First Thomas Pickering Memorial Lecture*: Ambulatory Blood Pressure Measurement is Essential for the Management of Hypertension

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THOMAS G. PICKERING

Dr Thomas George Pickering, physician, clinical scientist, professor and mentor, editor, husband, father, and grandfather, died on May 14, 2009, at the age of 69 from complications of brain cancer, an illness that he had fought with dignity and courage for more than a year[1] (Figure 1).

Tom was educated at Bryanston School in Blandford, England, where he won state and entrance scholarships. He went on to study medicine at Trinity College, Cambridge, and the Middlesex Hospital Medical School, London, where he graduated in 1966, being awarded the first Broderip Scholarship.[2] His early postgraduate years were spent at Middlesex Hospital and the Radcliffe Infirmary. He sat for the membership of the Royal College of Physicians of London in 1968 (becoming a fellow in 1980) and went on to earn a PhD degree at Oxford University in 1970. In 1972, he went to New York to take up appointments as Associate Physician at the Rockefeller University Hospital and Assistant Professor at Cornell University, and he spent 2 years as Assistant Professor at the Rockefeller University working with Neal Miller on biofeedback mechanisms. He was appointed Assistant Physician to the New York Hospital in 1974. He later returned to the Radcliffe Infirmary to work with Peter Sleight on research into baroreceptor function, the autonomic nervous system, and the emerging class of cardiovascular medications, known as the adrenoreceptor blockers. He was attracted back to New York City by the possibility of being able to work as both a practicing physician and a clinical investigator and he spent more than 20 years in a productive career in behavioral cardiovascular medicine, clinical hypertension, and blood pressure (BP) measurement research at Cornell University Medical College. In 2000, he became Director of Behavioural Cardiovascular Health and the Hypertension Program at the Cardiovascular Institute of Mount Sinai Medical Center and in 2003 he moved to Columbia University Medical College as Professor of Medicine and Director of the Behavioural Cardiovascular Health and Hypertension Program.[3]

So much for Dr Pickering, the scientist, what about Tom the man we came to love and admire? Tom was the quintessential Englishman, mannerly, gentle, and gentlemanly (the two must not be confused) whose enquiring mind was tinged with that spirit of philosophy whereby he knew nothing was new under the sun, but that what was fundamental to science was the expression of fact and the style of that expression. He was aware that each small brick added to the edifice of knowledge would enhance our understanding of hypertension and ultimately benefit those we graduated to serve as doctors—our patients.

My first contact with the Pickering family was with Tom's father, Sir George Pickering, when we were seated together on a bus taking us from the airport to a hotel in Valetta in 1975. I recall a man of small stature in an incredibly grubby raincoat who talked animatedly to me about the new drugs for the treatment of hypertension. However, my abiding memory is of his kindness to me the following morning when I was the first speaker in a session chaired by him in what was probably my first address to an international audience (Figure 2). As I prepared to begin my presentation there was the unmistakable sound of slides cascading from a carousel to the floor, whereupon Sir George looking encouragingly at me said "And now we will see how the young doctor from Dublin can convince us without slides!" Fortunately, during my sleepless night of rehearsing my lecture I had written prompt cards for each slide a precaution acknowledged by Sir George as "being a lesson to us all not to rely on slides." Tom's mother, Lady Carola, was a regular attendee at the British Hypertension Memorial Lectures named after her late husband. The most memorable of these was the ninth Sir George Pickering Lecture delivered in Dublin by Tom in September 1991 on "Ambulatory Monitoring and the Definition of Hypertension." At dinner at the Royal College of Surgeons she remarked to me: "Eoin, I am so pleased; I never thought Tom had it in him." How little moth-

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FIGURE 1. Thomas George Pickering (1940–2009).

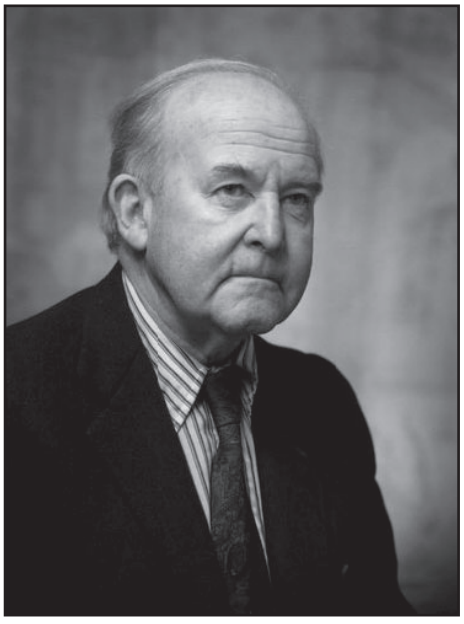


FIGURE 2. Sir George Pickering (1904–1980).

ers know their sons and how much more science Tom had in him!

THE ORIGINS OF AMBULATORY BLOOD PRESSURE MEASUREMENT

Ambulatory BP measurement (ABPM), which has been available in one form or another for some 40 years, was developed initially to determine the efficacy of BP-lowering drugs.[4,5] Although assessing the BP-lowering efficacy of antihypertensive drugs over the 24-hour period is a logical scientific premise, the ability to do so has been dependent on technological developments. The first advance was the introduction of a direct intra-arterial technique for the measurement of BP continuously over the 24-hour period.[5]

Direct Intra-Arterial ABPM

More than 30 years ago, a series of studies using direct intra-arterial ABPM to provide continuous 24-hour BP was conducted by Jim Raftery and his group at Northwick Park Hospital in London and by John Floras and Peter Sleight at the John Radcliffe Hospital in Oxford in which the value of ABPM in assessing the efficacy of BP-lowering drugs was dramatically demonstrated.[6–9] In the earliest of these studies, atenolol taken once daily in the morning was shown to lower BP during the day but to have little effect on either nighttime BP or the morning rise in BP (Figure 3). The prescient conclusions of this study merit quoting in full because they are as relevant today as when they were written in 1979:

> *The circadian rhythm of BP raises many questions about the timing of antihypertensive drug dosage and the effects of traditional regimens. Single measurements in outpatient clinics are unlikely to yield useful information on the effects of drugs on this basic cycle. If treatment aims at lowering BP to a 'normal' level (140/90 mm Hg) clearly it is desirable to lower it to that level throughout the 24-hour cycle.*[7]

The Oxford Group used intra-arterial ABPM to demonstrate the difference in efficacy and 24-hour duration of action between four β-blocking drugs—atenolol, metoprolol, pindolol, and slow-release

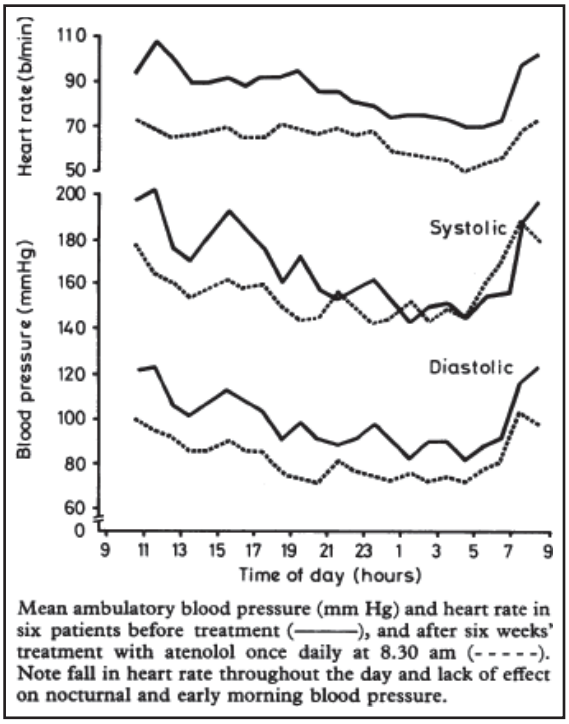


FIGURE 3. Plot of the effect of atenolol on 24-hour ambulatory blood pressure monitoring.[7] bpm indicates beats per minute.

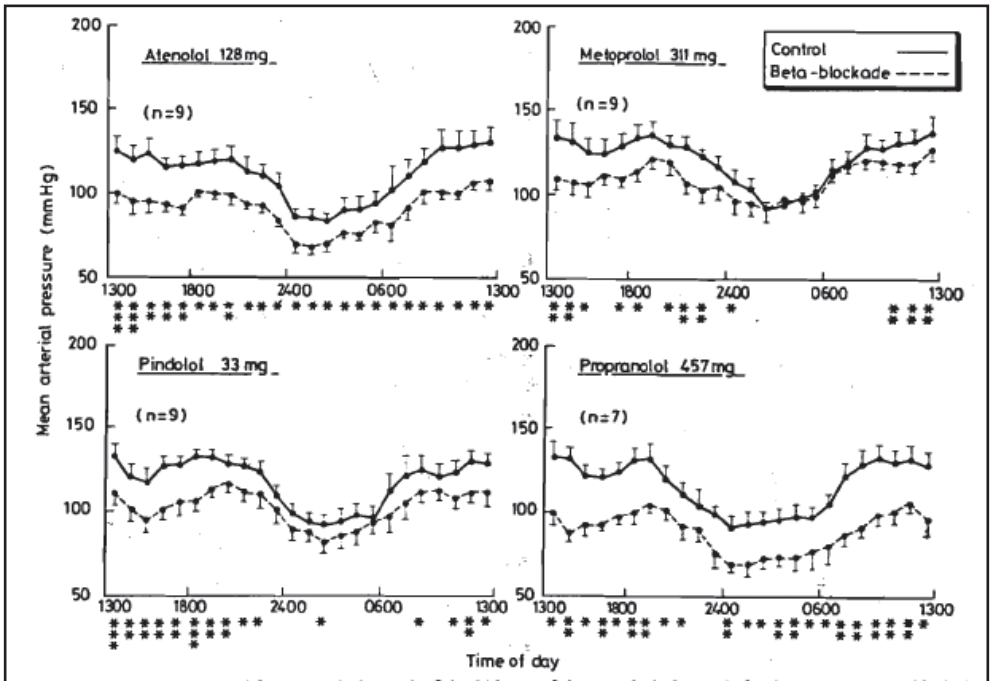


FIG 1—Mean ±SE mean arterial pressure during each of the 24 hours of the records, before and after beta-adrenoceptor blockade with one of atenolol, metoprolol, pindolol, and slow-release propranolol.
Comparison of each pair of hourly means: *p<0·05, **p<0·01, ***p<0·001 (one-tailed *t* test).

FIGURE 4. Plot of the effect of four beta-blockers on 24-hours ambulatory blood pressure monitoring.[8]

propranolol—in a double-blind randomized study (Figure 4). Whereas all 4 β-blockers achieved a significant reduction in mean arterial BP 28 hours after the last single daily dose was taken, the extent to which each drug lowered BP differed during 24 hours and had clinic BP only been measured no difference between these 4 drugs would have emerged.[8] However, direct intra-arterial ABPM was not without risk and the technique posed ethical issues that precluded its use except in a few specialized centers.[9]

Noninvasive ABPM

Efforts were focused, therefore, on developing a device that would record ambulant BP noninvasively and, in the 1960s, the Remler device, which was capable of measuring BP intermittently during the daytime period, provided clinicians with a new technique for evaluating antihypertensive drugs.[10,11] This device yielded interesting information on drug efficacy but was limited by having to be operated by the patient, which made the recording of nocturnal BP impractical. The early studies on drug efficacy using ABPM yielded interesting information on the discrepancy between clinic BP and ABPM.[9] First, ABPM could be in agreement with clinic BP measurements. In such studies, where a clinic fall in BP was confirmed by ABPM, the latter also demonstrated what conventional BP measurement can never show, namely, the duration of antihypertensive effect over the dosing interval. Second, clinic BP measurement could fail to detect the BP-lowering effect demonstrated by ABPM. The studies showing this phenomenon used smaller numbers, and for this reason their power to detect differences between treatments with clinic BP measurement was low. However, the greater number of observations available with ABPM, by reducing within-subject variability, compensated to some extent for this deficiency. Finally, reductions in clinic BP could be significant, but ABPM might be either nonconfirmatory or show that the clinic BP reduction coincided only with a brief period of BP reduction on ABPM. Of considerable practical importance was the fact that many drugs would have been declared as effective BP-lowering agents by conventional BP measurement, whereas ABPM showed a pattern of activity that was far less impressive.[9] That drugs continue to be assessed for efficacy with conventional clinic BP is an even greater indictment of clinical science today than when the following statement was made in 1989: "The time has surely come where studies of antihypertensive drug efficacy which do not assess BP over 24 hours should no longer be acceptable.[12]" Although ABPM was confined initially to clinical trials, the advent of automated devices capable of measuring BP at predetermined intervals over the 24-hour period in the 1980s allowed ABPM to be hailed as "an idea whose time has come.[13]"

The broader use of ABPM in clinical practice was given major expression with the publication of a semi-

nal paper by Dorothee Perloff and Maurice Sokolov in *The Journal of the American Medical Association* (*JAMA*) in 1983 when they showed for the first time that ABPM was superior to conventional BP in predicting cardiovascular outcome.[14]

These pioneering contributions provided Thomas Pickering with the solid foundations on which to build a lasting edifice to ABPM. Whereas Tom would be the first to acknowledge that his contributions were dependent on the supportive research from his many international collaborators and friends, the constraints of time and space do not make it possible for me to indicate these here.

Thomas Pickering's Contribution to ABPM

Pickering was an advocate of out-of-office BP measurement and his publications, particularly in the technique of ABPM, were influential in changing our approach to the diagnosis and management of hypertension. When he wrote, "The addition of ABPM to conventional clinic measurements for defining BP status in clinical practice has added a new complexity to the process, because the separation of normotension and hypertension can be assessed independently by each of the two methods,"[15] he effectively focused research and practice on two groups of patients who are of such importance that the practice of medicine has had to change radically to facilitate their identification, namely patients with white-coat and masked hypertension. Patients with these phenomena continue to intrigue and preoccupy researchers, but their impact on clinical practice is a tribute to Pickering's prescience in bringing them to attention. He also made a significant contribution to the BP behavior during the nocturnal period of ABPM. His contribution to other aspects of hypertension research, most notably the psychosocial determinants of hypertension[16] and the assessment of BP by self-measurement,[17,18] is outside the scope my remit.

White-Coat Hypertension

In his seminal paper published in *JAMA* in 1988, Pickering coined the term *white-coat hypertension* to describe patients whose BP is elevated in the medical environment, but not during daytime ABPM.[19] Using the 90th percentile of the distribution of the awake ambulatory BP in healthy normotensive volunteers (134/90 mm Hg) as a cut-off point, he showed that 21% of 291 patients with borderline hypertension and 5% of 42 patients with established hypertension had white-coat hypertension. He predicted that by combining conventional BP measurement with ABPM, it would become possible to identify patients at low risk, in whom the initiation of medical treatment might be questionable and in whom a longer period of observation might be appropriate. Or, as Pickering put it: "Taken on their own, the results of this study do not permit any definitive recommendations regarding prognosis or treatment. But when placed in the context of other reported data, they suggest the possibility of being able to identify a low-risk group in whom the need to initiate treatment is questionable.[19]"

A search in PubMed for white-coat hypertension or white-coat effect brings up over 2000 references to the condition that reflect the importance of the condition in clinical practice (PubMed search, June 2012). However, the practical relevance is perhaps best illustrated by a study showing that identification of white-coat hypertension with ABPM would result in antihypertensive drug treatment being postponed in 25% and multiple drug treatment being avoided in 15% of hypertensive patients.[20] At an epidemiological level, the benefit of identifying white-coat hypertension using ABPM has been clearly demonstrated in the Spanish Registry Study, which showed that if BP control was assessed by ABPM so that the white-coat effect was excluded, 52% of patients were controlled as compared with only 24% when BP control was assessed by conventional measurement.[21] These messages from clinical and epidemiological practice should find resonance with health care providers who should recognize that substantial financial savings could be made by making ABPM indispensible for the diagnosis and ongoing assessment of patients with hypertension (Figure 5).

Masked Hypertension

In another iconoclastic paper published in 2002, Pickering introduced the term *masked hypertension*[15] to describe what other researchers had called *reverse white-coat hypertension* and *white-coat normotension*.[22–24] This condition denotes patients who appear to be normotensive in a doctor's office but who have an elevated ABPM. Because of the proven superiority of ABPM over office BP measurement in predicting outcome, such patients can be regarded as genuinely hypertensive. In keeping with this reasoning, Pickering then showed that patients with masked hypertension have more extensive target organ damage than true normotensive patients.[25] He estimated that the prevalence of masked hypertension in adults seemed to be at least 10%, with a tendency to decrease with age.[25–27] It is a sobering thought that even if masked hypertension is only present in 5% of the population, this translates into 10 million people in the United States.[28] The clinical importance of the condition is that if BP is assessed with office BP measurement in a patient with a history of cardiovascular disease, eg, a stroke or heart attack, the doctor will prescribe aspirin and a statin but deny the patient the most important treatment to prevent a cardiovascular recurrence, namely BP-lowering medication in the belief that the patient is normotensive. The condition has subsequently been extended to children in whom the prevalence is as high 10%.[29] Once again, Pickering has challenged health care providers to face up to the serious issue of identifying masked hypertension in children and adults. Clearly, it is not practical to perform ABPM in all patients with normotension in the office or clinic to

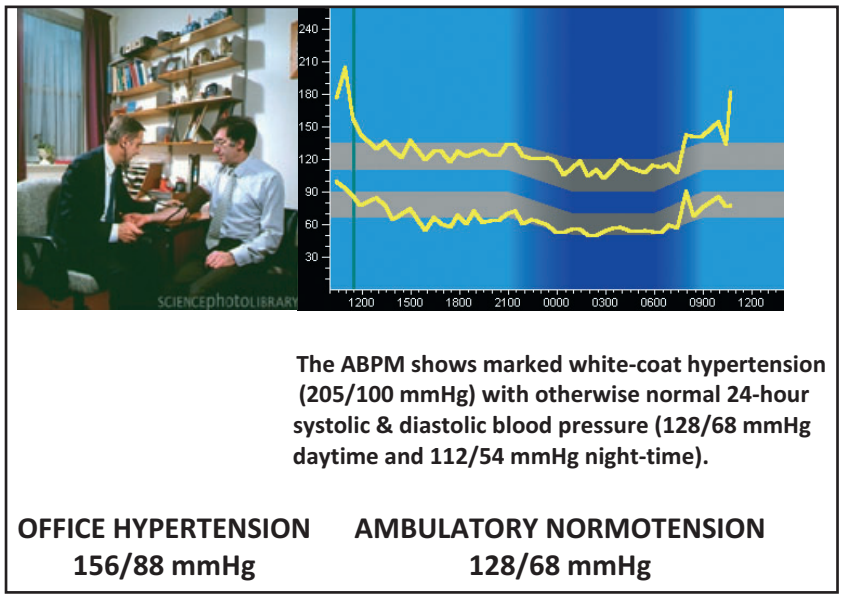


FIGURE 5. White-coat hypertension.

unmask those with ambulatory hypertension. Yet the consequences of not identifying masked hypertension carry serious implications for patients. The occurrence of masked hypertension in at least 10% of children and adults and the presence of the reverse phenomenon of white-coat hypertension in some 20% of hypertensive patients means that conventional office measurement has the potential for misdiagnosing more than 30% of patients who present to doctors to have BP measured. Leaving aside the many advantages of ABPM, this estimate alone, which is conservative, must surely make the case for ABPM being an indispensable investigation for the diagnosis and management of hypertension in children, adolescents, and adults (Figure 5).

Nocturnal Hypertension

Pickering regarded the nocturnal period of the 24-hour cycle as being of prime importance both as a measure of BP variability and also as a prognostic marker for outcome. Since we first coined the term *dipping* to denote patients who had a fall in nocturnal BP as distinct from those who had sustained elevation of nocturnal BP and a poorer cardiovascular outcome,[30]

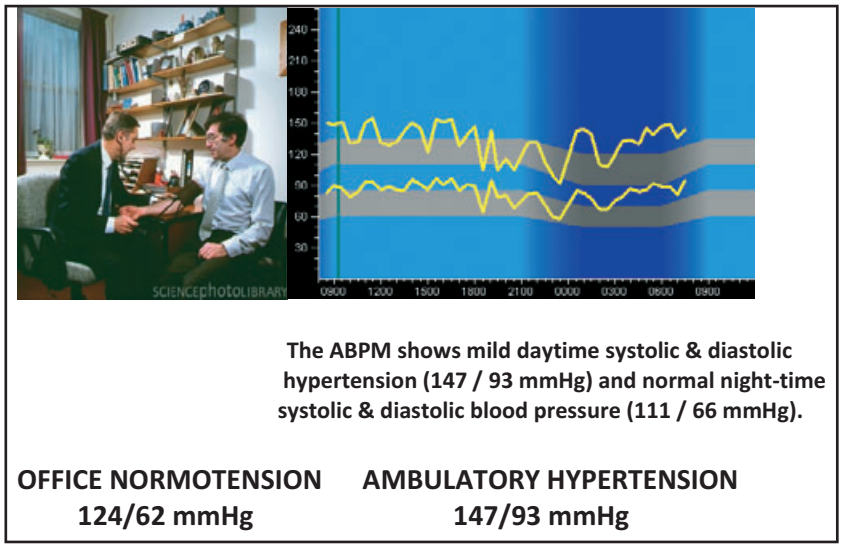


FIGURE 6. Masked hypertension.

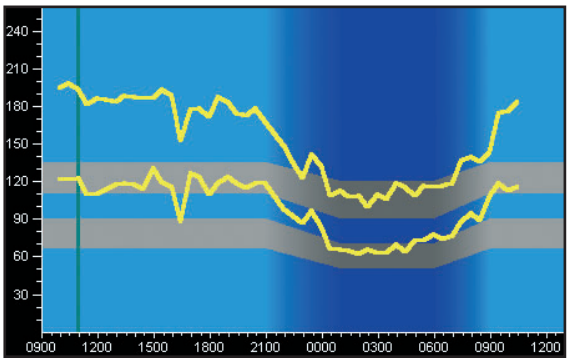


FIGURE 7. Dipping pattern: ambulatory blood pressure monitoring shows severe daytime systolic hypertension (181 mm Hg), moderate daytime diastolic hypertension (117 mm Hg), and normal night-time systolic and diastolic blood pressure.

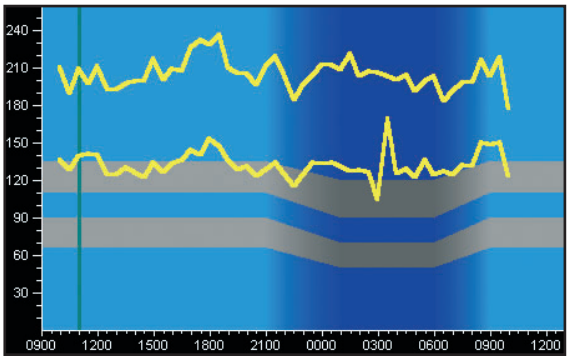


FIGURE 8. Nondipping pattern: ambulatory blood pressure monitoring (ABPM) shows severe 24-hour systolic and diastolic hypertension (210/134 mm Hg daytime and 205/130 mm Hg nighttime). Plots and reports generated by dabl Ltd., Dublin, Ireland.

numerous studies have corroborated this assertion.[31] In 1982, Pickering compared 24-hour BP in healthy patients, patients with borderline hypertension, and patients with established hypertension.[32] In this study he amplified the finding of his father some 20 years earlier (although he did not state this), showing that patients had their highest BP readings during work or at the clinic and the lowest readings during sleep. Subsequent studies have clearly demonstrated that ABPM should be recorded during the entire day so as to detect the patterns of BP behavior in the day time and nighttime periods, each of which carry important prognostic information[33,34] (Figure 6, Figure 7, and Figure 8).

One of Pickering's outstanding characteristics was the intellectual encouragement and friendship he extended to younger researchers.[35] This was particularly exemplified in the collaborative research he performed with his Japanese colleagues elucidating the role of the morning surge of BP in the pathogenesis of cardiovascular disease.[36] A subsequent study on the prognostic significance of the morning surge in 5645 participants randomly recruited form 8 countries established the prognostic value of the morning surge in BP in general populations. An exaggerated morning surge, exceeding the 90th percentile of the population, was an independent risk factor for mortality and cardiovascular and cardiac events, especially in smokers, whereas a sleep-through or pre-awakening morning surge in systolic BP <20 mm Hg was probably not associated with an increased risk of death or cardiovascular events.[37] The significance of the morning surge remains controversial, with the devil being in the detail as to how the phenomenon is defined.[37,38]

INTERNATIONAL STATUS OF ABPM IN 2012

In 1996, Pickering reviewed the international recommendations for ABPM and concluded that there was international agreement in support of the use of ABPM in clinical practice.[39] In a later review in 1999 in the *New England Journal of Medicine*, he anticipated the recent recommendations of the National Institute for Clinical Excellence in the United Kingdom[40] when he advocated ABPM for all patients suspected of having hypertension:

> *ABPM is currently used only in the minority of patients with hypertension, but its use is gradually increasing. The monitors are reliable, reasonably convenient to wear, and generally accurate. Ambulatory monitoring can be regarded as the gold standard for the prediction of risk related to BP, since prognostic studies have shown that it predicts clinical outcome better than conventional blood pressure measurements. Therefore, a good case can be made for using this technique in all patients in whom hypertension has been newly diagnosed by means of clinic blood pressure measurements.*[41]

It is timely, therefore, to review the international guidelines from 2000 to the present time to see whether the recommendations for the use of ABPM in clinical practice have changed since Pickering made his prescient statement. International guidelines not only influence the clinical practice of medicine, but they also serve as a barometer of world expertise. Of the 14 guidelines reviewed,[40,42–53] all were in agreement that ABPM is indicated for the exclusion or confirmation of suspected white-coat hypertension. All but one were in agreement that ABPM is indicated for the confirmation of a diagnosis of hypotension and to identify patients with resistant hypertension; just 80% recommended ABPM to assess drug efficacy over the 24-hour period and for the assessment of the nocturnal dipping status and more than half the guidelines recommended ABPM to identify masked hypertension (Table 1).

The National Institute for Health and Clinical Excellence (NICE) guideline published in 2011 has

TABLE 1. Indications for Ambulatory Blood Pressure Monitoring in Hypertension Guidelines in the Years 2000–2012

Guideline	Suspected White-Coat Hypertension	Identify Hypotension	Resistant Hypertension	Assess Drug Efficacy	Assess Nocturnal Dipping Status	Suspected Masked Hypertension	Assess Blood Pressure Variability	White-Coat Effect
British Hypertension Society 2000[42]	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes
Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) 2004[43]	Yes	Yes	Yes	–	–	–	–	–
European Society of Hypertension 2003[44]	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes
British Hypertension Society 2004[45]	Yes	Yes	Yes	Yes	Yes	–	Yes	–
American Heart Association 2005[46]	Yes	Yes	Yes	Yes	Yes	Yes	–	–
Brazilian Society of Cardiology 2005[47]	Yes	Yes	–	Yes	–	Yes	–	–
European Societies of Hypertension and Cardiology 2007[48]	Yes	Yes	Yes	Yes	Yes	–	Yes	–
Italian Society of Hypertension 2008[49]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Canadian Hypertension Education Program 2011[50]	Yes	Yes	Yes	Yes	Yes	–	Yes	–
National Institute for Clinical Excellence UK 2011[40]	Yes	No	–	No	No	No	–	Yes
South African Hypertension Society 2012[51]	Yes	Yes	Yes	–	–	–	Yes	–
Japanese Circulation Society 2012[52]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Australian Consensus Statement on Ambulatory Blood Pressure Monitoring 2012[53]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

generated a considerable amount of comment for its recommendations for ABPM.[40] Yet, when the NICE ABPM recommendations are examined closely, it will be seen that they are somewhat at variance with international recommendations in that NICE does not advocate the use of ABPM to identify patients with resistant hypertension, to asses drug efficacy over the 24-hour period, to assess nocturnal BP, or to identify masked hypertension on the basis that evidence as yet does not support recommending the technique in these circumstances. What makes the NICE guideline different form other international guidelines is that for the first time it is stated unequivocally that ABPM should be offered to anyone suspected of having hypertension by virtue of having had an elevated conventional BP measurement: "if the clinic BP is 140/90 mm Hg or higher, offer ABPM to confirm the diagnosis of hypertension." In short, the NICE guideline has effectively substituted "suspected hypertension" for what other international guidelines have been labeling as "suspected white-coat hypertension." This is not only a courageous step based firmly on evidence, but by doing so, NICE has laid to rest the ghost that white-coat hypertension can be suspected, when in fact there are absolutely no clinical or other criteria that give any hint of the condition.[54]

MESSAGES FOR SCIENCE AND SOCIETY

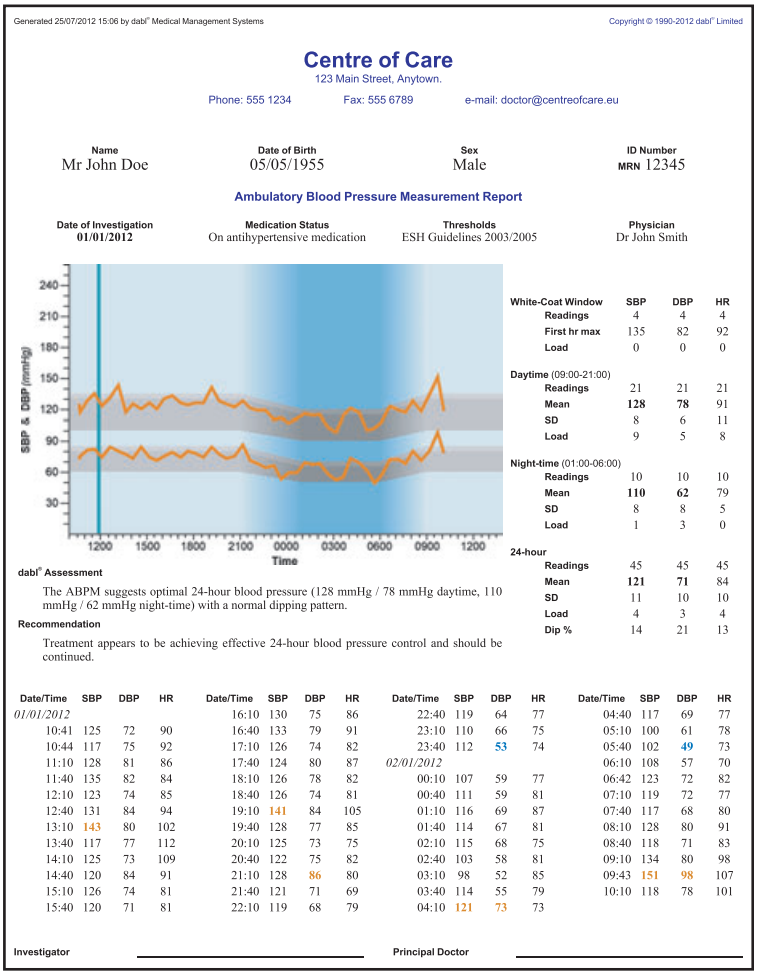
Based on the foregoing analysis, I believe it is now incumbent on all doctors who manage patients with hypertension to be able to offer ABPM to anyone suspected of having hypertension, which effectively means anyone whose office BP has been found to be high, and that the technique should be an integral component of ongoing management. Armed with this assumption and in keeping with what I know would have been Pickering's ethos, I will now address what I believe are important messages for science and society.

Making ABPM Accessible to Patients: The Role of the Pharmacist

No matter how good a technique may be if it is not made readily accessible and financially affordable, it will simply not achieve its potential. When I became interested in hypertension in the 1980s,[55] I was influenced by Sir George Pickering's data derived from direct 24-hour BP using direct intra-arterial BP measurement, but I realized that the technique would not be applicable to clinical practice. Using the Remler system as an alternative, the considerable potential of noninvasive ABPM soon became apparent:

> *Faced with a patient with borderline hypertension, the doctor should be slow to diagnose hypertension until some attempt has been made to categorize the behavior of BP over time: ambulatory BP measurement is the best way to do this.*[56]

When Pickering was preparing his review for the *N Engl J Med* in 2006, we discussed how ABPM might



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Name	Date of Birth	Sex	ID Number
Mr John Doe	05/05/1955	Male	MRN 12345

Ambulatory Blood Pressure Measurement Report

Date of Investigation	Medication Status	Thresholds	Physician
01/01/2012	On antihypertensive medication	ESH Guidelines 2003/2005	Dr John Smith

White-Coat Window	SBP	DBP	HR
Readings	4	4	4
First hr max	135	82	92
Load	0	0	0
Daytime (09:00-21:00)			
Readings	21	21	21
Mean	**128**	**78**	91
SD	8	6	11
Load	9	5	8
Night-time (01:00-06:00)			
Readings	10	10	10
Mean	**110**	**62**	79
SD	8	8	5
Load	1	3	0
24-hour			
Readings	45	45	45
Mean	**121**	**71**	84
SD	11	10	10
Load	4	3	4
Dip %	14	21	13

dabl® Assessment

The ABPM suggests optimal 24-hour blood pressure (128 mmHg / 78 mmHg daytime, 110 mmHg / 62 mmHg night-time) with a normal dipping pattern.

Recommendation

Treatment appears to be achieving effective 24-hour blood pressure control and should be continued.

Date/Time	SBP	DBP	HR	Date/Time	SBP	DBP	HR	Date/Time	SBP	DBP	HR	Date/Time	SBP	DBP	HR
01/01/2012				16:10	130	75	86	22:40	119	64	77	04:40	117	69	77
10:41	125	72	90	16:40	133	79	91	23:10	110	66	75	05:10	100	61	78
10:44	117	75	92	17:10	126	74	82	23:40	112	53	74	05:40	102	49	73
11:10	128	81	86	17:40	124	80	87	*02/01/2012*				06:10	108	57	70
11:40	135	82	84	18:10	126	78	82	00:10	107	59	77	06:42	123	72	82
12:10	123	74	85	18:40	126	74	81	00:40	111	59	81	07:10	119	72	77
12:40	131	84	94	19:10	141	84	105	01:10	116	69	87	07:40	117	68	80
13:10	143	80	102	19:40	128	77	85	01:40	114	67	81	08:10	128	80	91
13:40	117	77	112	20:10	125	73	75	02:10	115	68	75	08:40	118	71	83
14:10	125	73	109	20:40	122	75	82	02:40	103	58	81	09:10	134	80	98
14:40	120	84	91	21:10	128	86	80	03:10	98	52	85	09:43	151	98	107
15:10	126	74	81	21:40	121	71	69	03:40	114	55	79	10:10	118	78	101
15:40	120	71	81	22:10	119	68	79	04:10	121	73	73				

Investigator _____ Principal Doctor _____

FIGURE 9. Summary report of ambulatory blood pressure monitoring. ABPM report and plot generated by dabl Ltd., Dublin, Ireland.

be made more easily accessible to patients with hypertension and he reproduced the dabl system (dabl Ltd, Dublin, Ireland) for standardizing the data from a 24-hour ambulatory recording in this paper and later encouraged me to continue with my efforts to standardize ABPM and make it more cost-effective.[41] Towards this end I had developed with my colleagues the dabl software system[57] (dabl Ltd., Dublin, Ireland; www.dablhealth.ie) that was capable of providing the following facilities:

- A succinct 1-page report with standardized presentation and plotting of data with summary statistical data for day-to-day clinical use with storage of more detailed data for research.
- An interpretative report validated for accuracy against expert observers[58] so as to remove the need for a physician to report with substantial cost benefit (Figure 9).
- A trend report of successive ABPMs showing the efficacy or otherwise of treatment during the day time and nighttime periods.
- Online hosting of data to facilitate the establishment of patient BP registries.
- Electronic transmission of data to pharmacies and other health care outlets to allow ready access to ABPM by patients.

In recent years, pharmacists have been recognized as having an important role in health care delivery and particularly in improving BP control.[59–63] Recently, ABPM has been introduced to pharmacists in Ireland using the dabl system of analysis and reporting. The pharmacy-based service is proving popular with patients and is being increasingly adopted by pharmacies across the country. If the ABPM report in a pharmacy is normal, the patient is instructed to bring the report to his/her general practitioner at their next attendance, but if the ABPM is reported as abnormal, instruction is given to make an appointment as soon as possible. The advantages of an ABPM service in pharmacies are greater availability of ABPM to the public in a local and convenient pharmacy rather than having to attend a general practitioner or specialist clinic, the provision of an interpreta-

tive report and trend report to the patient who is informed as to the success or failure in achieving BP control, close collaboration between the pharmacist and the patient's general practitioner, and availability of data in a central database to provide demographic information in a patient registry on national BP trends. Another important consideration is that an ABPM provided by pharmacists costs substantially less than when it is performed by private specialist clinics.

The empowerment of patients in the management of hypertension has been one of the most gratifying aspects of the pharmacy-based ABPM service in Ireland.

Establishment of National BP Registries

In 2003, Pickering proposed for the first time that the pooling of data from national and other databases would provide a means of assessing the influence of different modalities of the ABPM profile and other biological markers on cardiovascular outcome and prognosis. Furthermore, he saw that having data from a number of national databases would allow for the identification of ethnic differences in the expression of cardiovascular disease.[64] Analyses from the international database showed that white-coat hypertension might not be a benign condition for stroke in the very long-term and that a nondipping or reverse-dipping pattern identified patients at increased cardiovascular risk at any level of 24-hour mean BP.[65]

Once again, Pickering was to lead the way in alerting his scientific colleagues to the value of patient disease registries, the value of which have since been well established. The purpose of a disease registry is to organize a system that uses observational study methods to collect uniform data so as to be able to define the prevalence and to study outcome related to specific strategies that may include scientific research and epidemiological and health economic methods of analysis.[66] There are many potential beneficiaries from disease registries. For a practicing doctor, a registry might provide data that can be used to assess the degree to which clinicians are managing a disease in accordance with evidence-based guidelines, focus attention on specific aspects of a particular disease that might otherwise be overlooked, or provide data for clinicians to compare themselves with their peers.[67] From a health care provider's perspective, registries can provide detailed information from large numbers of patients on how procedures, devices, or pharmaceuticals are actually used and on their effectiveness in different populations. This information may also be useful for determining private health insurance coverage.[68] For a drug or device manufacturer, a registry-based study might demonstrate the performance of a product in the real world, meet a post-marketing commitment or requirement, develop hypotheses, or identify patient populations that will be useful for product development, clinical trials design, and patient recruitment.[69] Patients themselves ultimately benefit by having their disease observed within the context of evidence-based guidelines, and should a new treatment become available, patients can participate in research. It has been shown that patients involved in clinical trials generally fare better than patients managed outside the research setting. For example, in patients with hypertension, participation in a clinical trial increases adherence to medication, which by leading to better BP control should reduce the occurrence of stroke and other cardiovascular consequence of hypertension.[70]

Studies from well-designed and well-performed patient registries can provide a real-world view of clinical practice, patient outcomes, safety, and comparative effectiveness and cost-effectiveness, and play an important part in improving health outcomes.[66] Through the use of such registries, health care providers can compare, identify, and adopt best practices for patients and, most importantly, disease registries can substantially reduce health costs.[71,72] To take just one example, in Sweden, which leads the drive for patient disease registries and is committed to increasing its annual financial support for disease registries from $10 to $45 million by 2013, Swedish surgeons avoided about 7500 hip revisions and saved $US 140 million in costs during 2000 to 2009. If the United States could reduce its revision burden of hip arthroplasty to 10% by 2015, it would save $2 billion of a predicted total cost of $24 billion.[71,72]

A number of countries have begun to establish patient registries for ABPM but it is fair to say that some of these registries are databases rather then registries in that they do not fulfill the full criteria for the establishment of a registry,[66] an example being the Dublin Outcome Study database, which has data from more than 25,000 patients observed over a 30-year period.[73] Such databases may serve, however, as the valuable starting point for a registry. The scientific move to establish registries of ABPM is now well underway with national registries of varying sophistication being established in Spain, Italy, Belgium, Germany, Ireland, France, Australia, Japan, and the United States. To be effective, a national registry of ABPM must use a system that is capable of providing online analysis and storage of data for demographic and scientific research. The advantages of national ABPM registries are that health care providers are able to rely on accurate demographic data for the management of hypertension and to ascertain the degree of BP control nationally.

The most successful example of a national ABPM registry has been the Spanish ABPM registry, which has changed the demographics of high BP in that country and altered the international approach to the diagnosis and treatment of hypertension.[74]

The call by Pickering to establish international ABPM databases by pooling national data has been realized with the establishment of two major international registries. The International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes (IDACO), has collected data

on ABPM from general populations in many countries and has published a number of papers on the prognostic value of ABPM.[75]

The ARTEMIS Project is an international ABPM registry of patients from hypertension clinics in different countries that aims to assess the prevalence of varying phenotypes of measurement in hypertensive patients.[76]

Ignore the Evidence at Our Patient's Peril!

Currently, cardiovascular disease is the leading cause of death in the United States and constitutes 17% of overall national health expenditures, which makes US medical expenditures the highest in the world. Medical expenditure has risen from 10% of the Gross Domestic Product in 1985 to 15% in 2008. This growth in costs has been accompanied, however, by an increase in life expectancy, suggesting that the increase in expenditure is a worthwhile investment, but there are clearly ways in which both cost-savings could be made and improved outcome could be achieved.[77] About 1 in 3 adults in the United States—an estimated 68 millions—have high BP, and less than half have it adequately controlled. It is now accepted that stroke and heart disease are at epidemic levels and are leading causes of death in the nation. If all hypertensive patients were treated sufficiently to reach the goal specified in current clinical guidelines alone, 46,000 deaths might be averted each year. The total annual costs associated with hypertension are $156 billion, including medical costs of $131 billion and lost productivity costs of $25 billion.[78] In an effort to redress these daunting health and economic statistics, the US Department of Health and Human Services has launched the Million Hearts initiative, which aims to prevent 1 million heart attacks and strokes in the next 5 years.[79,80] This initiative is commendable but it will not be achieved if BP measurement continues to be measured with conventional techniques in the office. I have emphasized and hopefully demonstrated that ABPM is not only mandatory for good clinical practice, but that it is also feasible to make it available on a cost-effective basis in the community. It is encouraging that the Million Hearts campaign states that two of its main initiatives will be to focus on the use of health information technology to improve management of risk factors and preventive care, and to make better use of team-based care that will include allied health workers, such as pharmacists, in educational interventions and risk factor measurement.[79]

Without wishing to be presumptuous as a guest lecturer from a small island that has had enduring associations with your country but made bold by the assurance of the ethos that Tom Pickering espoused, I would urge the hard-working committees that are deliberating on the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) to endorse what has been stated so boldly in the NICE guideline in relation to ABPM.[40] I would suggest, moreover, that JNC 8 should be iconoclastic in going one step further than NICE or other international guidelines in recommending not only ABPM as an indispensible technique in clinical practice, but that in addition, the data recorded from ABPM should be centrally hosted so as to provide a US BP patient registry. Together with the establishment of such a registry and the ready availability of ABPM in pharmacies and other health care outlets (as well as in doctors' offices and in specialist clinics), the laudable objectives of the Million Hearts initiative can be achieved and even surpassed.

> *Let us not banish reasoning in our headlong quest for evidence anymore than we should discard the search for evidence to support our intuitive reasoning.*

The hard-working members of the JNC 8 committees face the very real danger in the quest for irrefutable evidence that not only will intuitive reasoning be sublimated but the advancement of clinical science may be halted while the studies necessary to produce evidence are enacted—a process that in some instances could take more than a decade. This is not to say that the quest for evidence should be abandoned but rather that it should not impede progress by obscuring the weight of collective intuitive reasoning.

There is an epilogistic message that I have not seen stated elsewhere, but one which I believe the medical profession needs to acknowledge before the consequences of failing to do so redound on it with very negative consequences. With the overwhelming weight of international expertise in hypertension having voiced the opinion in many guidelines that ABPM should be offered to patients suffering from hypertension, surely the failure to provide such a facility for patients who experience the cardiovascular complications of mismanaged hypertension must soon be a cause for redress in the medico-legal forum? It behooves us as caring doctors and scientists to acknowledge the weight of opinion and no longer to resist the need to make ABPM available not only for the diagnosis but also for the proper management of patients with hypertension.

CONCLUSIONS

I hope that Tom would support the sentiments I have expressed in this, the first memorial lecture to honor his contribution to the science and practice of hypertension (Figure 10). I know that he would be in agreement with the efforts made in recent years to make ABPM more accessible to patients and that he would be pleased that international opinion, albeit belatedly, is at long last heeding his admonitions that the technique should be indispensible to good clinical practice. It is a pleasure to be able to acknowledge the presence of Janet, Robert, and William in this address. In thanking the American Society of Hypertension for honoring me with this lec-

FIGURE 10. Dr Pickering (left) in a discussion with the author (center) and a colleague at the Ambulatory Blood Pressure Monitoring Working Group meeting in the Royal College of Surgeons of Ireland, Dublin, 1991.

tureship, I would like to suggest that the Society might give consideration to now establishing a Thomas Pickering Scholarship to support young scientists involved in hypertension research.

Conflict of interest: Eoin O'Brien is Medical Director, Board Member, and Shareholder of dabl Ltd., Dublin, Ireland.

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