Hypertension: A Challenge in Preventive Medicine

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In discussing hypertension as a challenge in preventive medicine, I confine my remarks to benign essential hypertension, citing North American experience only, and I shall attempt to answer two questions—

‘Does the treatment of patients with benign essential hypertension do more good than harm?’ and ‘are those with benign essential hypertension receiving effective therapy?’

My answer to the first question will be ‘yes, with certain reservations’ and to the second ‘regrettably, but definitely no’.

Now to the first question. Good may come from the prevention of the complications of hypertension. This is easy to measure. Harm may arise from the side effects, expense and inconvenience of treatment, as well as from the worry of knowing one has hypertension. These factors are more difficult to quantify. However, on the basis of a double-blind randomised drug trial organised by the U.S. Veterans’ Administration Co-operative Study Group (VACSG), it would appear that treatment is likely to do more good than harm in hypertensive patients with the following characteristics: middle-aged and male, approximately 50 per cent black, diastolic pressures between 90 and 129, and with a prevalence of cardiovascular-renal abnormalities higher than in the general hypertensive population. The details of this drug trial are as follows (VACSG, 1967, 1970, 1972).

Patients were excluded from entry into the trial on the basis of failure to pass tests of reliability, and the presence, or history of, surgically curable hypertension, uraemia, concomitant fatal disease, grade III or IV changes in the optic fundi, cerebral or subarachnoid haemorrhage, dissecting aneurysm or congestive heart failure resistant to medical treatment.

It should be emphasised that the presence of conditions such as cerebrovascular thrombosis, myocardial infarction or diabetes mellitus did not exclude patients from the drug trial.

The tests of reliability were as follows. The initially selected patients entered a pre-trial period of 2 to 4 months during which they were given daily placebos containing riboflavin, a substance which produces fluorescence in
the urine. At each visit during the pre-trial period urine was examined for fluorescence and the remaining placebo tablets were counted. If on two successive clinic visits fluorescence was not noted in the urine or there was a greater than 10 per cent excess of the calculated tablets remaining, the patient was excluded from entry into the final trial. On this basis 50 per cent of the patients were excluded.

Active therapy for the final trial consisted of 0·2 mg of reserpine, 100 mg of hydrochlorothiazide and 150 mg of hydralazine daily.

The results of this trial were reported in 1967 for the group with diastolic pressures between 115 and 129, and in 1970 and 1972 for the group with diastolic pressures between 90 and 114.

First, the group with diastolic pressures 115 to 129. Table 1 shows the principal characteristics of the placebo and active therapy groups. All patients were male, and approximately half in each group were black. There was no significant difference between the two groups in mean age, duration of hypertension, diastolic pressure or, not shown here, in a complex score of degree of damage in kidneys, heart, fundi and cerebrovascular system. The mean duration of therapy was somewhat shorter in the placebo group. The mean change in diastolic pressure was 0 in the placebo group and −30 mm Hg in the active therapy group. Table 2 shows the number of patients with morbid events in each group. The total numbers of patients are shown in brackets. Neuroretinopathy refers to the appearance of grade III or IV changes in the optic fundi. The presence of coronary artery disease was inferred when myocardial infarction or sudden death occurred. It can be seen that there were 27 patients with morbid events in the placebo group and only two such patients in the active therapy group. Four deaths occurred in the former group, none in the latter.

Next the group with diastolic pressures between 90 and 114. Table 3 shows the principal characteristics of the placebo and active therapy groups. Again, all patients were male and somewhat less than half in each group were black. There was no significant difference between the two groups in mean age, duration of hypertension, diastolic pressure, duration of therapy or, not shown here, in a complex score of degree of damage in kidneys, heart, fundi and cerebrovascular system. The mean change in diastolic pressure was +1·2 in the placebo group and −17 mm Hg in the active therapy group. Table 4 shows the number of patients with morbid events in each group. The total numbers of patients are shown in brackets. Diastolic BP > 124 refers to those patients with this finding on three successive visits. Such patients were removed from the study. It can be seen that there were 76 patients with morbid events in the placebo group and 22 such patients receiving active therapy. Nineteen deaths occurred in the former group, eight in the latter. Treatment
Table 1. Characteristics of the group of patients with diastolic pressures 115–129 in the V.A. antihypertensive drug trial

| Characteristics                      | Placebo | Active therapy |
|--------------------------------------|---------|----------------|
| Number of patients                   | 70      | 73             |
| Number of blacks                     | 35      | 42             |
| Sex                                  | M       | M              |
| Mean age (years)                     | 51      | 50             |
| Mean duration hypertension (years)   | 5-4     | 5-3            |
| Mean diastolic BP                    | 121     | 121            |
| Mean duration therapy (months)       | 16      | 21             |
| Mean change of diastolic BP          | 0       | -30            |

Table 2. Morbid events in the group of patients with diastolic pressures 115–129 in the V.A. antihypertensive drug trial

| Morbid events                      | Placebo (70) | Active therapy (73) |
|------------------------------------|--------------|---------------------|
| Neuroretinopathy                   | 10           | 0                   |
| Cerebrovascular accident           | 4            | 1                   |
| Dissecting aneurysm                | 2            | 0                   |
| Renal damage                       | 2            | 0                   |
| Congestive heart failure           | 2            | 0                   |
| Coronary artery disease            | 3            | 0                   |
| Ruptured aortic aneurysm           | 1            | 0                   |
| Others                             | 3            | 1                   |
| Total                              | 27           | 2                   |

Table 3. Characteristics of the group of patients with diastolic pressures 90–114 in the V.A. antihypertensive drug trial

| Characteristics                      | Placebo | Active therapy |
|--------------------------------------|---------|----------------|
| Number of patients                   | 194     | 186            |
| Number of blacks                     | 81      | 76             |
| Sex                                  | M       | M              |
| Mean age (years)                     | 52      | 51             |
| Mean duration hypertension (years)   | 4-4     | 4-6            |
| Mean diastolic BP                    | 105     | 104            |
| Mean duration therapy (months)       | 3-3     | 3-2            |
| Mean change diastolic BP             | +1-2    | -17            |

was more effective in preventing stroke and congestive heart failure than in preventing the complications of coronary artery disease. The incidence of morbid events in relation to age at the start of the trial in this group of patients is shown in Table 5. The numbers in brackets in this table refer to the total number of patients in each group. It can be seen that the risk of developing a morbid event was markedly reduced by therapy even in the group of patients over 60.
Table 4. Morbid events in the group of patients with diastolic pressures 90–114 in the V.A. antihypertensive drug trial

| Morbid events                             | Placebo (194) | Active therapy (186) |
|-------------------------------------------|---------------|----------------------|
| Diastolic BP > 124                        | 20            | 0                    |
| Cerebrovascular accident                  | 20            | 5                    |
| Congestive heart failure                  | 11            | 0                    |
| Neuroretinopathy                          | 4             | 0                    |
| Renal damage                              | 3             | 0                    |
| Dissecting or ruptured aneurysm           | 2             | 1                    |
| Coronary artery disease                   | 13            | 11                   |
| Others                                    | 3             | 5                    |
| **Total**                                 | **76**        | **22**               |

Table 5. The incidence of morbid events in relation to age in the group of patients with diastolic pressures 90–114 in the V.A. antihypertensive drug trial

| Age at start | Incidence of morbid events |
|--------------|---------------------------|
|              | Placebo | Active therapy |
| <50 years old| 15% (99) | 7% (102) |
| 50–59        | 27% (52) | 9% (46) |
| 60+          | 63% (43) | 29% (38) |

Thus, it can be said from the V.A. study that treatment was effective in lowering the incidence of morbid events in a group of hypertensive subjects with the following characteristics: middle-aged and male, approximately 50 per cent black, diastolic pressures between 90 and 129 and with a prevalence of cardiovascular-renal abnormalities prior to entry that was higher than in the general hypertensive population.

In order to determine the effect of therapy in a more representative sample of the population with benign essential hypertension, the U.S. Public Health Service has launched a double-blind randomised drug trial. The patients in this trial differ from those in the V.A. trial just described. There is a lower percentage of blacks; approximately 20 per cent of subjects are female and the mean age is lower than in the V.A. study. The patients have a lower mean diastolic pressure and a lower prevalence of cardiovascular-renal abnormalities. A preliminary report of the results of this trial has appeared (U.S. Public Health Service Hospitals Co-operative Study Group, 1972).

While it shows a greater number of morbid events in the placebo group it is too early to assess the significance of this finding.

Now to the second question. Are those with benign essential hypertension...
receiving effective therapy? The answer to this question, for North America at least, is clearly 'no'.

Two surveys give evidence for this answer. The first was carried out by Schoenberger and his associates (1972) under the auspices of the Chicago Heart Association. Its purpose was to study the incidence of risk factors for coronary artery disease among industrial employees in metropolitan Chicago. To this end a series of tests was offered to all employees of a co-operating plant. The screening was carried out by nurse-technician teams. Among other tests, a single supine blood pressure reading was taken. The subject was said to be hypertensive if systolic pressure was equal to or greater than 160 and/or diastolic pressure was equal to or greater than 95 mm Hg. It is likely, with the single blood pressure reading and the criteria chosen for the diagnosis of hypertension, that the incidence of diastolic hypertension was over-estimated.

The results of this survey were as follows. Some 23,000 people were seen, the majority of whom were fairly evenly distributed between ages 20 and 59. Only eight per cent of patients were black. Twenty per cent of those surveyed were considered to be hypertensive by the criteria described. Of these, 60 per cent were unaware they had hypertension, 16 per cent knew but were on no therapy, 13 per cent knew, were apparently on therapy but were still hypertensive, and only 11 per cent who gave a history of hypertension were normotensive on treatment. Thus, 89 per cent of those deemed to be hypertensive were either not on therapy or the therapy was ineffective.

The second survey was more carefully done and was carried out by Wilber and his colleagues in Atlanta (Wilber and Barrow, 1972; Wilber et al., 1972). Women from the community were trained to take accurate blood pressures and to administer a questionnaire. Three sitting blood pressures were measured during a 15 minute interview. Subjects were said to be hypertensive on the basis of the following criteria. Those between the ages of 15 and 39 were deemed hypertensive, and were referred to their physician, if their mean blood pressure equalled or exceeded 160 systolic and/or 95 diastolic. The cut off point was 170/100 for the age group 40 to 64 and 180/100 for those over 64. With these criteria it is still possible that the incidence of diastolic hypertension was over-estimated.

The results of the survey were as follows. Some 6,000 people were seen in this middle-class black community. Twenty-three per cent of those surveyed were unaware they had hypertension, 23 per cent knew but were on no therapy, 12 per cent knew, were apparently on therapy but were still hypertensive, and 45 per cent who gave a history of hypertension were normotensive on treatment. Thus, 55 per cent of those considered to be hypertensive were either not on therapy or the therapy was ineffective.
Those who were found to be hypertensive in this survey were notified of this by letter, and were urged by phone or by letter at monthly intervals, for three months if necessary, to see their physician. Two hundred and eight of the untreated patients under 65 have undergone re-survey. One hundred and sixty-three of these had visited their physician and 120 had had antihypertensive drugs prescribed for them. Only 87 had persisted on treatment. Only 43 (21 per cent) of the total of 208 were normotensive on therapy.

Results similar to those of Wilber and his colleagues have been obtained by Silverberg (unpublished observations) in a survey of a predominantly white population in Edmonton, Alberta.

The reasons why so many patients in these surveys were not receiving effective therapy could lie at one or more of the steps required for the successful treatment of hypertension. These steps are shown in Table 6. The problem

| Table 6. Requirements for effective therapy of hypertension |
|------------------------------------------------------------|
| 1. Detection of hypertension                                |
| 2. Determination of type of hypertension                    |
| 3. Decision as to therapy                                   |
|    Yes or no                                                |
|    If yes—what regimen?                                     |
| 4. Convincing the patient to accept life-long treatment     |

with the patients, in the Atlanta survey at least, seemed to lie particularly in steps one and four, the detection of hypertension, and convincing the patient to accept life-long treatment.

With respect to step one in Table 6, I would strongly urge that everyone over the age of 40 have his blood pressure taken once a year. The means of achieving this goal require much study. One means that might be explored is the following. Each February in Canada there are long queues as people apply for their new automobile licence plates. On these occasions applicants might be given the opportunity to have their blood pressure taken with the understanding that, if they agreed, their licence plates would cost 50 cents less. With regard to two, the determination of the type of hypertension, I believe that in the vast majority of patients this process need not be difficult. I contend that, by means of careful history and physical examination and a few relatively simple tests, one can rule out, or be suspicious of the presence of, all secondary causes of hypertension (Table 7) except renal artery stenosis and primary aldosteronism. These tests are, for the renal diseases in this table, urinalysis,
Table 7. Classification of systemic hypertension

| Primary | Essential Hypertension |
|---------|------------------------|
| Second  | 1. Renal |
|         | (a) Glomerulonephritis |
|         | (b) Pyelonephritis |
|         | (c) Renal artery stenosis |
|         | (d) Coarctation of aorta |
|         | (e) Polycystic disease |
|         | (f) Collagen disease |
|         | (g) Eclampsia |
| Second  | 2. Neurogenic |
|         | (a) Anxiety |
|         | (b) Brain tumour |
|         | (c) Poliomyelitis |
| Second  | 3. Endocrine |
|         | (a) Acromegaly |
|         | (b) Primary hypothyroidism |
|         | (c) Phaeochromocytoma |
|         | (d) Adrenal cortical hyperfunction |
|         | (e) Oral contraceptive medication |

Table 8. Incidence (cases per 1,000) of secondary hypertension at the Cleveland Clinic during 1966 and 1967. Total number of hypertensive patients—4939

| Condition                     | Cases |
|-------------------------------|-------|
| Phaeochromocytoma             | 2     |
| Cushing’s syndrome            | 2     |
| Primary aldosteronism         | 4     |
| Coarctation of aorta          | 6     |
| Renal artery stenosis         | 45    |
| Renal parenchymal disease     | 50    |
| Essential hypertension        | 891   |

serum creatinine, urine culture and IVP. The tests for the endocrine conditions in this table are serum thyroxine, urine catecholamines, urine 17-hydroxy-corticoids and serum potassium. With respect to renal artery stenosis it is not a serious matter to miss this condition at first because in such patients one usually carries out a trial of drugs before considering surgery. And as far as primary aldosteronism is concerned, if the patient’s serum potassium is normal, the chance of his having this condition is extraordinarily small. But let us be more practical than this. Table 8 illustrates the incidence, in cases per 1,000, of secondary hypertension at the Cleveland Clinic during the years
1966 and 1967 (Gifford, 1969). At that time it was not fully realised that oral contraceptive medication could cause hypertension. It can be seen that almost 90 per cent of patients were found to have essential hypertension, approximately five per cent each had renal parenchymal disease and renal artery stenosis, and less than two per cent had other types of secondary hypertension.

On the basis of this information I would propose the following approach to the work-up of a new hypertensive patient: a careful history and physical examination plus urinalysis, serum creatinine and serum potassium determinations, and no further search for secondary types of hypertension unless indicated by clinical findings.

Now let us go on to the other requirements for effective therapy of hypertension (Table 6). Steps one and two have been discussed. With regard to step three, I believe that, in most cases, the treatment of benign essential hypertension can be made relatively simple.

But what about step four, convincing the patient to accept life-long treatment, realising full well that most patients will be asymptomatic at the time therapy should be begun and that therapy may be inconvenient, somewhat costly, at least in North America, and occasionally associated with adverse effects. Herein lies the problem of compliance which may be defined as the degree to which the patient adheres to appointment schedules and to the therapy prescribed. Published studies of this complex problem have not been models of scientific elegance (Haynes, 1973; Blackwell, 1972). Methods for assessing compliance have been imperfect. Description, let alone control, of the potential determinants of compliance has been inadequate. Properly designed clinical trials of measures which might improve compliance are hard to find. Nonetheless, some valuable information has emerged (Table 9). Education of patients with respect to the disease concerned, and the efficacy of preventive and/or therapeutic measures, has proved almost uniformly unsuccessful as a means of improving compliance. In contrast, tailoring has been successful in enhancing compliance with therapy in

| Table 9. Measures to improve patient compliance |
|-----------------------------------------------|
| Unsuccessful | Patient education |
| Successful | 'Tailoring' the regimen to the patient |
| | Fitting appointments to patient's schedule |
| | Minimising cost and complexity of regimen |
| | Fitting medications to patient's rituals |
| Under study | Behaviour modification techniques |

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a variety of diseases. For example, in an inner city hypertension clinic run by the Department of Medicine, Georgetown University, Washington, Finnerty et al. (1973) found that when particular attention was paid to ensuring that clinic waiting periods were short and drugs were given to patients without delay in the clinic, rather than with delay in the pharmacy, the number of drop-outs fell from 42 per cent to 8 per cent. Unfortunately, Finnerty et al. did not report the impact of these measures on the adherence of patients to their medical therapy.

Behaviour modification techniques have had little application in the field of patient compliance. At McMaster University Medical School, Dr David Sackett is now conducting a randomised trial of patient education, tailoring and behaviour modification techniques as means of improving compliance in hypertensive patients.

The delivery of effective therapy to hypertensive patients in the community at large is an enormous problem. Only a small fraction of these patients can be managed in university hospital clinics. The majority must be cared for by physicians in the community. The task of detecting, screening for secondary causes, and treating large numbers of hypertensive patients is an overwhelming one for the busy doctor. The magnitude of this task and the efforts that may be required to produce even a modest success are well illustrated by a recent study which took place in Berlin, a community of some 14,000 souls in New Hampshire (Charman, 1974).

The protocol for this study was organised jointly by physicians from Dartmouth Medical School and by the staff of the major community hospital in Berlin. An intensive pre-screening public and physician education programme was carried out by the New Hampshire Heart Association. The subjects of the study, some 2,700 persons, were employees of the two major industries in Berlin. Blood pressure detection teams were recruited from the community, trained at Dartmouth Medical School and subsequently worked in the industrial clinics. Blood pressures were measured in the supine position on three separate visits. Those persons who were found to have diastolic pressures of 90 or over on all three occasions were referred to their family physicians. Telephone contact was subsequently made with these patients and their physicians by staff from Dartmouth Medical School. The results of this study were as follows. The potential number of subjects to be screened was 2,760, of which 1,760 appeared for screening. One hundred and four of these, some six per cent, were found to be hypertensive by the criteria described. The lower prevalence of hypertension in these subjects was probably due to the fact that persons with hypertension had been given lower priority than normal subjects for jobs in these industries. Of the 104 persons with hypertension, a large
proportion, some 86, were still being followed up by their physicians at the end of one year. At that time 62 of these were apparently on antihypertensive medication. Unfortunately, the number who were normotensive on therapy was not reported. Thus, it took an immense effort to achieve moderate success in the detection and treatment of hypertensive patients in this small rural community.

In summary, despite the availability of beneficial antihypertensive drugs, there are many patients, in North America at least, who are not receiving effective therapy. To remedy this, great efforts are required in public and physician education, in health service research and in research on measures to improve patient compliance with antihypertensive treatment.

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