A Decade of Progress in the Management of Hypertension

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The central theme of this national conference on high blood pressure control is "A Decade of Progress in the Management of Hypertension." Before reviewing the past 10 years of progress, let me briefly describe the "Decades of Discovery" prior to 1973 when the National High Blood Pressure Education Program was established.

Background History
In the 1930s and early 1940s, little was known about the etiology of hypertension; management of the disease was primitive. We were able to discuss this common entity "unencumbered by scientific facts." Hypertension had been described as a symptom, not a cause, of arteriosclerosis. It was considered "essential" by some observers who believed that the increased pressure represented a necessary adjustment to supply adequate blood to the brain and kidneys. In fact, as late as 1949, the media had proclaimed, on the one hand, that hypertension was a serious disease, and on the other, that "when the facts are known about high blood pressure, we need not be alarmed and a brooding and paralyzing fear should lift from the land."

In the 1940s, facts began to replace the myths, and knowledge increased rapidly. Tobian, Dahl, and Menecley began to delineate the role of sodium in hypertension, when they demonstrated in rats that genetic susceptibility to hypertension could be unmasked by an increased sodium intake. Corcoran, Page, McCubbin, Braun-Menendez, and others began to define the role of baroreceptors and neurogenic stimuli. Goldblatt performed his ingenious experiments on the kidneys and renal arteries and demonstrated that a renal "hormone" might cause some cases of hypertension. Guyton's theory of autoregulation, and the investigations of Genest, Gunnells, Laragh, Conn, and Melby began to clarify the role of volume regulation, the renin-angiotensin system, and mineralocorticoids in hypertension.

In 1950, Drs. Page and Corcoran put these observations together as the mosaic theory, a theory that has stood the test of time (fig. 1).

Hypertension is indeed a mosaic, with a multifactorial causality that relates in part to a genetic predisposition, possibly to a defect in sodium handling by the kidney, or an inappropriately responsive sympathetic nervous system.

While these ongoing experimental studies continued in the 1940s to the 1960s, other data were being put in place to set the stage for the origination of the National High Blood Pressure Education Program in 1973. Kannel, Dawber, Castelli, Paul, Schoenberger, Stam...
and many others refused to accept the inevitability of an epidemic of cardiovascular disease that claimed more and more lives each year, and defined clinical clues that seemed to contribute to the epidemic.

Numerous epidemiologic studies including the Albany, Western Electric, Chicago People's Gas, Framingham, and L.A. County studies identified the risk factors as hypertension, smoking, elevated lipid levels, obesity, diabetes, and sedentary existence, which predispose us to cardiovascular diseases. They challenged clinicians and the public to change the risk factors and prevent the emergence of stroke, heart attack, or heart failure. They put in place the clinical observation that elevated blood pressure, whatever the cause, was a significant risk factor. In the 1950s and 1960s, as these facts were generated, treatment efforts were being increased.

Early treatments were primitive and often painful. It included the injection of typhoid bacilli or other pyrogens to lower blood pressure in patients with accelerated hypertension, with the explanation: “considering the dangers of the disease to the life of the patient, it is a small price to pay for its benefits.” Smithwick and Peet demonstrated that cutting the sympathetic nerves reduced blood pressure and saved lives, but fortunately, other methods were to supersede this extensive and painful surgery. The pioneering observations of Allen and Kempner that severe restriction of dietary sodium also lowered blood pressure were to set the stage for yet another approach to treatment.

Development of Antihypertensive Medications

In the 1950s, effective antihypertensive medications were finally made available. These early drugs were effective, but they had many side effects or disadvantages. A quote from an editorial in the Annals of Internal Medicine in 1955 summarized the state of the art at that time: “Treatment with antihypertensive drugs is in an experimental stage. They are dangerous if clumsily used. Treatment should be started in a hospital. The technique of administering them safely is too cumbersome for extensive use.”

Today, some of these early drugs are of historic interest only — hexamethonium, phenoxybenzamine, veratrum viride, ansolsylos. But these were the tools with which we treated hypertension in the 1950s when Page, Dustan, Gifford, Schroeder, Perry, Wilkins, Freis, Smirk, Moyer, Hooler, Pickering, and many others reported that hypertension could be controlled and lives prolonged with these “primitive drugs,” and with some of the newer drugs that had appeared — the thiazide diuretics, the rauwolfia drugs, and hydralazine. As more effective medications became available, it was necessary to document these initial experiences by long-term clinical trials.

Veterans Administration Study

The Veterans Administration Study, pioneered by Dr. Freis, examined a group of patients and demonstrated in the more severely hypertensive, that the lowering of blood pressure dramatically improved their outlook. Acute pulmonary edema and heart failure were virtually eliminated. Strokes, both hemorrhagic and thrombotic, were markedly decreased. Left ventricular hypertrophy was reversed and progression of renal disease halted in many patients whose blood pressure was lowered. A statistically significant decrease in the incidence of myocardial infarction or death from coronary artery disease was not, however, documented in treated hypertensives over a short period of time, and the benefits of treatment in the mildly hypertensive patient were not clearly established.

Public Health Study on Mild Hypertension

The Public Health Study on Mild Hypertension confirmed the Veterans Administration Study — hypertensive complications were reduced and progression to more severe disease prevented. Here again, however, no definite proof was forthcoming that the mortality from myocardial infarction or sudden death was reduced by therapy, although a trend in that direction was noted.

National High Blood Pressure Education Program

While other data were being gathered, but now with sufficient information in hand about the risk of hypertension and the benefit of treatment, the National High Blood Pressure Education Program was instituted in 1973. This program was parented by Mary Lasker and Secretary of Health Elliot Richardson and nurtured by Drs. Theodore Cooper and later by Dr. Robert Levy and Graham Ward; it was established to disseminate information about the “silent killer” and to initiate and expand detection and treatment programs.

Apparent from the beginning was the fact that the Federal Government, industry, organized medicine, many volunteer groups, and physicians, nurses, and other professionals could work together with a National High Blood Pressure Coordinating Committee to help control a major chronic illness. Task forces were established to summarize the “state of the art.”

Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure

The First Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure in 1977 established guidelines for the management of hypertension and introduced the Stepped Care approach to treatment. This was redefined in 1980 and is in the process of being updated for the third time. The program disseminated guidelines that stressed a scientifically acceptable and simplified diagnostic evaluation, encouraged community-wide screening programs, and elaborated on a method of treatment which, although not suitable for all patients, has been effective and widely accepted by professionals all over the world. I need not review the Stepped Care approach to treatment except to emphasize that it works in the majority of patients.
Position papers on hypertension in the elderly or in the adolescent, the role of weight control and sodium restriction in hypertension management, treatment at the worksite, and the problem of hypertension in minority groups were issued. The American Red Cross, pharmaceutical companies, the American Heart Association, the Citizens for the Treatment of High Blood Pressure, and many other organizations were in the forefront of this effort.

Volunteerism was an important factor in screening efforts in supermarkets, schools, and industry. Television and radio time were generously provided with help from the Ad Council. The Louisiana Program in Bogalusa, the Savannah Stroke Program, the Milwaukee Program, and our own program in Westchester County, where over 5000 individuals in the so-called “hard-to-reach group” are under therapy with excellent results are models of how communities can organize to combat a problem.

**Hypertension Detection and Follow-Up Program**

The recently completed Hypertension Detection and Follow-up Program (HDFP) Study attempted to clarify the effect of blood pressure lowering on less severe degrees of hypertension and on the incidence of myocardial infarctions and deaths from coronary heart disease. This was a multicenter study involving approximately 11,000 people; although it has been faulted in design, it has answered several questions. In this study, over 5000 individuals were randomly assigned to special treatment centers where they were rigorously treated so as to achieve goal blood pressure, utilizing the Stepped Care method of therapy (SC group). Another group of over 5000, the Referred Care (RC) group, were returned for usual and customary care. At the end of 5 years, blood pressure had been lowered in both groups, but to a lower level in a higher percentage of patients in the SC group. Overall mortality was reduced in the SC group; there was a 45% reduction in stroke death rates and, important, a reduction of 20% in deaths from myocardial infarction in the so-called mild hypertensive group (table 1). Benefit of therapy was noted in patients with mild degrees of hypertension, with diastolic pressures of 90–94, 94–99, or 100–104 mm Hg (table 2), even in those without evidence of prerandomization target-organ involvement. Benefit in black patients was especially marked. Recent data indicate that the incidence of angina and myocardial infarction was also decreased in the SC compared with the RC group.

The HFDP Study has been criticized because of the failure to include a placebo group. Some critics believe that it was not a trial of antihypertensive therapy but one that tested the effects of better overall medical care. There were no differences, however, in weight changes, smoking quit rates, and lipid levels between the RC and SC groups, and patients in both groups who survived had lower blood pressures (both systolic and diastolic) than those who died. Of importance was the finding that complications clearly linked to hypertension, specifically, left ventricular hypertrophy and strokes, were significantly reduced in the SC group. It would appear that the blood pressure levels made the difference. The HFDP Study, in my opinion, has answered the question — there is benefit from treating mild hypertension.

### Table 1. Results from the Hypertension Detection and Follow-Up Program (HDFP)

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>SC</th>
<th>RC</th>
<th>SC:RC % (reduction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke deaths</td>
<td>29</td>
<td>52</td>
<td>45</td>
</tr>
<tr>
<td>Myocardial infarction deaths</td>
<td>51</td>
<td>69</td>
<td>26</td>
</tr>
<tr>
<td>All coronary deaths</td>
<td>131</td>
<td>148</td>
<td>20</td>
</tr>
<tr>
<td>All cardiovascular deaths</td>
<td>195</td>
<td>240</td>
<td>26</td>
</tr>
<tr>
<td>All noncardiovascular deaths</td>
<td>154</td>
<td>179</td>
<td>13</td>
</tr>
<tr>
<td>SC = stepped care group; RC = referred care group (see ref. 7).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Percentage Reduction in Mortality in Stratum I Subjects According to Entry Characteristics in the Hypertension Detection and Follow-Up Program

<table>
<thead>
<tr>
<th>Entry characteristics</th>
<th>Stepped care</th>
<th>Referral care</th>
<th>Reduction in mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deaths (no.)</td>
<td>Rate/1000 patient-years</td>
<td>Deaths (no.)</td>
</tr>
<tr>
<td>Not on antihypertensive treatment and without target-organ damage*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entry diastolic blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90–94 mm Hg</td>
<td>36</td>
<td>7.0</td>
<td>54</td>
</tr>
<tr>
<td>95–99 mm Hg</td>
<td>39</td>
<td>8.4</td>
<td>53</td>
</tr>
<tr>
<td>100–104 mm Hg</td>
<td>31</td>
<td>9.3</td>
<td>44</td>
</tr>
</tbody>
</table>

*Target-organ damage included left ventricular hypertrophy on ECG, history of myocardial infarction, history of stroke, history of intermittent claudication, serum creatinine 1.7 mg/dl.
The Australian Therapeutic Trial in Mild Hypertension

The Australian Therapeutic Trial also demonstrated a reduction in cardiovascular mortality in treated patients compared to those on placebo, although the number of deaths and complications are few (table 3).

The Oslo Study

The Oslo Study, alone among the trials, appeared to demonstrate that there was no benefit to treatment. However, the artifact created by the Oslo Study was the result of small numbers of patients. The authors themselves have cautioned against the overinterpretation of their data, and yet some investigators point to this study to demonstrate the lack of benefit of treatment. Of great interest is that 17% of the patients maintained pressures at or progressed to pressures of 180/110 mm Hg or above and were transferred to the treatment group.

Discussion

A summary of the results of the therapeutic trials in hypertension is listed in table 4. It is clear that the treatment of mild hypertension is beneficial — and that benefit appears to outweigh risk (fig. 2).

Several prominent investigators have questioned the data above and have quite correctly noted that large numbers of patients may have to be treated to benefit a few; and that the benefit may not be worth the risk of treatment. When one reviews the results of the recent trials, however, it is apparent that the potential benefits are great; for example, in the HDFP Study, in mild uncomplicated hypertensives the deaths from cardiovascular disease were reduced from 8.7/1000 to 6.4/1000 patient years when the RC group was compared to the SC group, a potential decrease in deaths of 46,000/year, assuming that there are 20 million mild hypertensives. It is important, however, to select patients for therapy as carefully as possible and to minimize the risk of treatment by using drug therapy in minimal doses only when nonpharmacologic methods fail.
TABLE 5. Status of Hypertension Control

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. examined</td>
<td>6,672</td>
<td>22,929</td>
<td>6,012</td>
<td>158,906</td>
<td>11,534</td>
<td>117,954</td>
<td>1,656</td>
<td>56,078*</td>
</tr>
<tr>
<td>% DBP &gt; 95 mm Hg</td>
<td>15</td>
<td>20</td>
<td>23</td>
<td>13.2</td>
<td>23</td>
<td>13.2</td>
<td>14</td>
<td>7**</td>
</tr>
<tr>
<td>% Unaware HBP</td>
<td>43</td>
<td>59</td>
<td>19</td>
<td>25</td>
<td>21</td>
<td>11.9</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>% HBP being treated</td>
<td>36</td>
<td>25</td>
<td>57</td>
<td>54</td>
<td>60</td>
<td>76.1</td>
<td>69</td>
<td>87</td>
</tr>
<tr>
<td>% HBP under control</td>
<td>16</td>
<td>11</td>
<td>36</td>
<td>38</td>
<td>43</td>
<td>59.3</td>
<td>61</td>
<td>72</td>
</tr>
</tbody>
</table>

Data from Chicago were made available by Dr. David Berkson from the Chicago Board of Health.
*Includes unknown number of repeat examinations.

One of the issues that has been examined repeatedly over the past 10 years is the nonpharmacologic approach to hypertension management. Let us not forget that this was the approach that most investigators used in the 1940s and early 1950s, because there was nothing else to do. Although severe sodium restriction worked, it proved impractical. Moderate sodium restriction lowers blood pressure in some cases; in the majority, it is ineffective when used alone as therapy. Weight loss lowers blood pressure in many people; it is difficult to achieve and maintain. We must improve our approach to blood pressure management by behavioral modification, but we are not, however, at a point where these approaches can be advocated for definitive therapy in most patients. Certainly they are worth a try, along with a sensible exercise regimen prior to use of specific medications.

What have all of our efforts accomplished? We have begun to understand what hypertension is all about; we have much more to learn! We have learned that streamlining our diagnostic approach is effective. We have kept people out of the hospital. We have identified millions of individuals who were unaware of their hypertension, and we have got them under treatment. There has been a marked improvement in blood pressure control rates in the 1970s and 1980s, compared to the numbers of persons under effective treatment in the 1960s (table 5). There has been a marked decrease in the number of hypertensives who are not being adequately treated (as noted, the data from Westchester County and Chicago include an unknown number of repeat screenees and probably overstate the percentage of patients under treatment and control). Treatment has achieved blood pressure control in about 70% of the patients in many well-controlled treatment programs, including private practice experiences.

Has lowering blood pressure reduced mortality? The stroke death rate has decreased by over 45% in the past 15 years (fig. 3). Most of this change has occurred since the implementation of the National High Blood Pressure Education Program; a remarkable achievement. The downward slope of deaths that had begun in the 1960s and dropped at a rate of 1% to 1½% a year, has clearly accelerated to a rate of 5% to 6% a year since the institution of the program, despite an aging population. The dictum that the cardiovascular epidemic was unstoppable because our population was aging has proved to be false.

It is obviously simplistic to believe that the better management of hypertension was or is the sole reason for this dramatic change, since other modalities of care have also improved (table 6). Tobacco consumption is down by 22%, people are exercising more, saturated fat intake has been reduced by over 29% — but the coincidence is worth noting.

Figures for calculating these percentages were obtained from the U.S. Department of Agriculture.

TABLE 6. Change in Per Capita Consumption in the United States 1963-1975

<table>
<thead>
<tr>
<th>Product</th>
<th>Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>All tobacco products</td>
<td>22.4% decline</td>
</tr>
<tr>
<td>Fluid milk &amp; cream</td>
<td>19.2% decline</td>
</tr>
<tr>
<td>Butter</td>
<td>31.9% decline</td>
</tr>
<tr>
<td>Eggs</td>
<td>12.6% decline</td>
</tr>
<tr>
<td>Table salt (1971-81)</td>
<td>29.3% decline</td>
</tr>
<tr>
<td>Animal fats &amp; oils</td>
<td>56.7% decline</td>
</tr>
<tr>
<td>Vegetable fats &amp; oils</td>
<td>44.1% increase</td>
</tr>
</tbody>
</table>

Figures for calculating these percentages were obtained from the U.S. Department of Agriculture.
We have a long way to go. Our basic research efforts must continue. Behavioral and environmental research must help to define the aspects of hypertensive disease that can be prevented. We must clarify the roles of vasodilator substances in the kidney, of the newly discovered mineralocorticoids, of the sodium/potassium pump, and of genetic markers of hypertension. We must learn how to implement our knowledge that weight loss lowers blood pressure, redefine treatment practices to keep adherence to behavioral change or medication at a high level, and, above all, keep the cost of hypertension management at an affordable level. We must not overuse the newer medications and must continue to refine our uses of the old.

Finally, a cautionary note about overkill. Perhaps in our enthusiasm to conquer high blood pressure we have become alarmists. Hypertension is a risk, but in most cases it is not an immediate one and can be managed over time. Many patients may now be under treatment without having clearly established that they have hypertension. Let us be careful not to create a nation that is too blood pressure conscious. Sir George Pickering summarized some of these warnings in 1965 when he elaborated three cardinal rules for the management of hypertension: 1) "The first is never to frighten your patient. Many of the symptoms of those with mild or moderate elevations of pressure are due, not to the hypertension, but to the fear of the disease produced directly or indirectly by the doctor. Even when the hypertension is severe, it is nowadays usually treatable, and again there are no grounds for terrifying the patient to no good purpose." 2) "The second cardinal rule is to avoid petty interference with liberty and the enjoyment of life. Medicine is not yet liberated from the medical idea that disease is the result of sin and must be expiated by mortification of the flesh. Patients with elevated arterial pressure should not be allowed to become fat, otherwise restrictions should be imposed because of the presence of complications and not from fear of them." 3) "The third cardinal rule is no unnecessary instrumentation." These rules are perhaps even more important today than they were 30 years ago.

The decade of 1973–83 has indeed been a decade of progress, and I believe that we all can look forward to the challenge ahead with confidence.

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A decade of progress in the management of hypertension.

M Moser

_Hypertension_. 1983;5:808-813
doi: 10.1161/01.HYP.5.6.808

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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