OHE Early Diagnosis Paper 1

The Early Diagnosis of
Raised Arterial Blood Pressure

W. W. HOLLAND, BSc, MB, BS, MD
Reader in Clinical Epidemiology
St Thomas's Hospital Medical School, London

Published 1967

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Foreword

by the Chairman of the OHE Advisory Committee on Surveillance and Early Diagnosis in General Practice

In July 1965, the Office of Health Economics held a colloquium on Surveillance and Early Diagnosis in General Practice at Magdalen College, Oxford. It was apparent from the discussion at this meeting that General Practitioners believed that if they were to act effectively in this field, they had to have clear cut information on current screening methods and the impact of early diagnosis of disease on the long term health of the patient. As a result of this view an Advisory Committee was set up by the Office of Health Economics. After much discussion this Committee came to the conclusion that the best method of furthering this issue was to ask experts in a number of relevant clinical fields to write short papers specifically for General Practitioners. These were to conform to a general pattern, to be authoritative and to indicate clearly the limitation of existing methods and of our knowledge of the natural history of selected common disorders. The first two on early diagnosis of raised arterial blood pressure and on visual defects are now ready for publication. Others will follow on diabetes, anaemia, cancer of the cervix, diseases of the lung, cancer of the breast, kidney disease, coronary heart disease, overweight and depression. It is hoped to publish these in pairs at approximately two-monthly intervals.

These studies are being published at a time when early diagnosis is a subject of great interest and discussion. The acceleration of work in this area has not only provided us with increased knowledge but it has also drawn to our attention the limitations and problems involved in the development of such techniques. Firstly, it has indicated the limitation of our current knowledge of the natural history of the various diseases. Frequently the screening technique measures a symptom rather than the cause of a disease. Hence its discovery may be of little use because its significance is not fully understood. Secondly, it now seems unlikely that a single parameter can invariably be relied on to define the presence or absence of a particular disease. Thirdly, and directly leading from this, it is in many cases becoming clear that there is no sharp demarcation between the abnormal and the normal state. The 'normal' for different individuals may vary considerably; in consequence it is impossible to establish a single but meaningful definition of what constitutes disease in its early stages.

However, it would be wrong to be pessimistic about the future. Advances in medical care have a habit of moving through a number of stages. Initially there is a flush of excitement and hope as a new technique or concept emerges. There follows a period of gentle disillusionment. But solid and persistent research usually continues and ultimately establishes the real significance of the development. Often this culminates in substantial advance. In the field of early diagnosis we have entered the second stage; I am hopeful that we shall continue through to find its true place in medical care, and to establish clearly its benefits to the community. In the meantime I trust that this series of OHE booklets will give a useful analysis of the present position and encourage medical practitioners and workers in the public health field to undertake selected studies in this field so that we can rapidly establish sound programmes to prevent a number of disorders which today cause so much morbidity.

R. E. Tunbridge

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HIGH blood pressure is not in its own right a common cause of death or of admission to hospital. It is however, a major factor associated with atherosclerosis and its complications. Arterial blood pressure tends to rise with age; in the sixth decade half of the population have blood pressures which would be defined as 'abnormal' by conventional criteria. Those with high blood pressure run a greater risk of mortality than those whose blood pressure is 'normal'.

However, the correlation between blood pressure and mortality is statistical rather than individual. Thus, hypertension as a disease must be defined by the presence of signs and symptoms in conjunction with the pressure level. It can be classified in three stages. At the first stage there is no objective sign of organic change in the cardio-vascular system. There is no evidence so far that treatment is effective at this time and there is a need for controlled studies to clarify this point. Should the value of treatment be established, the cost would be considerable because as many as ten per cent of the population might be eligible for it. At the second stage, objective signs of left ventricular hypertrophy appear. This may be most readily established with the electro cardiogram, but this is still a highly sensitive technique providing many false positives. Evidence suggests that the reduction of the level of blood cholesterol and of weight may prove effective as may the use of hypotensive agents. Detection of the disease at this stage is vital since effective therapy may prevent the onset of further serious conditions. Stage 3 occurs when the signs and symptoms of heart failure or manifestations of ischaemic heart disease are apparent. Treatment with hypotensive drugs must always be considered at this stage.

Effective treatment of hypertension requires the diagnosis of patients with early raised blood pressure and the regular surveillance of these patients even if treatment is not initially justified. The precise measurement of pressure is less important than the careful observation of other signs and symptoms.

However, more precise measurements are important for the epidemiological studies which are needed to determine the natural history of the disease, and the value of long-term treatment in Stage 1. The two usual ways of measuring arterial blood pressures are the intra arterial method and the cuff and sphygmonanometer. Variations in readings frequently occur between these two methods. One factor causing variation may be the effect of arm circumference on the cuff measurement. Variability may also be due to variations in the subject's arterial pressure at different times and to other aspects of the measuring technique. A clear understanding of 'high risk groups' necessitates a standardisation of the methods of measurement if we are to advance our knowledge of the true significance of variations in blood pressure.

THE importance of high blood pressure is that it is a major factor associated with atherosclerosis and its complications, mainly coronary and cerebrovascular disease. Tables A and B illustrate that high blood pressure on its own is not a common cause of death nor of admission to hospital (Table C). For coronary heart disease it is now well established that two-thirds of new cases in middle-aged men develop among those who have elevated blood pressure or serum cholesterol, or both.[1] These two latter risk factors carry approximately equal weight. It must be obvious, therefore, that prevention of coronary heart disease, not to mention other atherosclerotic disorders, depends, in part, in finding means to prevent high blood pressure. The problem is, however, one of definition and measurement—as to what levels of blood pressure are to be considered as raised.

Table A
Age-Sex Specific Mortality Rates for Hypertensive Disease per 100,000 England and Wales, 1965 (ISC 440-447)

Age (years)	*Male*	*Female*
15-44	1·7	0·8
45-64	27·7	21·4
65+	173·7	177·7
All ages	24·0	30·2

Table B
Proportionate Mortality (%) of Hypertensive Disease Compared to All Causes of Deaths England and Wales, 1965

Age (years)	*Males*	*Females*
15-44	1·1	0·9
45-64	1·9	2·0
65+	2·2	3·1
All ages	2·0	2·8

Table C
Discharge rates (spells) for hypertensive disease per 100,000 population in 1962 (Hospital In-Patient Enquiry)

Age (years)	*Male*	*Female*
15-44	20·0	19·0
45-64	127·0	88·0
65+	196·0	207·0

Proportion (%) of hospital discharges (spells) due to hypertensive disease compared to all diseases in 1962 (Hospital In-Patient Enquiry)

Age (years)	*Male*	*Female*
15-44	0·4	0·1
45-64	1·6	1·2
65+	1·3	1·8

THE MEASUREMENT OF BLOOD PRESSURE

Rose, Holland and Crowley[2] have summarised some of the principal sources of variation as a result of which different observers studying the same subject may obtain different blood pressure readings. This variability is due partly to true variation in the subject's arterial pressure and partly to measuring techniques. Well-known factors such as recent physical activity, the emotional state, room temperature, the position of the subject and arm, the absence of all restricted clothing, are liable to cause variations in the measurement of blood pressure. There are other abnormalities arising from instrumentation. The ordinary sphygmomanometer may provide inaccurate and biased readings of blood pressure due to a systematic error whereby one observer tends habitually to read higher or lower than another, terminal digit preference and prejudice for or against certain values. The first of these is serious because it leads to a false estimate of the mean pressure and the last two distort the frequency distribution curve. A further source of error is the size of cuff. Orma et al.[3] observed that blood pressure readings obtained with a sphygmomanometer using a cuff bag of 23 cm. in length were on average 23 mm. systolic and 19 mm. diastolic higher than the values obtained using the same apparatus with a cuff bag 33·5 cm. long. This error was

definitely correlated to the magnitude of the upper arm circumference. Karvonen et al.[4] demonstrated that the arm circumference as such had no effect on the error of the indirect blood pressure measurement when cuff size was taken into account. However, the thickness of the triceps skin-fold was negatively correlated with the error of the systolic measurement when a small cuff was used and with that of the diastolic phase 4 measurement with both large or small cuffs. They found that with a large bag random error was significantly smaller both for systolic and diastolic pressure.

In recent years numerous reports have appeared of discrepancies between arterial blood pressure measured by an intra-arterial method and by the usual cuff and sphygmomanometer. Part of this discrepancy has been attributed to the effect of arm circumference when arterial pressure is measured with a cuff. Corrections based on measurements made by Ragan and Bordley[5,6] have been published. The relation between sphygmomanometer reading and arm circumference is of more than academic interest. It has obvious implications in that arm circumference varies with sex, age, weight and physical demands of occupation, while clinically whether or not a man is accepted for life insurance or for a particular occupation may turn on an estimate of his arterial pressure made with a sphygmomanometer.

Several workers report good agreement between systolic blood pressure when determined by intra-arterial and cuff methods, but there is disagreement over which of the two phases, phase 4—muffling, or phase 5—disappearance, represents the true diastolic pressure. Pickering[7] concludes that indirect methods will under-estimate systolic and over-estimate diastolic pressures in adults of normal weight, while in the very obese both values will be over-estimated. Holland and Humerfelt[8], using a Hansen manometer and a method of recording blood pressure free from observer bias, found that the difference between direct and indirect methods was greater than had been previously assumed. They showed that there was a significant relation between differences in indirect and direct blood pressures and the level of direct blood blood pressure, particularly for diastolic pressure, so that the higher the direct blood pressure the greater the difference. In addition, there was a correlation between arm circumference and level of direct arterial blood pressure.

In an analysis of data on physique and occupation with indirect readings of arterial blood pressure for a population of over 5000 men aged 15 to 69, Lowe[9] confirmed that for a given age sphygmomanometer readings increase with body weight and that weight and arm circumference are highly correlated. When weight was corrected for, he found that the effect of arm circumference upon pressure reading was negligible and he concludes that the greater part, perhaps all, of the observed relationship between arm circumference and sphygmomanometer reading is attributable to close association between arm circumference and weight. On re-analysis of the data using a multiple regression technique, Khosla and Lowe[10] found that of the three variables, age, body weight and arm circumference, only age and body weight appear

to be significant predictors for sphygmomanometer readings of systolic and diastolic arterial pressure. They, therefore, conclude that the influence of arm circumference upon sphygmomanometer readings is indirect only and is due to high correlation with body weight. In effect, therefore, any attempt to correct sphygmomanometer pressure readings for arm circumference will eliminate the important influence of body weight. It must, however, be emphasised that this is indirect reasoning. Actual proof that the differences between intra-arterial and cuff blood pressures are not due to the effect of arm circumference will depend upon confirmation of Holland and Humerfelt's findings.

All these studies demonstrate some of the variability in the commonly-used method of recording arterial blood pressure. The finding of these inaccuracies and biases is of considerable importance for it is unquestionable that individuals with higher levels of blood pressure experience higher mortality from cardiac infarction[11].

There is, however, no statistically reliable cut off point. The risk is graded and to have arbitrary limits for selection and prognostication is in our present state of knowledge nonsensical, although pragmatic figures are essential if the effect of long-term treatment on the natural history is to be studied.

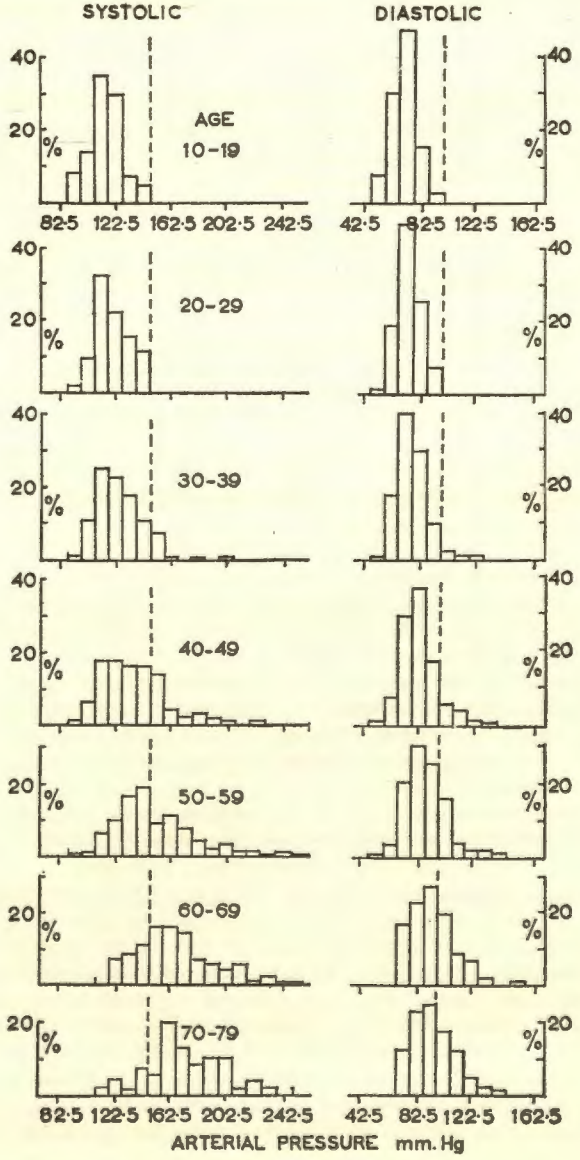
THE NATURAL HISTORY OF THE DISEASE

In patients with raised arterial blood pressure both systolic and diastolic pressures are usually elevated. Only in the elderly may systolic blood pressure be raised while diastolic pressure is normal or only slightly elevated. Such cases should probably be considered separately as the increased blood pressure probably represents a response to increased rigidity of the larger arteries. A minority of cases are due to recognisable causes such as renal or endocrine disease, coarctation of the aorta, or toxemia of pregnancy. However, for the great majority of individuals with elevated blood pressure no cause can be found.

When arterial hypertension runs an accelerated course leading in particular to severe renal and retinal lesions (including papilloedema), the term 'malignant hypertension' is used. This condition will not be referred to further.

Arterial pressure tends to rise with age. After age 40 the rise is faster in women than in men[12]. It has been common practice to regard as abnormal systolic pressures above 140 mm. and diastolic pressures above 90 mm. In the absence of a recognised abnormality known or suspected to be associated with hypertension, patients with pressures above these values have been labelled 'essential hypertension' and thus deemed to have a disease. Miall and Oldham's curves show that these values are exceeded by the bulk of the population aged 50 in females and aged 57 in males. That in the sixth decade half of the population seems to be abnormal should at least raise a doubt in the mind whether we are not 'being led up the garden path' intellectually speaking. This doubt is fortified by finding that there is no actual dividing

Figure 1
Frequency distribution of systolic and diastolic blood pressure for females of the population sample arranged by age in decades.



line in the frequency distribution curves and that the relation between arterial pressure and expectation of life is quantitative. No discontinuity has ever been demonstrated. (Figure 1).

Life insurance companies have the largest collective stake in relating measurable quantities to subsequent life expectation. Dublin et al.[13] state that it is clear that mortality rises steadily and markedly with increasing elevation of both systolic and diastolic pressure. The excessive mortality of individuals with hypertension is primarily due to cardiovascular-renal diseases. In the group with highest blood pressures included in this experience, and these are not conceived as seriously high by many clinicians, the mortality from cardiovascular-renal disease was nearly four and a half times the average for all standard risks.

Essential hypertension is usually classified into three stages. In Stage 1 there are no objective signs of organic change in the cardio-vascular system. Nevertheless, symptoms may be present which may be related to anxiety, but in some cases appear to be attributable to the raised blood pressure level. Stage 2 is based on the objective signs of left ventricular hypertrophy which may be established either by physical examination, radiography or electrocardiography.

The chief clinical sign of left ventricular hypertrophy is the heaving apex beat, especially if this is displaced downwards. There is considerable variation between different observers in evaluating this sign so that other methods of investigation are usually necessary to establish the presence of left ventricular hypertrophy.

Radiologically the heart may appear normal even when left ventricular hypertrophy is considerable. The relative lengthening and increased convexity of the left lower border in the postero-anterior position is strongly suggestive. Marked enlargement of the heart indicates that dilation is present as well as hypertrophy. Such individuals are properly placed in Stage 3.

The electrocardiogram probably provides the most reliable indication of left ventricular hypertrophy but at present there is no generally acceptable set of criteria. Unfortunately, too many criteria have been employed in the diagnosis and it has become clear that any one of these which is highly sensitive tends to produce many false positive results. It is probable that in the near future improved techniques will lead to revision of current concepts. With these reservations, high voltage criteria, as described by Sokolow and Lyon[14], R.V.5 or L.V.6+S.V.1=35 mm. or more, provide a reasonably clear basis for a provisional diagnosis of left ventricular hypertrophy in the adult. If these voltage criteria are extended to peripheral leads and if ST segment and T wave changes of the hypertrophic type are included, specificity is increased.

Stage 3 results from damage in various organs due to the hypertensive process or secondary vascular lesions. Characteristics of Stage 3 are the signs and symptoms of heart failure or manifestations of ischaemic heart disease, consequent on accelerated atherosclerotic changes in the coronary arteries. Physical examination may reveal dis-

placement of the apex beat outside the mid-clavicular line due to cardiac dilatation and this will be confirmed by marked widening of the heart shadow in the postero-anterior and left-anterior oblique views. Pulmonary congestion leads to increasing dyspnoea on exertion, although breathlessness as an isolated symptom is not sufficient to classify the patient in Stage 3. Paroxysmal nocturnal dyspnoea and other signs of heart failure may develop. There may be radiographic evidence of pulmonary congestion.

Cerebrovascular accidents are manifested by signs of persistent brain damage. Transient attacks of paralysis or sensory disturbance or hypertensive encephalopathy may occur and may be followed by persistent signs of organic vascular lesions. The term 'hypertensive encephalopathy' is used to indicate sudden and reversible attacks in which headaches,blindness, disorientation, convulsions and coma may occur.

The appearance of exudates, retinal oedema, haemorrhages and vascular thrombosis are unequivocal signs of Stage 3 arterial hypertension. The additional findings of bilateralpapilloedema indicates the development of the malignant course.

Difficulties may arise in distinguishing renal damage due to essential hypertension from primary renal disease. In the malignant phase renal involvement is almost invariable and progresses rapidly. In other cases of essential hypertension renal damage is not usually severe enough to give rise to symptoms. Nevertheless, proteinuria and impairment of renal function may be indicated by laboratory tests, particularly when the blood pressure is long-standing.

THE TREATMENT OF HIGH BLOOD PRESSURE

Real doubt exists as to the value of treatment of Stage 1 hypertension. There is evidence that nervous or emotional stress may be of importance at this stage. The role of environmental stress may vary in different age groups. It is generally agreed, therefore, that what may be described as common-sense psychotherapy is the most effective treatment, possibly combined with change in environment where symptoms are referable to anxiety. There is, as yet, no evidence that treatment with drugs is effective at this stage of the disease, either in prognosis or in the factors which may determine transition to later stages.

We do not know whether treatment of hypertension in Stage 1 can prevent development of Stage 2. Well-controlled studies should be undertaken, however, in order to clarify this question. The Anti-Coronary Club of New York[15] has demonstrated that since high levels of blood pressure are often associated with high levels of cholesterol and with obesity, reduction of the cholesterol diet and weight reduction may prove effective at this stage. Further controlled trials for this and for the use of hypotensive agents as well as any other suitable measures are necessary in order to determine whether Stage 1 hypertension is of any significance or not.

Detection of subjects with Stage 2 essential hypertension is important, since these

have definite evidence of impairment other than that of a purely raised blood pressure. Effective therapy may delay or avoid the severe developments of Stage 3. Thus congestive heart failure can be prevented and there is evidence that the risk of malignant hypertension is reduced. Whether cerebrovascular accidents can be prevented is a more controversial question but there are some reports that the incidence may be diminished.

It is obvious that patients in Stage 3 of essential hypertension must be considered for treatment with hypotensive drugs. In the treatment of heart failure, for example, these drugs can be extremely effective. Careful selection is necessary since the presence of certain complications may contra-indicate sudden or severe lowering of blood pressure. Apart from the urgent treatment of acute complications such as heart failure and encephalopathy blood pressure reduction should be carried out with caution in patients with severe ischaemic heart disease, renal stenosis or cerebrovascular disease.

In Stage 2 and Stage 3 essential hypertension there is no question that treatment should be given and is already being given but it is Stage 1 that would be discovered by screening or early diagnosis. If it is established that the treatment of raised blood pressure without any of the known symptoms or complications is of value then the implications in terms of cost and resources are considerable. At least 5-10 per cent of the population would be eligible for such treatment.

In order to diagnose patients with early raised blood pressure it is probably essential that individuals be examined at regular intervals and their blood pressure measured under standard conditions. By this means it may be possible to detect raised blood pressure soon enough and indicate those that are most susceptible.

The object of treatment of asymptomatic patients with hypertension is to improve prognosis while causing as little disturbance as possible to their lives. In the absence of complications treatment with drugs should not be instituted unless there is a clear indication. There is fairly convincing, although not unequivocal, evidence that the amount of benefit that the patient receives from treatment is proportional to the level to which the arterial pressure can be decreased. Statistically a patient will have a better prognosis if diastolic pressure is controlled below rather than at 105 mm. Hg. This must, however, be balanced against the difficulties and side effects that may accompany energetic efforts to control the blood pressure at a lower level. The patient's age must also be considered. The younger the patient the greater his potential life span and hence the greater potential benefits of good control of blood pressure.

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Office of Health Economics
162 Regent Street London W1

Series Editor John McKenzie

Printed by The Leagrave Press Ltd, Luton and London Nov 67.5