, cusum values, etc, may be required.

The use of ABPM in clinical practice could be greatly facilitated by two developments. Firstly, if the graphic presentation of ABPM data was standardised, much as is the case for ECG recordings, the presentation of data would be independent of the type of ABPM monitor used and the user would not have to become familiar with a variety of programs. Moreover, standardisation would facilitate the interchange of ABPM recordings between databases, such as a hospital and primary care practice. Secondly, if ABPM software programs could provide a printed report of the ABPM data, as is possible with ECG recordings, doctors and nurses unfamiliar with the technique would be assisted in learning the variety of patterns generated by ABPM; most importantly, the time needed for a physician to report on each ABPM would be greatly reduced, thereby reducing the cost of the technique. The dabl® ABPM Program (ECF Medical Ltd, Blackrock, Co Dublin, Ireland, www.ecfmedical.com) has been designed to provide a graphic display of ABPM data (on screen or printout) showing a visual graph with blood pressure plotted on the vertical axis and time on the horizontal axis, and the range of normal systolic and diastolic pressures are also depicted.^{77 78} The transitional periods between retiring at night and arising in the morning are excluded from the analyses so as to reduce variability in the day and night time recordings. The first hour of recording, when the blood pressure may still be influenced by the medical environment, can be excluded from the analysis. The program also provides a printed report derived from a computer data set of some 7000 permutations (fig 1).

FINANCIAL CONSIDERATIONS

ABPM is more expensive than CBPM but the benefits to patients more than justify the additional expense. Subjects

Some clinical indications for ABPM

- ▶ Exclusion of white coat hypertension
- ▶ Deciding diagnosis in borderline hypertension
- ▶ Elderly patients
- ▶ Identification of nocturnal hypertension
- ▶ Hypertensive patients resistant to treatment
- ▶ As a guide to antihypertensive drug treatment
- ▶ Hypertension of pregnancy
- ▶ Diagnosis of hypotension

with white coat hypertension, which is present in about a quarter of people who appear to have hypertension with conventional measurement, may be spared years of unnecessary and expensive drug treatment.¹¹ Likewise, ABPM may spare patients with white coat hypertension being penalised for insurance or employment by having the diagnosis of "hypertension" misapplied.⁹⁹ It has been shown that when ABPM is used as the basis for prescribing rather than clinic blood pressure, significantly less antihypertensive medication is prescribed.¹² The financial saving from less drug prescribing has been analysed in a cost-benefit comparison of ABPM with CBPM in Switzerland; over a 10 year period 2 million Swiss francs could be saved if therapeutic decisions were based on ABPM rather than CBPM.¹³

AGREEMENT ON DEFINITION OF NORMALITY FOR ABPM

As with conventional measurement, normal ranges for ABPM have been the subject of much debate over the years. Currently, an average daytime ABPM of less than 135 mm Hg systolic and 85 mm Hg diastolic is generally considered normal, but lower levels are being advocated in high risk groups, such as diabetic patients, in whom levels less than 130/80 mm Hg are considered optimal (table 1).^{1 4 14 w10 w11}

CLINICAL INDICATIONS FOR ABPM

ABPM is useful in both diagnosing and managing hypertension, and it is used, at least in European countries, for a broad range of indications in clinical practice (see box above). However, if one had to single out one clinical indication over and above all others in which the technique is so valuable as to be indispensable, that would have to be the identification of white coat hypertension, and this condition will therefore be reviewed in detail.

White coat hypertension

The importance of white coat hypertension rests on a curious haemodynamic phenomenon, which has quite profound clinical relevance. Patients—let us call them people, because they may not be ill—who appear to have hypertension when their blood pressure is measured by the traditional Riva-Rocci/Korotkoff method, have normal blood pressures when ABPM is used to record their blood pressures away from the medical environment. Put another way, CBPM is misleading in people with white coat hypertension, and if decisions are based on these measurements, inappropriate diagnosis and treatment may result.

The CMS in the USA has recently approved ABPM for reimbursement, but only for "patients with suspected white coat hypertension" in whom the CMS believes the information deriving from the technique "is necessary in order to determine the appropriate management of the patient".³ Faced with the difficult dilemma of being unable any longer to

deny the evidence showing the value of ABPM on the one hand, and the need to prevent indiscriminate use of the technique on the other, the CMS has therefore selected white coat hypertension as the only indication for ABPM that is approved for reimbursement.³ This decision, which is likely to change the clinical management of hypertension in the USA, makes white coat hypertension a condition of major importance. The decision by the CMS begs the question as to how the practising physician can select patients with white coat hypertension. It might indeed be argued that all patients with a raised clinic blood pressure are candidates for ABPM.

The most popular definition of white coat hypertension requires a blood pressure measured by conventional techniques in the office, clinic or surgery to be above 140/90 mm Hg, with normal ABPM measurements throughout the 24 hour period, except perhaps during the first hour of the 24 hour recording when the patient is under the pressor influence of the medical environment while having the monitor fitted.³ White coat hypertension is common, being present in about a quarter of people who appear to have hypertension with conventional measurement.¹¹

Self measured home blood pressure has been used to identify subjects with white coat hypertension,^{w12} though its role in this regard remains to be validated in further clinical studies.^{w13} Subject to this caveat, a report of the first international consensus conference on self measured home blood pressure recommended that the upper limit of normal home blood pressure should be 135/85 mm Hg based on the average of two measurements in the morning and in the evening for at least three working days.¹⁵

Are people with white coat hypertension at risk? This is an important question because future management is dependent on it. The clinical significance of white coat hypertension has become clearer from a growing mass of data, including some event based cohort studies,^{16 w14 w15} which suggest that subjects with raised office/clinic blood pressure, who have normal average daytime pressures on ABPM, have a risk of major cardiovascular events comparable to that of clinically normotensive subjects and less than that of subjects with raised daytime pressures. On the other hand, some studies have suggested that patients with white coat hypertension may be at increased risk, albeit a smaller risk than patients with sustained hypertension.^{5 w16}

Several hypertension guidelines^{w17-19} stipulate that suspected white coat hypertension is an indication for ABPM. However, none of the guidelines elaborate as to how the practising physician may “suspect” white coat hypertension, and in fairness it has to be admitted that data allowing an estimate of the probability of white coat hypertension according to the clinical characteristics of subjects are very scarce (table 2). An analysis of data from a number of studies^{11 17 w20-22} indicate that in untreated subjects with essential hypertension, the probability of white coat hypertension increases in subjects with:

- ▶ office systolic blood pressure 140–159 mm Hg or diastolic blood pressure 90–99 mm Hg
- ▶ female sex
- ▶ non-smokers
- ▶ hypertension of recent onset
- ▶ limited number of blood pressure measurements in the office
- ▶ small left ventricular mass.

The consequences of failing to identify white coat hypertension are considerable. Young (and indeed not so young) people may be penalised for insurance and pension policies,

Table 2 Features of white coat hypertension

Definition	<ul style="list-style-type: none"> ▶ Abnormal office blood pressure \geq 140/90 mm Hg ▶ Normal daytime ABPM <135/85 mm Hg
Prevalence of white coat hypertension	<ul style="list-style-type: none"> ▶ 15–30% general population ▶ 30% pregnancy
Risks from white coat hypertension	<ul style="list-style-type: none"> ▶ Considerably less than sustained hypertension ▶ Probable small risk compared to normotensives ▶ Possibly a pre-hypertensive state? ▶ May not be an entirely innocent condition
Clinical implications	<ul style="list-style-type: none"> ▶ Few clinical characteristics to assist diagnosis ▶ Must be considered in newly diagnosed hypertensives ▶ Should be considered before drug prescribing ▶ Must be placed in context of overall risk profile ▶ Reassurance for employment ▶ Reassurance for insurance and pension liability ▶ Common in the elderly and pregnancy ▶ Less drug prescribing ▶ Need for follow up and re-monitoring

and for employment. Life long treatment may be prescribed unnecessarily, and if antihypertensive medication is given to people whose 24 hour pressures are normal they may be made unwell by the adverse effects of medication. In the elderly, in whom white coat hypertension is common, the inappropriate use of drugs may have serious debilitating consequences. It is recommended that people with white coat hypertension should be followed at yearly intervals with ambulatory measurement.¹

White coat effect

White coat hypertension must be distinguished from white coat effect, which is the term used to describe the rise in pressure that occurs in the medical environment regardless of the daytime ABPM level. In other words the term indicates the phenomenon found in most hypertensive patients whereby CBPM is usually higher than the average daytime ABPM, which is none-the-less raised above normal. The importance of the phenomenon is that patients diagnosed as having severe hypertension by CBPM may have only moderate or mild hypertension on ABPM because of a pronounced white coat effect. Although the white coat effect may contribute to white coat hypertension, there seems to be no predictive association between the two entities.^{w23} The term white coat effect has also been used by some authors^{w24 w25} to categorise individuals with an unusually large difference between office and ambulatory readings, regardless of the actual level of either. According to this line of thinking, a clinically significant white coat effect has been defined as an office blood pressure exceeding mean daytime ambulatory blood pressure by at least 20 mm Hg systolic and/or 10 mm Hg diastolic.^{w24} Such a large white coat effect has been found in as many as 73% of treated hypertensive subjects^{w25} and it may occur more frequently in women than in men.^{w26}

Masked hypertension (reverse white coat hypertension)

Recently, a group of patients have been identified in whom CBPM levels of pressure are normal but ABPM levels are elevated. This phenomenon has been previously given the awkward titles of “reverse white coat hypertension” or “white coat normotension”. Pickering and his colleagues have proposed the more sensible term of “masked hypertension” to denote blood pressure elevation which is hidden until ABPM

ABPM patterns in the elderly

- ▶ White coat hypertension
- ▶ White coat effect
- ▶ Isolated systolic hypertension
- ▶ Postural hypotension
- ▶ Postprandial hypotension
- ▶ Daytime hypotension/nocturnal hypertension
- ▶ Drug induced hypotension
- ▶ Autonomic failure

is performed.¹⁸ If, as has already been shown, ABPM gives a better classification of risk than CBPM, then it follows that these people should be regarded as being genuinely hypertensive. The problem for clinical practice is how to identify these subjects, who it is estimated may number as many as 10 million people in the USA.¹⁸ The phenomenon might be suspected in subjects who have had a raised CBPM at some time, subjects with a family history of hypertension in two parents, patients with multiple risks for cardiovascular disease, and perhaps diabetic patients.

Systolic and diastolic hypertension

Combined systolic and diastolic hypertension is the most common form of hypertension, and ABPM allows for a more detailed assessment of the severity of elevation of systolic and diastolic pressures as well as the duration of elevation throughout the 24 hour period. Moreover, the degree of white coat effect can be quantified. In patients with resistant hypertension, defined as a CBPM which remains consistently above 150/90 mm Hg in spite of treatment with three antihypertensive drugs, ABPM may indicate that the apparent lack of response is caused, in fact, by the white coat phenomenon.

Hypertension in the elderly

A number of ABPM patterns may be found in elderly subjects (see box above). The results of the ambulatory study of the systolic hypertension in Europe (Syst-Eur) trial show that systolic blood pressure measured conventionally in the elderly may average 20 mm Hg higher than daytime ABPM,¹⁹ thereby leading to inevitable overestimation of isolated systolic hypertension in the elderly and probably excessive treatment of the condition. Moreover, results from this study also show that ambulatory systolic blood pressure was a significant predictor of cardiovascular risk over and above CBPM. Among the many ambulatory patterns found in the elderly are a number of hypotensive states caused by baroreceptor or autonomic failure. As the elderly can be particularly susceptible to the adverse effects of blood pressure lowering drugs, identification of hypotension becomes particularly important,^{w27} though its management may present a considerable therapeutic challenge.

Hypertension in pregnancy

As in the non-pregnant state, the main use for ABPM in pregnancy is the identification of white coat hypertension, which may occur in nearly 30% of pregnant women.^{w28} Its recognition is important so that pregnant women are not admitted to hospital or given antihypertensive drugs unnecessarily or excessively. Normal values for ABPM in the pregnant population are available, and the changes in pressure, which occur during the trimesters of pregnancy and in the postpartum period, have been defined.^{w29} The evidence that ABPM may predict pre-eclampsia is not yet conclusive.^{w30}

However, ABPM correlates better with proteinuria than does conventional sphygmomanometry,^{w31} it is a better predictor of hypertensive complications,^{w32} and women diagnosed by the technique as having hypertension give birth to infants with lower birth weight than normotensive women.^{w33} Moreover, women with white coat hypertension tend to have more caesarean sections than normotensive women, suggesting that if ABPM was used to measure blood pressure rather than the conventional technique, caesarean delivery might be avoided.^{w28}

Nocturnal hypertension

ABPM is the only non-invasive blood pressure measuring technique that permits measurement of blood pressure during sleep. Blood pressures are generally recorded every 30 minutes during sleep, and though ABPM may disturb sleep in some people, it is generally well tolerated. Moreover, the nocturnal fall in blood pressure is more a result of cessation of activity than of sleep. The relevance of nocturnal hypertension has been controversial, but recent evidence has shown that a non-dipping nocturnal pattern is a strong independent risk for cardiovascular mortality.^{6 7 w3 w34-36} In a recent study Ohkubo and his colleagues extended their previous preliminary findings^{w36} in 1542 inhabitants of Ohasama, Japan by increasing the mean follow up from 4.1 years to 9.2 years. There was a linear and inverse relation between cardiovascular mortality and the nocturnal decline in blood pressure, which was independent of the overall blood pressure load during 24 hours and other cardiovascular risk factors. Overall, each 5% increment in the systolic or diastolic night-to-day ratio was associated with a 20% rise in the risk of cardiovascular death, even when 24 hour ambulatory blood pressure was within normotensive range (< 135/80 mm Hg).²⁰ It has also been shown that absence of nocturnal "dipping" of blood pressure to lower levels than during the day is associated with target organ involvement, and may be a useful (though non-specific) clue as to the presence of secondary hypertension.¹

Ambulatory hypotension

Reference has already been made to the clinical use of ABPM in identifying hypotensive episodes in the elderly, but it may also be used in young patients in whom hypotension is suspected of causing symptoms.^{w27} ABPM may also be used to demonstrate if drug induced hypotension in treated hypertensive patients is associated with symptoms. The demonstration of excessive blood pressure lowering with antihypertensive medication is important as it may have untoward effects in patients with a compromised arterial circulation, such as those with coronary and cerebrovascular disease.^{w37}

ABPM as a guide to drug treatment

The role of ABPM in guiding drug treatment is currently the subject of much research, and its place in this regard has not yet been fully established. However, recent reviews have highlighted the potential of 24 hour ABPM in guiding antihypertensive medication.^{w38 w39} Furthermore, in a well controlled study by Staessen and colleagues, adjustment of antihypertensive treatment based on either ABPM or CBPM resulted in less intensive drug treatment in the ABPM group despite comparable blood pressure control in both groups; importantly, patients in the ABPM group, who received less drug treatment, were not disadvantaged as judged by left ventricular mass on echocardiography.¹²

CONCLUSION

After a long gestational period in research ABPM has now become an indispensable technique in the management of

hypertension. This being so, there is a need to encourage the use of ABPM in general practice rather than restricting its availability to specialist hospital centres as has tended to be the case so far. However, diagnostic and management decisions based on the interpretation of ABPM patterns are more complex than has been the case with conventional measurement of blood pressure, and suitable educational processes must also be initiated. Standardisation of data handling and presentation, the display of normal bands, the delineation of the windows of the 24 hour profile, and computer generated reports as physician assistance are steps that should make the technique easier to use and interpret so that its manifest advantages can be utilised to improve the management of hypertension, which remains so abysmally poor.

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Competing interests: The author is director of the Blood Pressure Unit at Beaumont Hospital, which has been contracted from time to time to conduct validation studies of ambulatory blood pressure measurement devices; the results of these studies have been published. The author has advised ECF Medical Ltd on the development of the dabl® ABPM Computer Program, and he holds a minority financial interest in the programme.

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Additional references appear on the Heart website—www.heartjnl.com/supplemental