# Warning—The Physician's Clinical Judgment Can Be Hazardous to Your Health: Withdrawing Drugs in Patients With High Blood Pressure

In this issue of the *Journal*, Froom and colleagues review a series of reported clinical observations concerning the advisability of drug withdrawal in patients whose hypertension has been treated successfully.[1] From their review the authors infer that it is advisable to attempt to withdraw drugs from these patients. They note that a considerable portion of these patients will not be hypertensive on early follow-up after drug withdrawal. Thus these newly unmedicated patients will be relieved of the risk of side effects, adverse quality of life, and financial costs that have been associated with antihypertensive drug treatment.

The authors acknowledge the problems caused by combining these study results because of the many methodologic variations: different blood pressure criteria for restarting drugs, lack of standardization, different groups studied for various lengths of time, missing data, and so on. Although a meta-analysis could not be carried out because of these variations, after examining these disparate studies, the authors use clinical judgment to conclude that it is advisable to withdraw antihypertensive drugs in many patients whose blood pressure is well controlled.

This conclusion must be questioned, however, because without a meta-analysis inferences drawn from reviewing reported clinical observations are notoriously unreliable. Furthermore, it should be noted that most of the studies cited by Froom et al use either extraordinarily high blood pressure levels or stringent criteria (multiple visits) for restarting drugs. If more conventional blood pressure levels were used, these same studies would indicate that there is a group of patients (approximately 25 percent) whose blood pressures do increase rapidly (in 6 to 8 weeks) on drug withdrawal. The rest experience a gradual return to drugs during a longer follow-up period, so that at 4 years essentially all patients (97 percent) are back on drugs.[2]

In addition, the two largest studies, which are not included in Table 1, had the same blood pressure criteria for return to drugs. The sample size for these omitted studies is 475, substantially larger than most of the studies cited in Table 1. In both of these studies identical criteria were used to restart drug therapy, with qualifying levels of blood pressure consistent with the Fifth Joint National Committee on the Detection, Evaluation and Treatment of High Blood Pressure (JNC V) guidelines.[3] These researchers observed a pattern of return to drug therapy that was quite similar; that is, there was an initial group (approximately 25 percent) that returned to drug treatment rather quickly, within 6 months. The rest gradually returned to drug treatment with time: 60 percent at 2 years, and 97 percent at 4 years in the Hypertension Control Program (HCP).[2]

Moreover, Froom et al base their conclusions on several faulty assumptions. First, they assume that blood pressure is bimodal, that is, that there exist, on the one hand, normotensive patients who are not at risk for cardiovascular disease and, on the other hand, hypertensive patients who are at risk.

Second, they assume that drug treatment of hypertension is less than desirable because of substantial risks of side effects, impaired quality of life, and excessive financial cost.

Third, they assume that many patients who are currently taking antihypertensive medications are not truly hypertensive. They suggest that some patients whose hypertension was correctly diag-

Submitted 25 March 1997.

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nosed before drug treatment might no longer be hypertensive because their blood pressure could have reset to "normal" levels after years of taking drugs. Or, perhaps some patients were originally misclassified and were really normotensive or had "white coat hypertension" all along. These normotensive patients should be detected with drug withdrawal and subsequent monitoring.

With regard to the first assumption, it is emphasized that there is no scientific basis for the widely accepted, bimodal view of blood pressure. Data from all major observational studies of cardiovascular disease (Framingham, Multiple Risk Factor Intervention Trial [MRFIT], Treatment of Mild Hypertension Study [TOMHS], and others) show that the relation of blood pressure to risk of cardiovascular disease is continuous rather than bimodal.[4] Understandably, clinicians need cutoff points to guide them in the management of blood pressure; however, it is important to emphasize that these cutoff points are in actuality imaginary. Because blood pressure risks exist along a continuum, the higher the blood pressure, the higher the risk. At no point along the continuum can blood pressure be sharply defined as normal, high, or low. Rather, the current recommendation of the JNC V is to classify patients with higher blood pressure according to four stages, all of which need to be controlled by lifestyle changes, drug treatment, or both.

In TOMHS one group of hypertensive patients was instructed in lifestyle change and given drug therapy, whereas the other group was instructed in lifestyle change and was given a placebo.[5] The first group had average systolic and diastolic blood pressures of 124/78 mmHg. The second group had average systolic and diastolic blood pressures of 133/82 mmHg. Both groups would be considered well controlled according to the currently used cutoff point of 140/90 mmHg; however, it was also observed that the lifestyle-drug group had a 34 percent lower incidence of combined cardiovascular events than the lifestyle-placebo group. Thus, TOMHS clearly established, prospectively and experimentally, that—other than acute emergencies and perhaps patients with clinical coronary heart disease—the lower the blood pressure, the lower the risk of cardiovascular disease.

With regard to the second assumption, Froom et al believe that drug therapy for hypertension has substantial side effects, impairs quality of life, and is unduly costly. The major unconfounded clinical trials showing efficacy of drugs in lowering cardiovascular events have revealed few side effects.[4,5] In the TOMHS study, although there were some specific side effects attributed to medications (ie, angiotensin-converting enzyme inhibitors causing persistent cough), overall, the drug-therapy group experienced the same or even fewer side effects than the placebo group. Quality-of-life measures for the 4 years showed significantly more improvement in patients with lifestyle changes and drug therapy than in patients with lifestyle changes and placebo.[6] Furthermore, although costs of antihypertensive drugs vary widely, many efficacious, lower cost drugs (ie, diuretics and generics) are readily available. By contrast, costs incurred from fatal and nonfatal cardiovascular events and hospitalizations, which can result from unnecessary drug withdrawal, are astronomical.

Finally, the authors believe that many hypertensive patients are misclassified because they have so-called white coat hypertension, uncharacteristically elevated blood pressures that are caused by the clinic visit itself. In fact, it is extremely unlikely that white coat hypertension, if it exists, is clinically important. Research shows that blood pressure is highly variable in the same patient from one clinic visit to another. The high within-individual variability of systolic and diastolic pressures (approximately 11 mmHg and 6 mmHg under ideal conditions) makes it impossible to ascertain true blood pressure from one or even a few clinic visits. Only by standardizing the measurement with multiple readings or by measuring ambulatory blood pressure can the true mean blood pressure be determined.[7] Thus, any patient whose blood pressure is found to be above some arbitrary cut point above the mean on one clinic visit will inevitably be found to have lower pressures on subsequent visits regardless of whether treatment is started. This tendency of regression to the mean is what actually accounts for the phenomenon some regard as white coat hypertension, rather than any emotional impact caused by the physician or the clinic visit itself.

The vast majority of patients on drug therapy should continue to take their blood pressure medicine indefinitely, probably for life. In fact, the National Health and Nutrition Examination

Survey III (NHANES III) data, which show a control rate (less than 140/90 mmHg) in patients on drugs of only 29 percent nationally, indicate that we should be working aggressively to get more patients on medication and under good control.[8] As in the JNC V recommendations, patients with stage 1 hypertension should initially be advised to make lifestyle changes (weight loss, dietary sodium and alcohol reduction, increased physical activity). But many patients with stage 2 hypertension will ultimately need medications as well. Patients with stage 3 through 4 hypertension frequently initially require lifestyle changes and drug treatment. Once drugs are started, patients should continue with their medication, with goal blood pressures in those with uncomplicated hypertension ideally less than 130 mmHg systolic or 80 mmHg diastolic for optimal benefit to the patient. Although there are patients who make considerable lifestyle changes and succeed in drug withdrawal, the main priority for physicians is to get more hypertensive patients on lifestyle and drug treatments, not off.

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The author wishes to acknowledge and thank Jeanne Grimm, PhD, for her valuable assistance in preparing this paper.

## References

1. Froom J, Trilling JS, Yeh S, Gomolin IH, Filkin A, Grimson RC. Withdrawal of antihypertensive medications. J Am Board Fam Pract 1997;10:249-58.
2. Stamler R, Stamler J, Grimm RH, Gosch FC, Elmer P, Dyer A, et al. Nutritional therapy for high blood pressure. Final report of a four-year randomized controlled trial—the Hypertension Control Program. JAMA 1987;257:1484-91.
3. 1993 Joint National Committee. The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). Arch Intern Med 1993;153:154-83.
4. MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, et al. Blood pressure, stroke, and coronary heart disease. Part 1. Prolonged differences in blood pressure: prospective observational studies corrected for regression dilution bias. Lancet 1990;335:765-74.
5. Neaton JD, Grimm RH Jr, Prineas RJ, Stamler J, Grandits GA, Elmer PJ, et al. The Treatment of Mild Hypertension Study: final results. Treatment of Mild Hypertension Study Research Group. JAMA 1993; 270:713-24.
6. Grimm RH Jr, Grandits GA, Cutler JA, Stewart AL, McDonald RH, Svendsen K, et al. Relationships of quality of life measures to long-term lifestyle and drug treatment in the Treatment of Mild Hypertension Study (TOMHS). TOMHS Research Group. Arch Intern Med 1997;157:638-48.
7. Pearce KA, Grimm RH Jr, Rao S, Svendsen K, Liebson PR, Neaton JD, et al. Population-derived comparisons of ambulatory and office blood pressures. Arch Intern Med 1992;152:750-6.
8. Burt VL, Cutler JA, Higgins M, Horan MJ, Labarthe D, Whelton P, et al. Trends in the prevalence, awareness, treatment and control of hypertension in the adult US population. Data from the health examination surveys, 1960 to 1991. Hypertension 1995; 26:60-9.

# The Role of Procedures in Family Practice: Is There a Right Answer?

As family medicine matures and attempts to define its scope, as managed care programs move patients out of hospital settings, and as a progressively increasing percentage of health care services are performed in ambulatory settings, a large number of thorny questions arise regarding the proper role of procedures in family practice. The article by Prislin, Dinh, and Giglio[1] in this issue of the *Journal* addresses the following general and specific questions:

What is the impact of incorporating procedural activities into the clinical domain of family practice?

What effect does the availability of a procedure (in this case colposcopy) within a family practice clinic have on the test-ordering behavior of the physicians practicing there?

What effect does the availability of a diagnostic procedure within a family practice clinic have on the compliance of patients for whom the procedure is recommended?

Submitted 21 February 1997.

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