Non-Drug Treatment of Hypertension

Medical Grand Rounds

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"The only way to keep your health is to eat what you don't want, drink what you don't like, and do what you'd rather not" - Mark Twain

"If we do not change our direction, we are likely to end up where we are headed" - Chinese proverb

Mild hypertension, defined as a diastolic blood pressure of 90 to 104 mm Hg, has become a therapeutic dilemma: the steadily rising pressure to treat is bringing many millions of asymptomatic people into lifetime drug therapy; at the same time the results of clinical trials have indicated that the risks of the drugs, for some, outweigh the benefits that can be gained from the lowering of the blood pressure that they accomplish. As the levels of hypertension considered to be in need of reduction have progressively come down, what was only recently a therapeutic adventure in balancing intolerable side effects against dangerously elevated blood pressures has now become commonplace: the treatment of hypertension is now the leading indication for the use of licit drugs (1).

The ever expanding drug therapy of mild hypertension fulfills a number of public and professional needs and wants: to justify the recognition of an asymptomatic disease present in millions of people -- why bother unless something will be done; to provide presumed protection, with the fond hope that here is a place that prevention can be actively practiced rather than passively preached; to fulfill the physician's role as healer; in short, to do something. Once having identified the danger, the availability of effective counter-measures almost guarantees their widespread use. In other words, "technological optimism and therapeutic activism" have been potent forces toward the increasing use of drugs to manage mild hypertension (2).

The increased use of drugs and the larger number of treated hypertensives likely has played a role in the significant declines in both coronary and stroke mortality rates in the United States that have occurred since 1968 (3). However, the impact of drug therapy of mild hypertension is hard to gauge: in the population of Rochester, Minnesota, stroke mortality rates have declined 76 per cent since 1950, primarily from a decrease in the incidence of new cases of cerebral infarction and hemorrhage (4), but these rates began falling in the early 1950s at a time before any but the most severe, malignant forms of hypertension were being treated, long before the advent of widespread therapy of mild hypertension.

I. CURRENT STATUS OF TREATMENT OF HYPERTENSION

A. Drug Therapy

In the United States, hypertension is now the leading indication for both outpatient visits to physicians (5) and the prescription of drugs (1). Of the drugs prescribed, diuretics are the most popular (Figure 1), reflecting the widespread acceptance of the "diuretic-first, stepped-care" approach (6).

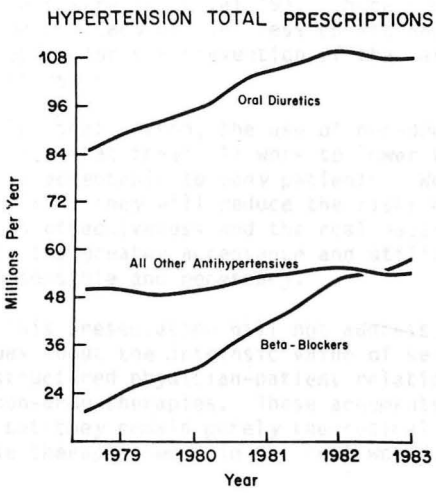

Figure 1: Estimates of the numbers of prescriptions filled in the United States for antihypertensive drugs from 1979 to 1983.

B. Non-Drug Therapy

On the other hand, non-drug therapies are less seldom applied for various reasons, including the common beliefs that they are relatively ineffectual (7) and very difficult to implement (8). In Wechsler et al's survey of primary-care physicians in Massachusetts, only 40 per cent felt that decreasing salt consumption was "very important" for the average person and only 7 per cent felt they were "very successful" in helping patients change their diets.

The lack of confidence in the effectiveness of non-drug therapies is almost certainly, at least in part, a reaction by physicians against the overly-enthusiastic advocacy of these manuevers by "true believers," as well as quacks and health gurus who promise major benefits, with little or no supporting evidence. Since they are constantly being admonished to accept no therapy until it has been found effective in properly performed clinical trials, physicians are only naturally suspicious of the claims of long-term benefits from non-drug therapies. Many likely are unwilling to spend the considerable time and effort needed to implement non-drug therapies in the absence of proof of their efficacy.

This leads to another dilemma: the nature of mild hypertension, slowly accelerating the development of atherosclerotic vascular disease, mandates massive and prolonged clinical trials to uncover protection by any therapeutic manuever. Witness the best of the currently available therapeutic trials: it took over 4 years of careful observation of over 3400 patients to demonstrate overall benefits of drug therapy over placebo

in the Australian trial (9). There seems no way to provide such evidence on the efficacy of even less potent and more difficult to monitor non-drug therapies for the prevention of the cardiovascular complications of mild hypertension.

For that reason, the use of non-drug therapies must be accepted on the evidence that they: 1) work to lower the blood pressure, 2) are safe, and 3) are acceptable to many patients. We do not and likely will not have proof that they will reduce the risks of hypertension. Considering the spotty effectiveness and the real hazards of currently used drug therapies (10), the greater acceptance and utilization of non-drug therapies seem both sensible and necessary.

This presentation will not address further the more philosophical issues about the intrinsic value of self-help and the need for a re-structured physician-patient relationship which are involved in the use of non-drug therapies. These arguments are strong justifications for their use but they remain purely theoretical in the absence of evidence that these therapies work in the real world.

II. PROBLEMS WITH CURRENT PRACTICE

Most physicians began to treat mild hypertension with drugs before there was any evidence that such treatment was beneficial. Once drug therapy had been proved effective in prevention of cardiovascular complications in patients with more severe degrees of hypertension in the late 1960s, the multiple forces previously identified began the inexorable push toward active therapy of those with mild hypertension as well.

A. Controlled Trials

At the same time, controlled clinical trials were started. Currently, 4 have been completed (9,11-13) and one more is in progress (14), along with at least 2 on the more restricted area of the elderly with pure systolic or combined hypertension (15,16). Yet another, on hypertensive patients who had survived a cerebrovascular accident, has been completed (17). Despite its provocative conclusions that drug therapy did not significantly reduce the rate of stroke recurrences or cardiovascular disease endpoints except for congestive heart failure, it will not be covered since the hypertension in these patients cannot be considered to be truly "mild." Similarly the results of the VA Cooperative (18) and USPHS (19) trials will not be included since they involved too few patients with mild hypertension to provide statistically valid data.

The designs of the 4 completed trials are shown in Table 1. They all used a diuretic as the first and often only drug in a stepped-care approach. The doses of diuretic, considered appropriate in the early 1970s, might be considered too large today and there were few attempts made to counter any metabolic aberrations induced by the therapies.

TABLE 1: TRIALS OF DRUG THERAPY FOR MILD HYPERTENSION

Trial	Range of DBP (mmHg)	Number of patients	Duration of Follow-up (years)	Drug regimen First	Second
Drugs vs Placebo					
Australian, 1980	95-110	3427	4	Chlorothiazide 500-1000	Propranolol, pindolol, methyldopa
Oslo, 1980	95-110	785	5.5	Hydrochloro-thiazide 50	Methyldopa, propranolol
More vs Less Drugs					
HDFP, 1979	90-104	7825	5	Chlorthalidone 25-100	Reserpine, methyldopa
MRFIT, 1982	90-	8012	6	Hydrochloro-thiazide 50-100 or chlorthalidone 50-100	Reserpine, methyldopa, propranolol

The Australian (9) and Oslo (11) trials were straightforward drug versus no-drug comparisons in patients with diastolic pressures between 95 and 110 mm Hg at the end of the screening process. Though this range extends 5 mm Hg beyond the usual definition of "mild" hypertension, the patients were all free of obvious cardiovascular complications at entry. On the other hand, the HDFP (10) and MRFIT (11) trials enrolled patients with all degrees of hypertension, with or without pre-existing cardiovascular disease. (Only the group with DBP between 90 to 104 mm Hg in the HDFP trial are included in the tables). Because they enrolled patients with all degrees of hypertension, the investigators felt obligated to offer therapy to all, but they provided more therapy to the half they managed than was given to the other half who were referred back to usual sources of care.

B. Results of Trails (Table 2)

The use of drugs (or more drugs) uniformly reduced mortality from cerebrovascular disease. But the mortality rates from coronary disease were less affected in the HDFP trial and adversely affected in the Oslo trial and the one-third of the MRFIT patients who had abnormal electrocardiograms on entry into the trial.

TABLE 2: TRIALS OF DRUG THERAPY FOR MILD HYPERTENSION
MORTALITY RATES PER 1000 PERSON-YEARS

TRIALS	Cerebrovascular Disease			Coronary Heart Disease		
Drugs vs Placebo	No Rx	Rx	Difference	No Rx	Rx	Difference
Australian, 1980	0.9	0.4	-56%	1.6	0.7	-56%
Oslo, 1980	1.0	0	-100%	1.0	2.7	+170%
More vs Less Drugs	Less	More		Less	More	
HDFP, 1979	1.6	0.9	-41%	5.6	4.5	-20%
MRFIT, 1982						
Normal ECG	not reported			3.4	2.6	-24%
Abnormal ECG	not reported			2.9	4.9	+70%

Most of the excess deaths in the treated half of the Oslo patients and the sub-group of the MRFIT population were sudden deaths. Though there is no way to ascertain the reason, the association between the larger doses of diuretics, the higher incidence of hypokalemia observed in the treated half, and the arrhythmogenic potential of hypokalemia strongly points to a connection between diuretic-induced hypokalemia and sudden deaths.

As of now, there is no evidence that one form of drug therapy is either safer or more protective against coronary disease than another. Hopefully the on-going MRC trial, comparing placebo against either a diuretic or a beta-blocker, will provide such evidence.

For now, drug therapy of mild hypertension can be said to have shown protection against stroke, as well as against congestive heart failure and progression of hypertension -- worthwhile and significant accomplishments. But, the spotty effects against what is by far the most serious and common complication of hypertension, coronary artery disease, must give pause to those who would advise routine, "early and aggressive" drug therapy for all patients with mild hypertension. As discussed elsewhere (20), the decision to use drugs seems best made on a consideration of all risk factors along with the level of blood pressure.

In keeping with this call for caution, the need to address the risks of even minimally elevated blood pressure while causing no harm brings us to consider the use of non-drug therapies.

III. NON-DRUG THERAPIES

As noted previously, the use of non-drug therapies must be predicated upon their antihypertensive efficacy, safety and acceptance by patients. The following will provide a critical look at their efficacy as demonstrated in published trials. Safety is rarely an issue, though all good things carried to an extreme may be harmful, despite Mae West's advice that "Too much of a good thing is wonderful." Patient acceptance is rarely mentioned, but it is likely that about as many patients will use a non-drug therapy as will take drugs, although the long-term adherence to drug therapy is probably better. Remember that in clinical practice as many as half of patients started on antihypertensive drugs will have stopped therapy one year later and, in some community surveys, only 20 to 30 per cent of known hypertensives are under good control (21).

Whatever the evidence that either drug or non-drug therapy lowers the blood pressure, that evidence must be weighed against claims for an antihypertensive effect from virtually everything that has been tried, including some - such as dilute hydrochloric-acid (22) and cholecystectomy (23) - that almost certainly are not effective. These "non-specific" effects likely reflect the progressive fall in blood pressure that occurs with repeated measurements (24), which could represent the statistical phenomenon of regression toward the mean or, more likely, the dampening of the psychological stress of the blood pressure measurements. Thus, blood pressures usually fall over the first few weeks of any therapy. Studies to demonstrate the efficacy of any therapy, drug or non-drug, must control for this effect. It may require more readings over a longer time than the 4 to 6 weeks most utilize: in the Australian Therapeutic Trail, the blood pressures of the patients on placebo continued to fall throughout the 36 months of observation, though most of the fall occurred between the third measurement taken at 4 weeks and the fourth at 4 months (25). (Figure 2).

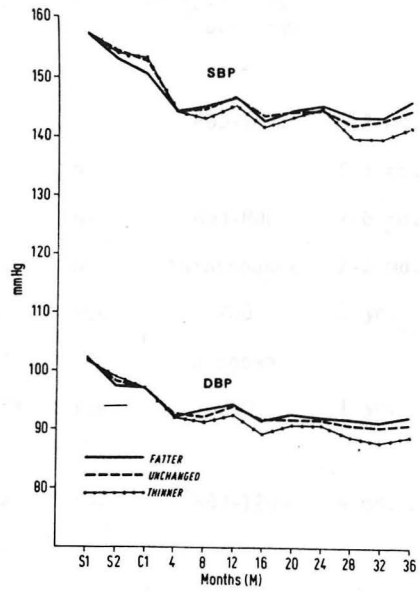

Figure 2: The mean systolic and diastolic blood pressures of the 1119 subjects who remained on placebo for 36 months in the Australian therapeutic trial in relation to weight changes. From Management Committee (25).

A. Weight Reduction

When people gain weight, their blood pressure usually increases and the frequency of hypertension is about two times higher in the obese than in the non-obese (26). In one study of obese hypertensives, blood pressure was positively correlated with fat-cell size but not fat-cell number (27). The mechanism by which weight gain induces hypertension is unknown, though hemodynamic studies usually find cardiac output to be elevated more than peripheral resistance (28). Increased levels of plasma norepinephrine have been found (29).

1. Effects of weight reduction

In careful studies involving small groups of patients, when weight is reduced, the blood pressure usually falls and the changes tend to go together. Both cardiac output and plasma norepinephrine levels usually fall in concert with the blood pressure (30).

The larger clinical evidence concerning the effect of weight loss is generally considered to be very strong (31) but as pointed out by Hovell (32), there have been pitifully few controlled studies to document the effects of weight loss on hypertension (Table 3). There are, in fact, only 4 published studies in which weight loss has been clearly dissociated from dietary sodium restriction (30,34,40,41).

TABLE 3: THE EFFECTS OF WEIGHT LOSS ON HYPERTENSION

STUDY (REF)	NO. PATIENTS	RANDOM SELECTION	DIET (calories per day)	DURATION	SODIUM INTAKE (mmol per day)	ANTI-HYPERTENSIVE DRUG TREATMENT	WEIGHT LOSS (kg)	BLOOD PRESSURE (mm Hg)	
								Initial	Change
Fletcher 1954	38	No	600-1000	6.4 mo.	unknown	No	-14.7	196/116	- 33/16
(33)	30	No		5.2 mo.	unknown	No	- 1.9	184/110	+ 0.5/1
Dahl 1958	6	No	600-800	2-6 mo.	175	No	-16.3	184/106	+ 3/4
(34)	6	No	Maintenance	2-6 mo.	5	No	- 2.4	195/108	- 52/23
Tyroler 1975	63	Yes	700	1 yr.	1 gm	18/63	- 8.2	167/103	- 18/13
(35)	64		unknown		unknown	36/64	- 1.8	168/101	- 12/8
Ramsay 1978	27*	Yes	800	1 yr.	unknown	Some	> 3.0	167/102	- 16/11
(36)							< 3.0		+ 6/4*
Reisin 1978	24	Yes	800-1200	4 mo.	+ 165	No	- 8.8	157/106	- 26/20
(37)	57				+ 185	Yes	- 9.8	172/113	- 37/23
	26				+ 155	Yes	- 0.7	171/109	- 7/2
Stamler 1980 (38)	67	No	unknown	5 yr.	unknown	No	- 4.5	147/96	- 12/9
Tuck 1981	15 (8HT)	Yes	320	12 wk.	120	No	-20.2	MAP=100	- 18
(39)	10 (4HT)				40	No	-20.2	MAP=105	- 19
Reisin 1983	12	No	800-1000	6 mo.	+ 176	No	-10	159/90	- 10/9
(30)	9				+ 168	No	+ 1	157/92	- 3/2
Fagerberg 1984	13	Yes	1200	8-12 wk.	190	No	- 9.2	151/89	- 5/5
(40)	3				87	No	- 8.8	151/89	- 13/10
Maxwell 1984	18	Yes	320	12 wk	40	No	-28	152/100	-30/21
(41)	12				210	No	-26	144/95	-26/23

* Only patients whose antihypertensive drugs were not changed during study

\+ 24 hour urine collected at end of study

MAP = Mean arterial pressure

In two of these studies, significant weight loss without sodium restriction was accompanied by either no fall in blood pressure (34) or less of a fall (40) than when sodium was restricted. The study often used as a clear demonstration that weight loss without sodium restriction is effective (37) suffers from the availability of only one 24 hour urine sodium determination at the end of the second month of a low calorie diet that was not designed to maintain a fixed level of sodium intake. Similarly, in the 1981 study by Tuck et al (39), both groups of patients were on a reduced sodium intake.

Two recent studies, however, show that weight loss is antihypertensive in the absence of dietary sodium restriction (30,41). In the 1983 study by Reisin et al, weight loss was effective without sodium restriction. In the study by Maxwell et al, weight loss was equally and significantly effective whether dietary sodium intake was 40 or 210 mmol per day.

2. Practical aspects

If the evidence is accepted that weight loss exerts an independent antihypertensive effect, the larger question still remains: how often does weight loss occur and persist in clinical practice. For the overall obese population, the results are poor, at best (42). In this review of all studies published from 1966 to 1977, the average weight loss was 5.4 kg and only about 20 per cent lost more than 9 kg. Though some find that more people in the general population have successfully lost weight than those who have been involved in a special weight loss program (43), the overall long-term success rate is likely no better than 20 per cent even with multidisciplinary programs involving very low calorie diets, nutritional education, behavior modification, and exercise (44). The problem may, at least in part, relate to diminished energy requirements in obese patients after they have lost weight, so that they must restrict their food intake to approximately 25 per cent less than anticipated on the basis of presumed metabolic needs (45). (Figure 3).

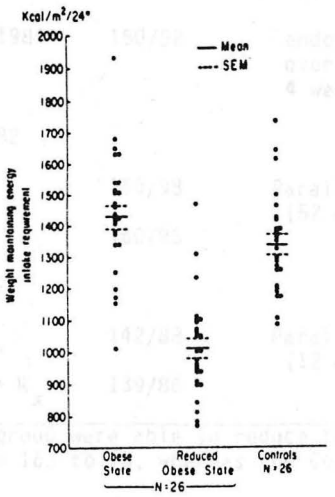

Figure 3: Seven-day weight maintaining energy intake requires (kcal/m^2/d) in 26 patients studied when obese and after substantial weight loss (reduced-obese state) in comparison to requirements of 26 never-obese normal weight controls. In all instances except one in which there was no change, per square meter energy requitements declined with weight loss. From Liebel and Hirsch (45).

In summary, weight loss though fairly easy to achieve seldom lasts; however, even small amounts of weight loss will usually lower the blood pressure. It seems logical to use the likelihood of a fairly certain fall in blood pressure to further motivate obese hypertensives to reduce their calorie intake. The observation of a falling blood pressure along with the falling weight should help keep them on a diet.

B. Sodium Restriction

High sodium intake is associated with a high frequency of hypertension and a marked reduction of sodium intake has long been known to cause a significant decrease in blood pressure (46). In more recent times, the effects of a more modest restriction of dietary sodium have been examined but the studies reported in the 1970s were poorly controlled, neither randomized nor blinded and often admixed with diuretic therapy (47-50).

1. Controlled trials

More recently, the results of more carefully controlled trials have been published (51-55) (Table 4).

TABLE 4: STUDIES OF MODERATE SODIUM RESTRICTION IN MILD HYPERTENSION

Reference	Initial BP	Design	Level of Urinary Sodium			Reduction in BP	
			Initial	- Low Sodium	- High Sodium	Low - Sodium	High Sodium
MacGregor, 1982 (51)	156/98	Random, cross-over, blind (8 week)	191	86	162	-12/6	-2/1
Watt, 1983 (52)	150/91	Random, cross-over, blind (8 week)	149	59	139	-10/5	-10/5
Richards, 1984 (53)	150/92	Random, cross-over; (three 4 week periods)		80	180	-5/2	
Silman, 1982 (54)							
Diet	165/98	Parallel (52 week)	143	117		-29/18	
Control	160/98		133		159		-20/11
Beard, 1982 (55)							
Diet + R_x	142/88	Parallel (12 week)	150	37		-11/6*	
Control + R_x	139/86		175		161		-6/3*

*The Diet group were able to reduce their daily total number tablets of antihypertensive drugs from 163 to 75, whereas the Control group reduced theirs only from 146 to 140.

The studies by MacGregor et at (51) and Watt et al (52) were similar in design, with small groups of patients initially placed on a diet containing 60 to 100 mmol per day of sodium and then randomly assigned to take either sodium chloride capsules to return sodium intake back to the pre-study level or identical-appearing placebo capsules, in a double-blind fashion. After 4 weeks, the order of capsules was crossed over for another 4 week interval.

The average blood pressure fell significantly in both studies during the lower sodium periods, 12/6 mm Hg in one (51), 10/5 in the other (52). However, the blood pressures in MacGregor et al's study returned almost to the pre-study level when sodium chloride capsules were taken (Figure 4), whereas the pressures were the same during both the lower and higher sodium periods in the study by Watt et al.

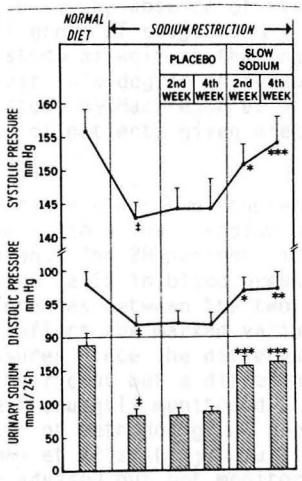

Figure 4: Average systolic and diastolic blood pressure and urinary sodium excretion on normal diet, two weeks on dietary sodium restriction alone, and at two weekly intervals during the randomized crossover trial of sodium capsules (slow sodium) versus placebo. From MacGregor et al, 1982 (51).

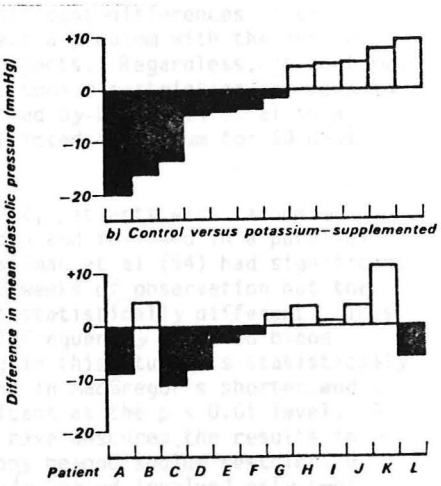

Figure 5: Differences in intra-arterial diastolic blood pressures (mean level recorded over 24h) for patients A to L between the control and sodium-restricted diets (top panel), and between control and potassium-supplemented diets (bottom panel). From Richards et al (53).

In the study by Richards et al (53), twelve hypertensives were randomly given, each for 4 to 6 weeks, one of 3 diets: a control diet with 180 mmol sodium and 60 mmol potassium; a sodium-restricted diet with 80 mmol sodium and 60 mmol potassium; a potassium supplemented diet, the same as the control diet plus 140 mmol per day of a flavored potassium elixir. In addition to repeated outpatient measurements of blood pressure and urinary electrolytes, the study involved 4 days of inpatient study at the end of each regimen. On the last day, 24-hour intra-arterial blood pressures were monitored. The differences of the mean 24-hour level between the control and the two other periods are shown in Figure 5.

Neither of these altered diets were associated with significant overall falls in blood pressure although 7 of the 12 had some fall on the lower sodium diet. Interestingly, all 5 whose blood pressures were higher on the sodium-restricted diet had taken that diet first, before the control diet. The patients displayed a trend for the blood pressure to fall with each succeeding period and there was a diet and order interaction approaching statistical significance ($p=0.09$).

Thus, the absence of statistically significant differences in this small group of subjects may partially reflect a problem with the design of the study as well as the small number of subjects. Regardless, it confirms the variable degree of response to moderate sodium restriction, as seen in the study by MacGregor et al (51) and reported by Longworth et al in a group of patients given diets variably restricted in sodium for 10 days (56).

In the other two studies shown in Table 4, patients were randomly placed into a lower-sodium or a control group and followed in a parallel fashion. The 28 patients in the study by Silman et al (54) had significant average falls in blood pressure over the 52 weeks of observation but the differences between the two groups were not statistically different. This may reflect the marked variability in the infrequently measured blood pressures since the difference of 9/7 mm Hg in this study was statistically insignificant but a difference of 10/5 mm Hg in MacGregor's shorter and more frequently monitored study was significant at the $p < 0.01$ level. A number of methodological problems may also have obscured the results in Silman et al's study: multiple interventions beyond sodium restriction were advised but not monitored; the pre-study period involved only two blood pressure recordings taken one month apart; half of the patients did not collect urine samples at 6 or 12 months, so that adherence to the diet cannot be documented.

The last study (55) involved 90 hypertensives who remained on antihypertensive drug therapy for 12 weeks during which half sharply reduced their dietary sodium intake to an average of only 37 mmol per day. This group had a greater fall in blood pressure despite the purposeful discontinuation of more than half of their daily total number of antihypertensive tablets, whereas the control group had to remain on almost the full amount of medication to achieve a lesser fall in blood pressure.

2. Practical aspects

In none of these studies did all hypertensives have a fall in blood pressure on a reduced sodium intake. Some have postulated that there are two populations, one sodium sensitive, the other sodium resistant (57), but there is more likely a continuum of responsiveness, with a greater response usually observed in the older, those with higher levels of blood pressure and those who have a lesser rise in renin-aldosterone levels (58).

There is no apparent potential for harm from moderate sodium restriction to a level of 75 to 100 mmol per day, achievable by deleting most high sodium foods from the diet and adding no extra sodium at the table or in the cooking. More rigid sodium restriction, to a level below 50 mmol per day, may not only be so difficult for patients to achieve that few would make the effort but may so stimulate the renin-angiotensin (59) and sympathetic nervous systems (60) as to limit both the antihypertensive and potassium sparing effects (61) of more moderate sodium restriction.

The proportion of patients who will follow a diet that is moderately reduced in sodium is not known. But the more convenient monitoring of urinary sodium chloride levels likely will help (62) and the increasing availability of processed foods that are either low in sodium or labelled with their sodium intake should make it relatively easy to reduce the daily sodium intake to a level of 75 to 100 mmol. Moreover, the taste preference for sodium has been shown to decrease after 3 months of moderately reduced (77 mmol per day) intake (63), so that such a diet should be more acceptable with time.

3. Sodium versus chloride

Until recently, all have assumed that the problems with sodium chloride relate to the sodium ion. However, studies on rats with two forms of sodium-dependent hypertension have shown that sodium in the form of sodium bicarbonate (64) or bicarbonate and ascorbate (65) did not raise the blood pressure, whereas sodium chloride did. Morgan gave 8 hypertensive men who were on a moderately low sodium diet (urinary sodium = 84 mmol per day), 70 mmol of either sodium chloride or sodium bicarbonate for 2 weeks each in a random, cross-over fashion (66). The mean supine blood pressures rose by 19/14 mm Hg with the sodium chloride but only 12/5 mm Hg with the sodium bicarbonate. There are no other such controlled studies of the affects of different forms of sodium in man, so the general applicability of these studies remains unknown. Since it is in the form of table salt or sodium chloride that most sodium is added to our food, the reduction of dietary sodium chloride will handle the problem, regardless of which component turns out to be the culprit.

4. Potential for prevention

Beyond the likelihood that moderate sodium restriction will lower the blood pressure of those with hypertension, there is hope that, if started early enough, it might prevent the development of the disease. In a study done on almost 500 infants in Belgium, the half who were given one-half as much sodium as usual for the first 6 months of life had a significantly lower blood pressure at the end of the 6 months than did those given the usual amount (67). Young, borderline hypertensives given a diet with 50 to 85 mmol of sodium per day for 6 weeks had a decrease in two features that may be involved in the pathogenesis of the disease, the intracellular concentration of sodium and the pressor responsiveness to stress (68).

In summary, then, moderate restriction of sodium intake may prevent or delay the development of hypertension; however, even if that turns out not to be true, there seems good reason to encourage all hypertensives to reduce the unnaturally high levels of sodium intake that we have only recently begun to consume. Since the taste preference we acquire for sodium has been shown to diminish after a few months of dietary restriction (63), there should be no permanent discomfort and, potentially, considerable benefit from moderate sodium reduction.

C. Potassium Supplementation

Both experimentally and clinically, many of the reported benefits of a reduced sodium intake may reflect an increased potassium intake since, whenever sodium is deleted from the diet, particularly by the substitution of natural foods for processed products, potassium intake increases. For many years, Meneely and co-workers have held that the high ratio of sodium to potassium in the diet of acculturated people was the important factor in the development of hypertension and that the reversal of this ratio back to that consumed by more primitive man would both prevent hypertension and help reduce that which has already developed (69). There is some evidence for this view in man: the blood pressure was inversely correlated with dietary intake and urinary excretion of potassium in blacks (but not whites) living in Evans County, Georgia (70). A meticulous analysis of body electrolyte content in 91 patients with essential hypertension also found an inverse correlation between plasma, exchangeable and total body potassium and the blood pressure (71). The lower blood pressure of vegetarians has been ascribed to their large intake of potassium (72).

1. Controlled trials

The intake of additional potassium has been shown to lower the blood pressure, some time ago in poorly controlled trials (73-75), more recently in somewhat better controlled ones (53,66,76-79) (Table 5). Though most of these are of short duration and open design, they show a uniform, albeit limited, fall in blood pressure by the addition of from 64 to 175 mmol of extra potassium a day. However, half of the 12 patients studied by Richards et al had some rise in their intra-arterial diastolic blood pressures on the potassium supplementation (Figure 5).

TABLE 5: STUDIES OF POTASSIUM SUPPLEMENTATION IN MILD HYPERTENSION

Reference	Inital BP	Design	Level of Urinary Excretion Sodium Control	Potassium Control	Potassium Added KCL	Reduction in BP Control	Reduction in BP Added KCL
Iimura 1981 (76)	114(MAP)	Open; 10 days of diet with 25 or 175 mmol KCL	158	41	123		-11(MAP)
Morgan 1982 (66)	158/101	Open; 2 weeks of 70 mmol KCl	156	46	113		-10/8
MacGregor 1982 (77)	154/99	Random, cross-over, double-blind; 4 weeks each of placebo or 64 mmol KCl	152	68	118	+1/0	-6/4
Smith 1983 (78)	156/93	Open; 12 days of 96 mmol KCl	134	65	128		-8/2
Overlack 1983 (79)	152/98	Open, 8 weeks of 100 mmol KCl	181	66	153		-17/10
Richards 1984 (53)	150/92	Random, cross-over (three 4 week periods)	180	60	200		-2/1

2. Mechanisms

The slight antihypertensive effect may reflect the natriuresis that follows the addition of potassium, as suggested by Addison in 1928 (73) and shown in numerous studies in animals (80,81) and man (82-84). The natriuresis is short in duration and moderate in degree but could explain much of the limited antihypertensive effect of potassium supplementation. A number of other mechanisms may also be involved, including: neural effects, direct vasodilation, suppression of renin secretion, and antagonism of natriuretic hormone or other inhibitors of cellular transport mechanisms (85). Hypokalemia is known to increase sodium content within cells by decreasing active transport (86). Potassium supplements appear to decrease intracellular sodium by activation of the Na-K-ATPase pump (87).

In summary, though the addition of potassium may reduce the hypertensive effect of a high sodium intake (88), the potential hazards and considerable cost of large amounts of potassium supplements make this practice unacceptable. A much more sensible approach is to reduce the intake of high sodium-low potassium processed foods and increase the intake of low sodium-high potassium natural foods (Table 6). In addition, KCL should be substituted either completely or partially for NaCl in cooking and at the table (89).

TABLE 6: COMPARISON OF SODIUM AND POTASSIUM IN PROCESSED AND UNPROCESSED FOODS (mg/100g)

Unprocessed foods	Na	K	Processed foods	Na	K
Flour, wheat	2	95	White bread	503	100
Rice, raw brown	8	210	Rice, instant	270	trace
Peas, uncooked	2	316	Peas, canned	236	96
Ham, fresh lean	71	288	Ham, cured lean	1,110	340
Beef, lean flank	65	360	Beef, corned	1,310	60

From: Church CF and Church HN. Food Values, 12th ed., J.B. Lippincott, 1975.

D. Calcium Supplementation

As highlighted by Blaustein (90), idiopathic (essential) hypertension is thought to represent an increased peripheral vascular tone as a consequence of increased intracellular calcium. Interestingly, the free calcium level within blood platelets, which was elevated in a manner closely correlated to the level of the blood pressure in patients with essential hypertension, was found to fall after successful lowering of the blood pressure not only by calcium-entry blockers, but also by beta-blockers or diuretics (91). The close relation was taken by the investigators to "provide further evidence for the important role of intracellular free calcium in vasoconstriction and points to a common calcium-related pathway of antihypertensive drug action" (91).

1. Controlled trials

On the other hand, evidence has recently been presented that the intake of too little, not too much, calcium is associated with hypertension and that oral calcium supplements may lower, not raise, the blood pressure (92). Belizan and Villar observed an increase in pregnancy-induced hypertension among women with a low calcium intake (93) and subsequently reported a fall in blood pressure after supplementation of the diet with 1 gram per day of elemental calcium, both in normal pregnant women (94) and in normal young adults (95). McCarron et al found that calcium intake, assessed by a 24 hour diet recall, was 22% less in 46 hypertensives than in 44 age-, race- and sex-matched normotensives (96). When similar data from a much larger, representative sample of the United States population were analyzed, the hypertensives again were found to have an 18% lower estimated calcium intake (92) (Figure 6).

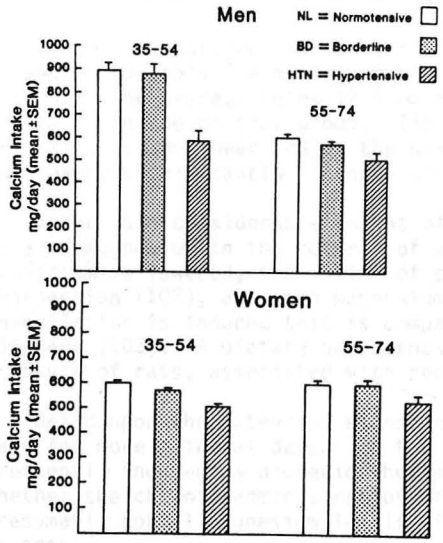

Figure 6: Mean ± SE of the calcium intake (mg/d) for men (top) and women (bottom) aged 35-54 and 55-74, categorized by blood pressure. Data from Health and Nutrition Examination Survey I, as reported by McCarron (92).

Subsequently, both McCarron and Morris (97) and Resnick et al (98) have presented preliminary data on the effects of supplemental calcium in patients with essential hypertension. In both studies, only a portion of the patients had a significant fall in blood pressure: 7 of the 15 in Resnick et al's fell more than 5%; 15 of the 32 in McCarron and Morris's fell more than 10 mm Hg.

2. Possible mechanisms

Obviously the evidence is incomplete. A number of possible abnormalities in calcium homeostasis may be at work in essential hypertension and, strange as it may seem, an increase in extracellular calcium concentration may inhibit calcium channels in vitro (99), so there is some experimental basis to the concept that extra calcium may lower the blood pressure. However, in rats, the antihypertensive effect of a high calcium diet appeared to be mediately entirely by concomitant phosphate deficiency and was independent of changes in PTH, blood calcium levels and fluid volume (100).

For now, the wisest course may be to ensure that, in the attempt to reduce dietary sodium and cholesterol, the dietary sources of calcium, mainly milk and cheese, not be reduced. Since many people are likely not ingesting an adequate amount of calcium, some increase in calcium intake should be helpful in reducing osteoporosis if not hypertension.

E. Magnesium Supplementation

Though long known to lower the blood pressure acutely in patients with hypertensive encephalopathy and renal insufficiency, the administration of magnesium on a more chronic basis may also lower the blood pressure (101). In this study, 20 of 39 hypertensive patients, all receiving a diuretic and potassium supplements, were randomly assigned to receive 15 mmol per day of

magnesium as aspartate hydrochloride for 6 months, while the other 19 served as controls. Nineteen of the 20 given magnesium had a fall in blood pressure, the average being 12/8 mm Hg (supine), whereas the average fell 0/4 mm Hg in the control group. Interestingly, the serum magnesium levels, initially at the lower end of the normal range at 0.76 mmol per liter, did not change significantly in those given the magnesium.

There is a considerable amount of experimental evidence for a major role of magnesium in the control of vascular tone. When extracellular magnesium is lowered, the influx of calcium into cells is enhanced causing contraction (102), and when magnesium is infused into human subjects, vasodilation is induced that is comparable to that seen with calcium entry blockade (103). A dietary deficiency of magnesium will raise the blood pressure of rats, associated with reduced microvascular lumen sizes (104).

Based upon the extensive experimental evidence, there is obviously a need for more clinical data. In the meantime, hypomagnesemia, which is frequently induced by diuretic therapy, should be avoided and corrected. Whether the chronic administration of extra magnesium to people with presumably normal magnesium levels will lower the blood pressure remains to be seen.

F. Other Dietary Changes

Other than for rare instances of toxic exposure to heavy metals inducing hypertension, there is no convincing evidence for a role of trace elements in the pathogenesis or treatment of hypertension (105).

1. Fat and fatty acids

On the other hand, a few controlled studies have shown that the blood pressure may respond to alterations in the type of macronutients. One of these examined the effect of a decrease in total fat along with an increase in polyunsaturated fat in people living in North Karelia, Finland (106) (Table 7).

TABLE 7: CONTROLLED TRIAL OF LOWER FAT OR LOWER SODIUM INTAKE
(data from Puska et al. Lancet 1981;1:1-5)

	Blood Pressure						All Patients Weights (Kg)	
	Normotensives			Hypertensives				
	No.	Initial	End	No.	Initial	End	Initial	End
Control	19	129/81	129/81	19	146/97	143/93*	70.6	70.8
Low Sodium (192 to 77 mmol)	19	132/83	130/80	15	148/98	147/94*	76.2	75.3
Low Fat (108 to 52 g)	19	127/80	122*/75*	16	152/99	139*/89*	75.1	74.4

*Difference from initial level significant at $p < 0.05$

Fifty seven couples were randomly allocated to 3 different diets for 6 week intervals: one group continued their usual diet, the second reduced their daily sodium intake from 192 mmol to 77 mmol, the third reduced their daily total fat intake from 108 g to 52 g and increased the polyunsaturated to saturated fat ratio from 0.27 to 0.98. In each group, about half of the subjects were hypertensive. There was little change in body weight or urinary potassium excretion. The systolic and diastolic blood pressures fell significantly in both the normotensive and the hypertensive subjects on the low saturated fat diet, whereas only the diastolic pressures fell to a lesser degree in the other two hypertensive groups on the control and low sodium diets.

A few other studies in man and a number of studies in hypertensive animals have shown an antihypertensive effect of increased intake of polyunsaturated fatty acids such as linoleic acid (107). Though the assumption has been made that the effect is mediated by way of an increased synthesis of vasodilatory prostaglandins, at least one study in hypertensive rats found an antihypertensive effect which was not mediated by changes in prostaglandin synthesis (108).

2. Vegetarian diets

Adherence to a vegetarian diet seems to be associated with a lowered blood pressure. When a group of 59 healthy omnivorous subjects were randomly assigned to a control group whose diet was unchanged or to either a vegetarian or an omnivorous diet for 6 weeks and then crossed-over to the other diet for another 6 weeks, a 5 to 6 mm Hg systolic and 2 to 3 mm Hg diastolic fall was observed with the vegetarian diet (109) (Figure 7).

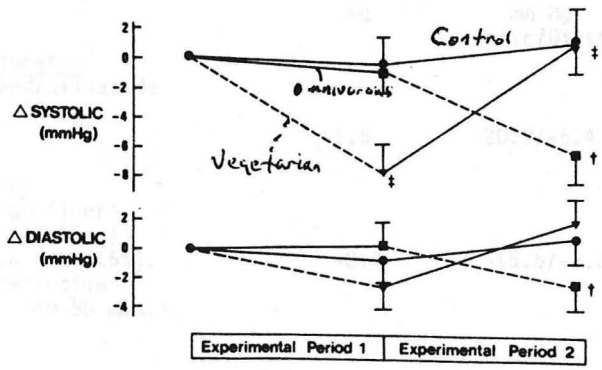

Figure 7: Mean ± SEM changes in resting blood pressures in control groups, experimental group I given omnivorous diet first, and experimental group II given vegetarian diet first. Broken line = vegetarian diet, solid line = omnivorous diet. From Rouse et al (109).

What it is about a vegetarian diet that lowers the blood pressure is unknown but, in addition to the possible effect of its increased potassium content (72), its increased amount of fiber may also play a role (110).

3. Others

Dietary protein intake is thought to markedly affect renal function but it seems to bear no relationship to levels of blood pressure (111). Similarly, variations in the amount and character of dietary carbohydrate intake seem to have little beyond a transient effect (112).

In animals, garlic extract has a potent though transient antihypertensive effect (113). Despite its wide use as a folk remedy for many ailments, no controlled trials of its use in man have been reported.

Just eating less may help: rats maintained on only 40% of the usual laboratory rat diet have an increased life span (114). The life-span increased from 18 months to over 30 months in spontaneously hypertensive rats and from 24 to over 32 months in normotensive rats.

The long-term value of these diverse dietary changes in the practical management of hypertension remains largely unknown but a number of simultaneous changes in diet may make a major difference, as shown in the study by Pacy et al (115) upon 50 hypertensive diabetics randomly assigned to either a daily dose of a diuretic or a low sodium, low fat, high fiber diet (Table 8).

TABLE 8: CHANGES AFTER 3 MONTHS THERAPY WITH DIURETIC OR DIET

25 Diabetic Hypertensives in Each Group

	Weight kg	Blood Pressure mm Hg Systolic/Diastolic	Total Cholesterol mg/dl	HDL_2 Cholesterol mg/dl	Glycosylated Hemoglobin %
Diuretic Bendrofluazide 10 mg	-1.6	-20.9/-6.4	+8	+4	+0.9
Diet High fiber (30-45 g) low fat (15%), low sodium (40-50 mmol)	-2.9	-15.5/-8.6	-4	+8	-1.6

From: Pacy PJ et al (115)

Not only was the mean blood pressure equally lowered by the diet but the blood lipids and diabetic control that were adversely affected by the diuretic were favorably changed by the diet. Thus, for many hypertensive patients, a major overhaul of the diet may be an effective way to lower the blood pressure.

G. Exercise

Beyond all of these alterations in diet, a number of other practices have been advocated as effective ways to lower the blood pressure, none more fervently than physical exercise. There is some evidence that those who are physically active and fit may develop less hypertension (116,117) and even more evidence that those who are hypertensive will achieve a lowering of their blood pressure by regular isotonic exercise (118-127). For at least 30 minutes after a period of isotonic exercise, the systolic blood pressure remains 25 per cent below the pre-exercise level (128). But the persistent effect of intermittent periods of exercise has been more difficult to document, in part because of the difficulty in isolating the effects of exercise per se from a variety of changes that usually occur with regular vigorous physical activity.

1. Effects on development of CHD and hypertension

Data from the Framingham study show that those who are more physically active, based on the number of hours spent at activities with assigned calorie expenditures, have a lower risk of developing or dying from coronary heart disease (129) (Figure 8). Furthermore, in this population, those who displayed objective evidences of poor physical fitness, i.e. more obesity, faster heart rate and lower vital capacity, had a higher risk of CHD mortality. In these and other such data, there lurks the confounding effect of selection: those who exercise and become fit may already be protected by various features ranging from a lesser genetic load of traits that predispose to early CHD disease, to a less atherogenic diet, to a more relaxed mood. Most investigators try to adjust for these variables but the possible bias remains a problem.

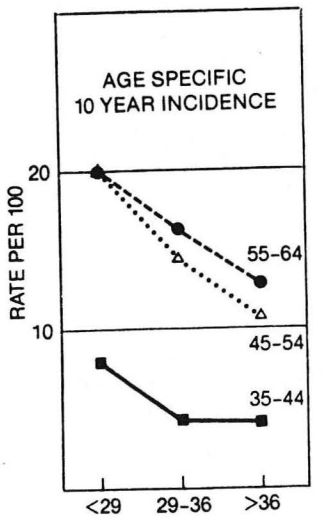

Figure 8: Risk of coronary heart disease in 10 years according to age and physical activity status of men 35-69 at exam 4 of the Framingham study. The higher the score, the greater the level of physical activities. From Kannel (129).

The manner by which exercise may protect against cardiovascular disease likely involves a number of mechanisms, including these: reduction in cigarette smoking and obesity, improvement in blood lipid profiles (130), changes in carbohydrate metabolism (131), increased tissue perfusion (132), reduction in perception and response to psychological stress (133) and remodelling of cardiac and arterial structure (134).

The prevention of hypertension is another possible way by which exercise may help. Paffenbarger et al followed 14,998 Harvard male alumni for 16 to 50 years and found that those who did not engage in vigorous sports play were at 35 per cent greater risk for developing hypertension, whether or not they had higher blood pressures while at Harvard, a family history of hypertension, or obesity, all of which also increased the risk of hypertension (116) (Figure 9). In a similar vein, normotensive people who were at a low physical fitness, assessed by maximal treadmill testing at the Aerobics Center in Dallas, had a 52 per cent greater relative risk for developing hypertension over the next 1 to 12 years when compared to people initially at high physical fitness (117).

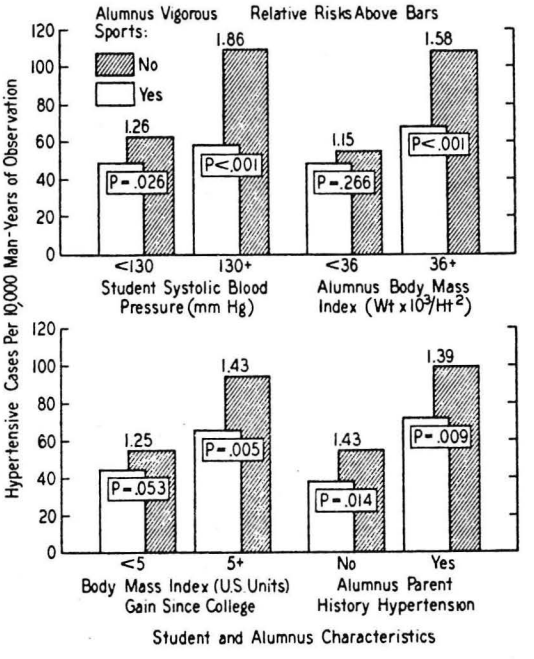

Figure 9: Age-adjusted incidence rates and relative risks of hypertension by paired combinations of vigorous sports play and other characteristics of Harvard male alumni 16 to 50 years after graduation over a 6-10 year follow-up (1962 or 1966 to 1972). From Paffenbarger et al (116).

2. Effects on established hypertension

Beyond these possible preventive effects, exercise may lower blood pressures that are already elevated (Table 9). All of these studies involved isotonic exercise. During isometric exercise, both systolic and

diastolic pressures rise, often to very high levels (135). Beyond one uncontrolled study (136), there are no data showing a beneficial effect of isometric exercise in patients with hypertension. In view of the potential for acute vascular damage from the high levels of pressure during static muscular contractions, the prudent course would be to caution against isometric exercise. This caution should not be carried too far: the largely isometric exercise of sexual intercourse may cause the blood pressure to rise in concert with the passion but, like handgrip, the rise is transient (137).

TABLE 9: EFFECTS OF ISOTONIC EXERCISE TRAINING ON SELECTED HYPERTENSIVE PATIENTS

Reference	No. of Subjects	Pre-Exercise BP Monitoring	Anti HT Therapy	Exercise Hours Per Week	Program Duration (Months)	Resting Blood Pressure Initial mm Hg	Resting Blood Pressure Change mm Hg	Weight Change kg
Johnson, 1967 (119)	4	Yes	No	1/2 x 3	?	188/103	+7/2	"None"
Hanson, 1970 (120)	6	Yes	2/6	1 x 3	7	150/86	-16/11	
Boyer, 1970 (121)	23	Yes	Yes	1/2 x 2	6	MAP=105	-13/12	-1.1
Sannerstedt, 1973 (122)	5	No	No	1 x 3	1.5	MAP=108	-5	-3.2
Choquette, 1973 (123)	37	No	No	1 x 2	6	136/90	-15/8	+0.2
Ressl, 1977 (124)	10	No	No	1/2 x 5	1	182/99	-6/1	-3.0
Krotkiewski, 1979 (125)	27	No	No	1 x 3	6	134/87	-9/7	+1.2
Roman, 1981 (126)	27	Yes	No	1/2 x 3	3-24	182/113	-20/18	
Hagberg, 1983 (127)	9	Yes	No	1/2 x 5	6	141/91	-8/11	"None"

On the other hand, when hypertensives who are not trained or conditioned perform isotonic exercise, they usually undergo hemodynamic changes which are moderately accentuated beyond those seen in untrained normotensives (138). Those who are soon to become hypertensive may have an even greater rise in systolic pressure compared to those who remain normotensive or a rise in diastolic pressure (139), suggesting that the response to isotonic exercise may become a practical prognostic indicator for the appearance of hypertension.

After training, hypertensives display indications of a lower level of sympathetic activity (133,140) which may be responsible for their lower resting and post-exercise blood pressures. The studies of the effects of isotonic exercise upon hypertensive patients mostly involved enough exercise to reach a trained or conditioned state. In all but one, falls in resting blood pressures were observed which usually could not be attributed to weight loss (Table 9). However, none of these studies involved randomly chosen patients who were compared in a parallel fashion with similar patients who did not exercise and few involved repetitive pre-exercise monitoring of the blood pressure.

The studies by Roman et al (126) and Hagberg et al (127) involved continued monitoring of the patients after cessation of the exercise. In both, the blood pressures tended to return near, though not quite to, the pre-exercise level, providing additional evidence that the fall in blood pressure observed during the exercise was related to the exercise per se.

3. Effects of antihypertensive therapy upon exercise

In view of the apparent benefits of regular isotonic exercise, more and more hypertensives will likely engage in this activity, many of them while taking antihypertensive drugs. Some of these drugs may pose problems to those who exercise: diuretic-inducted hypokalemia may decrease muscle blood flow (141); beta-blockers inhibit exercise-induced increases in heart rate and cardiac output and may blunt performance (142). Nonetheless, the hemodynamic responses to both isometric (143) and isotonic exercise (144) can break through beta-blockade and a training effect can be achieved. Moreover, hypertensives made normotensive with a diuretic and a beta-blocker may still show a significant rise in diastolic blood pressure with isotonic exercise (145). In the future, the normalization of the response to exercise may be used to document the optimal level of blood pressure control.

4. Practical aspects

Regardless of whether exercise can lower an elevated blood pressure, it offers multiple attractive - though largely unproved - advantages. Transient beneficial effects are fairly easy to demonstrate, particularly when combined with a stringent diet (146). But, in the absence of any proof of longer survival of those who exercise regularly, it may be true that "joggers don't live longer, it just seems like it." Perhaps there is a lesson to be learned from studies done at SMU on houseflies: those whose normal flight activity was restricted had a twice longer life span than did high-activity flies (147).

If we encourage hypertensives to exercise, we should not promise more than it can provide. The majority of those who start an exercise program do not stick with it (148). We should guard against zealous over-sell and coercion, as might arise in work-site programs. As stated by Haynes: "Until better evidence is produced demonstrating substantive and persisting benefits of exercise programs, potential and actual participants should decide for themselves whether they will comply with all or part of the program." (148).

H. Relaxation

Some of the antihypertensive effects of exercise could reflect the more relaxed feeling that may accompany physical activity. On the other hand, purposeful muscular relaxation has long been noted to lower the blood pressure in many hypertensives (149, 150). In recent years, considerable evidence from studies in both animals and humans has implicated a role of behavorial stress in the pathogenesis of primary (essential) hypertension, often in concert with a high sodium intake (151, 152). Along with this evidence, an increasing number of studies, a few well controlled, have shown that reduction of behavorial stress by various techniques will reduce the blood pressure, both during the relaxation therapy and for prolonged periods thereafter (153-158) (Figure 10). However, a smaller number of similarly controlled studies have failed to show a significant effect in most patients (159-161).

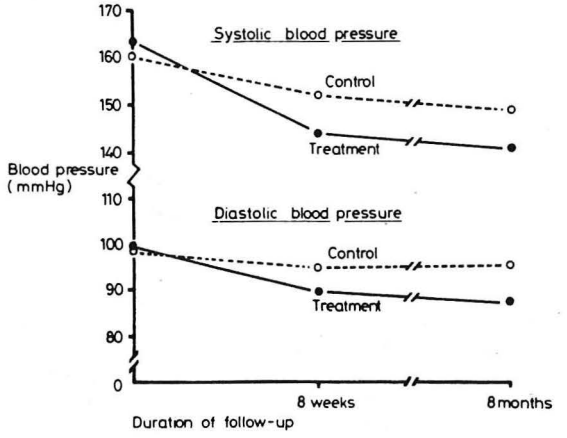

Figure 10: Changes in systolic and diastolic blood pressures at 8 weeks and 8 months in 50 hypertensive patients who received biofeedback and relaxation therapy and 43 similar patients wh did not. From Patel et al (153).

A number of reviews of the evidence on the effectiveness of relaxation therapy available prior to 1980 were cautiously optimistic but uniformly decried the lack of carefully controlled studies and long-term follow-up (162-164). The additional studies shown in Table 10 provide some additional evidence of a statistically (and perhaps clinically) significant fall in blood pressure, greater than that seen by other patients followed in parallel without relaxation.

TABLE 10: EFFECTS OF RELAXATION THERAPY ON HYPERTENSIVE PATIENTS

Reference	No. of Subjects	Anti HT Therapy	Relaxation Program	Duration of followup	Resting Blood Pressure Initial mm Hg	Change mm Hg
Patel, 1981 (153)	43	No	None		160/98	-11/3
	50	No	Biofeedback-relaxation	6 mo	163/100	-22/11
Luborsky, 1982 (161)	7	Yes	None	6 weeks	138/89	-12/10
	15	No	Relaxation		142/88	-8/3
	9	No	Biofeedback		140/87	-4/1
	8	No	Exercise		137/87	+2/1
Glasgow, 1982 (154) and	20	44/90	None	6 months	143/94	-5/3
Engel, 1983 (155)	70		Relaxation and/or Biofeedback			-5/3
						-8/5
	60 (of 90 above)	33/60	Relaxation and/or Biofeedback	6 months later		-5/7
Peled-Ney, 1984 (158)	30	Yes	None	6 months	147/98	-1/+1
	40	Yes	Group therapy		152/100	-21/13
			Group therapy	3 months later		-16/11

The study by Patel et al (153) remains the best designed: it randomly allocated a group of newly recognized untreated hypertensives to either no therapy or a behavorial modification program involving one-hour group biofeedback sessions once a week for 8 weeks and twice daily relaxation at home. After the active phase, the treated patients were asked to continue to practice relaxation twice a day but they were not seen again until 6 months later. The differences in both systolic and diastolic blood pressures were highly significant both at 8 weeks and 6 months later, as shown in Figure 10.

In addition, the patients followed by Engel et al (155) and Peled-Ney et al (158) for at least 3 to 6 months generally showed continued lowering of the blood pressure. These patients were also randomly assigned to relaxation therapy, so the evidence from these studies does appear to be methodologically strong.

1. Mechanism of action

The manner by which various relaxation therapies lower the blood pressure may be akin to that often observed with placebo and almost always observed with bed rest (165). These manuevers all tend to lower the plasma level of catecholamines (165) and renin-aldosterone (153). Contrary to these observations, Hoffman et al reported that plasma norepinephrine levels after standing and isometric exercise rose to a higher level in subjects who elicited the relaxation response than in a control group (166). However, the responses of heart rate and blood pressure to these stresses were similar in the two groups. The dichotomy between higher plasma norepinephrine levels but no greater changes in pulse and blood pressure was interpreted as reflecting reduced end-organ responsivity to norepinephrine after regular elicitation of the relaxation response (166).

In whatever manner the effect of relaxation is mediated, it may depend upon the patient's expectations: when a group of 30 hypertensives underwent the same relaxation training, the 15 who were told to expect immediate lowering of their blood pressure had a 17.0 mm Hg lowering of the systolic level; the 15 who were told to expect a delayed effect had a 2.4 mm Hg lowering during the same interval (156). The diastolic levels fell equally in the two groups, by 7.1 and 6.3 mm Hg, respectively.

2. Practical aspects

In some of the experimental studies, fewer than half of the enrolled subjects are willing to continue relaxation therapy for 3 to 6 months (154) although others are able to retain most of their subjects for even longer (153,158). In clinical practice, it is likely that only a minority of hypertensives will choose to try one or another of these relaxation procedures and that only a minority of them will continue the procedure for long. Nonetheless, most of those who stick with it likely will achieve some antihypertensive effect and a few may achieve a considerable effect. At the same time, they may be less anxious and feel better (167) so that the effort may provide multiple dividends.

It should be noted that sedatives and tranquilizers have not been shown to exert an antihypertensive effect, though there really are very few well-controlled trials in the literature (168). On the other hand the inhalation of tetrahydrocannabinol may decrease the blood pressure for 3 to 4 hours (169).

I. Alcohol

Relaxation of another sort can be achieved by drinking alcohol. The effects of alcohol upon the hypertensive patient are both good and bad: good because, in moderate amounts, alcohol somehow protects against coronary heart disease; bad because, even in moderate amounts, alcohol may elevate the blood pressure.

1. Cardioprotection

The epidemological evidence for a cardioprotective effect of moderate alcohol intake against CHD is quite strong and consistent (170), despite the deleterious effects of larger amounts of alcohol on myocardial cells

(171). The protection has been ascribed to alcohol-induced rises in plasma HDL-cholesterol. But, the type of HDL-cholesterol that is increased by the moderate intake of alcohol, the HDL_3 fraction, is not considered cardioprotective, whereas the HDL_2 fraction, which is considered protective, appears not to be increased (172). Therefore the mechanism is, at present, obscure.

2. Pressor effect

On the other hand, the evidence that even a little alcohol will raise the blood pressure has become equally convincing (173-176). Perhaps the most careful examination of the relationship is that reported on 20,920 persons not receiving antihypertensive therapy who were screened at the Sydney, Australia Hospital (175) (Figure 11). The blood pressures were progressively higher with increasing alcohol consumption and the relationship was even closer after statistical correction for age, obesity and smoking by multiple regression analysis, as shown by the solid lines in Figure 11.

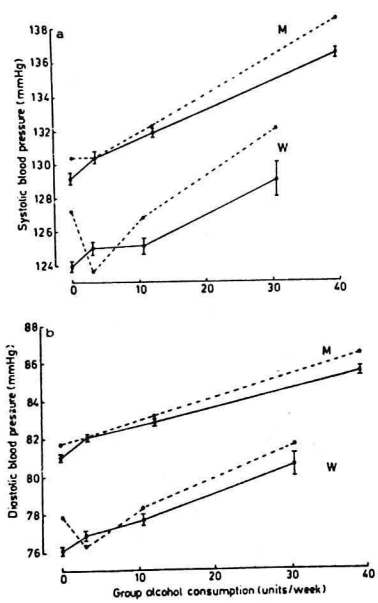

Figure 11: Mean systolic and diastolic blood pressures, uncorrected (dashed lines) and corrected (solid lines) for age, obesity and smoking, in relation to alcohol consumption for men and women. One unit of alcohol consumption = 10 g of ethanol. Twenty units per week translate to about one ounce per day. From Cooke et al (175).

Beyond such epidemiological evidence, the administration of alcohol under controlled conditions has been shown to raise the blood pressure of hypertensive men (176), in keeping with even more precise evidence that alcohol acutely increases heart rate and cardiac output, as first shown by Arthur Grollman in 1930 (177) and amply confirmed (178). Beyond these

acute effects, alcohol exerts more chronic pressor actions, which cannot be tightly connected to known pressor mechanisms (176). In addition, the blood pressure may rise even further during alcohol withdrawal.

All things considered, alcohol in more than moderate amounts, i.e., more than 2 ounces per day, may raise the blood pressure enough to make it the most prevalent cause of reversible hypertension. Though some have attributed as much as 30% of hypertension to alcohol consumption, more careful analyses suggest that the correct figure is around 10% of hypertensive men and 1% of hypertensive women (179), a sizeable group, nonetheless.

When both the good and bad are balanced, a reasonable position would seem to allow for, and maybe even encourage, up to 2 ounces of alcohol a day. Certainly those who drink more should be firmly counseled to cut back, both for their blood pressure and for multiple other health and social reasons.

J. Other Factors

The caffeine in coffee and the nicotine in cigarettes have been incriminated as possible hypertensive agents. Though both raise the blood pressure acutely (180), neither has been clearly associated with induction of permanent hypertension, likely because of the development of tolerance to their hemodynamic effects (181). Patients should be advised to avoid both for an hour before blood pressure measurements but it seems unlikely that more sustained avoidance will have much of an antihypertensive effect. In fact, the blood pressure may go up a few millimeters when people quit smoking, likely because of weight gain (182).

In 1979, two papers suggested that malignant hypertension was more likely to develop among smokers (183, 184) but no subsequent documentation of the relationship has been published.

Beyond caffeine and nicotine, a host of other drugs, some readily available "over-the-counter" and widely used for very common problems, may accentuate hypertension. Some do so by direct stimulation of pressor mechanisms, such as diet pills and cold remedies containing phenylpropanolamine, adrenal steroids, and oral contraceptive pills. Others interfere with antihypertensive therapy, such as high-sodium antacids and non-steroidal anti-inflammatory drugs. As with excessive alcohol intake, their discontinuation may be effective non-drug therapy.

IV. An Overall Perspective

When all of the evidence concerning the efficacy and applicability of non-drug therapies for the treatment of hypertension is considered, the more liberal and optimistic might say: "Everything works at least for awhile and patients should be enthusiastically encouraged to use them before, and hopefully instead of, drug therapy."; whereas the more conservative and pessimistic might say "Nothing has been shown to work over the long-term and patients should be protected by antihypertensive drugs as soon as their disease is recognized."

A more balanced view is provided in the 1984 report of the Joint National Committee (185), which recommends that "Nonpharmacologic approaches (be) used both as definitive intervention and as an adjunct to drug therapy." In addressing the 40% of all hypertensives who are in the 90 to 94 mmHg range, the report states" Nonpharmacologic therapy should be pursued aggressively while blood pressures are carefully monitored. However, the report cautions that "Physicians who elect not to use drug therapy for patients with diastolic blood pressures in the 90-to-94-mmHg range should follow up these patients' condition as closely as if they were on pharmacologic therapy, because many will progress to higher levels of diastolic BP that all agree should be treated with antihypertensive agents".

We obviously need better controlled, long-term efficacy data, along the lines of the Chicago Coronary Prevention Evaluation Program (186) (Table 11). Until such data are available, the wisest course would seem to be to enthusiastically offer a sensible, broad-based, non-drug regimen to all hypertensives, while providing some of the various motivational tools and follow-up procedures that are readily available to maximize their acceptance and effectiveness.

TABLE 11: THE RESULTS OF A NUTRITIONAL-EXERCISE PROGRAM ON 67 HYPERTENSIVE MEN OVERWEIGHT AT THE ONSET

Year	Weight	Blood Pressure		Serum Cholesterol
		Systolic	Diastolic	
0	196	147	96	258
1	183	134	86	227
5	186	135	87	233

(from Stamler et al: JAMA 243:1819, 1980)

A. A practical prescription

The non-drug prescription should be:

- For those who are overweight, weight reduction should be the primary goal.
- For all hypertensives, dietary sodium should be restricted to a 2 g (88 mmol/d) level, with caution not to reduce the consumption of milk and cheese products so as to maintain calcium intake.
- More fiber and less saturated fat are beneficial for other reasons and may also help lower the blood pressure.
- Alcohol should be limited to 2 ounces per day.
- Regular isotonic exercise should be encouraged, both as an aid to weight loss and as a likely independent antihypertensive modality.

- Potassium intake need not be specifically addressed since it will rise with a lowered sodium intake.
- Supplemental magnesium and calcium should only be given to those who are deficient until additional evidence of their efficacy for the larger population is available.
- Those who are willing and able should be encouraged to perform some type of relaxation therapy.

B. Benefits versus costs

This prescription may lower the blood pressure of a significant portion of the large population with mild hypertension to below 140/90 so as to eliminate, postpone, or at least minimize the need for drug therapy. Even if it does not lower the blood pressure, it will do no harm and it may provide a number of other benefits, including a reduction in most of the other risk factors for premature cardiovascular disease.

The intensive incorporation of all of these non-drug therapies into a given patient's management could entail considerable expense, far beyond that of one or two doses a day of an antihypertensive drug. However, for most patients, the regimen need only require a few extra visits to a dietician and, for those over age 40, perhaps an exercise stress test before beginning a strenuous isotonic exercise program. The majority of follow-up visits, mainly for maintaining the patient's motivation, can be handled by nurses or other non-physician personnel. Overall, the expense may be greater but the potential for improvement in overall health makes the cost seem trivial. Moreover, the use of drugs to lower the blood pressure does not relieve the patient of the need to lose weight, exercise regularly, eat a prudent diet, and learn to relax. Therefore, non-drug therapies likely have a place in the management of all patients with hypertension.

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