Reprinted from Medical Annals of the District of Columbia Vol. XXIII, No. 7, July, 1954 Printed in U.S.A.

# THE DISCREPANCY BETWEEN HOME AND OFFICE RECORDINGS OF BLOOD PRESSURE IN PATIENTS UNDER TREATMENT WITH PENTAPYRROLIDINIUM. IMPORTANCE OF HOME RECORDINGS IN ADJUST-ING DOSAGES\*

## EDWARD D. FREIS, M.D.

Clinical Adjunct Professor of Medicine, Georgetown University School of Medicine

ARLY in the course of investigations on antihypertensive drugs it became evident that many if not the majority of patients who exhibited favorable responses to certain agents while in the hospital appeared to lose this reactivity after they left the hospital. With the advent of the ganglionic-blocking agents it became necessary to follow the blood pressures more closely than could be accomplished with occasional visits to the office or clinic. As a result, certain patients were taught to record

their blood pressures in the home or while at work. It soon became evident that in many instances there often was a striking difference between the level of blood pressure as recorded in the home and as recorded in the office. It was found that the majority of the patients did not lose their responsiveness to the medication after discharge from the hospital. Rather, the visit to the doctor was a pressor stimulus of such magnitude that the hypotensive effects of the drug frequently were overcome.

This observation seemed to have obvious clinical importance, since, if the physician depends only upon office recordings of blood pressure in such cases, he will be unable to recognize the point at which a therapeutic dose level has been obtained. The development of pentapyrrolidinium (Ansolysen, M&B 2050) has given the doctor an oral antihypertensive agent which is effective even in the severe cases of hypertension.<sup>1, 2</sup> But, because of its potency and the

<sup>\*</sup> From the Cardiovascular Research Laboratory, Georgetown University Hospital, and the Veterans Administration Hospital, Washington, D. C.

This study has been supported in part by Research Grant H-720, National Heart Institute, U. S. Public Health Service; The Squibb Institute for Medical Research, New Brunswick, New Jersey; and Irwin, Neisler and Company, Decatur, Illinois.

Sponsored (in part) by the VA and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

variability of dosage requirements from one patient to another, it is vital that the physician have an accurate record of the extent of blood pressure reduction. If his readings are misleadingly high, he may unwittingly increase the dosage beyond the therapeutic range and thus precipitate severe side-effects. The purpose of the present study is to document observations on home versus office or clinic blood pressures in patients receiving pentapyrrolidinium.

## MATERIALS AND METHODS

A sample of 32 patients was selected who received a period of hospitalization for at least 1 week prior to the institution of therapy. The blood pressure was recorded 4 to 6 times daily by the nursing staff. The blood pressure values recorded during the last 2 days of pre-treatment observation were averaged, and this value was used as the pre-treatment level of blood pressure. Only patients whose average blood pressure was 180/110 or higher at the end of the observation period were treated with pentapyrrolidinium.

Twenty-three of the patients were males and 9 were females. According to the Keith, Wagener and Barker classification,<sup>3</sup> 2 of the patients exhibited Grade I, 11 Grade II, 5 Grade III, and 14 Grade IV changes in the optic fundi. No effort has been made to select the patients who later showed the greatest discrepancy between home and office blood pressure readings.

In each case the patient or a member of the family was taught to record the blood pressure, and such readings were taken 2 to 4 times daily after discharge from the hospital. The blood pressure values recorded with the patient in the sitting position were averaged to obtain the mean of the home readings. The office or clinic pressures were taken under the following circumstances: The patient and the physician were alone in a quiet room. Following a report by the patient of his symptoms and side-effects, if any, the blood pressure was recorded 5 times with the patient in the sitting position using

the standard auscultatory method. The patient then was asked to stand, and the blood pressure was recorded twice in the erect position. The lowest of the 5 pressures recorded in the sitting position during each visit was used in computing the average of the office readings.

Although the average period of treatment in this group of patients has been 9 months, only the data obtained during the first 3 months of treatment were used in the present study. The reasons for this are twofold: First, the early months represented the period of adjustment of dosage when accurate blood pressure was of greatest importance in regulating dosages, and second, in some of the patients, after a number of months had passed, the office recordings began to approach more closely the home recordings.

In each instance, when a discrepancy was found between office and home recordings, the patient or another individual who took the blood pressure at home was asked to repeat his readings in the office immediately after the physician finished his recording. In only 1 instance was the technic of home recordings found to be inaccurate, and this case was not used in the present series.

#### Results

In regard to systolic blood pressure, the average of the home post-treatment recordings was 30 mm. Hg or more lower than the pretreatment hospital readings in 31 of the 32 cases (table 1). In 22 or 68 per cent the average home reading was 50 mm. Hg or more lower than the pre-treatment reading, and in almost half of the cases the mean systolic pressure was 70 mm. Hg or more lower than the pre-treatment values. Thus, on the basis of home recordings, all except 1 case exhibited a significant reduction of systolic pressure.

When the blood pressures recorded in the office or clinic following discharge of the patient from the hospital are used as the standard for judging therapeutic results, 12 patients, or 37

per cent of the group, showed less than 20 mm. Hg reduction of pressure, and 22 or 68 per cent less than 30 mm. Hg reduction. Thus, on the basis of office or clinic readings, 68 per cent of patients failed to maintain a significant reduction of systolic blood pressure following discharge from the hospital.

#### TABLE 1

Difference between Home and Office or Clinic Post-treatment Recordings of Blood Pressure as Compared to Pre-treatment Hospital Blood Pressure in 32 Patients under Treatment with Pentapyrrolidinium

| TYPE OF COMPARISON   | NO. OF<br>CASES | PER<br>CENT OF<br>TOTAL |
|--|-----------------|-------------------------|
| Systolic Pressure  |                 |                         |
| Post-treatment home compared to pre-treat-   |                 |                         |
| ment hospital blood pressure   |                 |                         |
| Home pressures less than 30 mm. Hg lower.  | 1               | 3                       |
| Home pressures 30 mm. Hg or more lower.  | 31              | 97                      |
| Home pressures 50 mm. Hg or more lower.  | 22              | 68                      |
| Home pressures 70 mm. Hg or more lower.  | 15              | 47                      |
| Post-treatment office or clinic compared to<br>pre-treatment hospital blood pressure | ,               |                         |
| Office pressures less than 20 mm. Hg lower   | 12              | 37                      |
| Office pressures 30 mm. Hg or less lower   | 22              | 68                      |
| Office pressures 40 mm. Hg or less lower   | 28              | 88                      |
| Diastolic Pressure   |                 |                         |
| Post-treatment home compared to pre-treat-<br>ment hospital blood pressure           |                 |                         |
| Home pressures less than 20 mm. Hg lower   | 5               | 16                      |
| Home pressures 20 mm. Hg or more lower.  | 27              | 84                      |
| Home pressures 30 mm. Hg or more lower.  | 18              | 56                      |
| Home pressures 40 mm. Hg or more lower.  | 8               | 25                      |
| Post-treatment office compared to pre-treat-<br>ment hospital blood pressure         |                 |                         |
| Office pressures less than 10 mm. Hg lower.  | 13              | 41                      |
| Office pressures 20 mm. Hg or less lower   | 26              | 81                      |

In regard to diastolic blood pressure, the average post-treatment home recording was 20 mm. Hg or more lower than the mean pretreatment reading in 27, or 84 per cent, of the cases, whereas the average follow-up office recording was 20 mm. Hg or more lower than the pre-treatment reading in only 6, or 19 per cent, of the patients. On the basis of home recordings more than half of the patients exhibited

reductions of diastolic pressure of 30 mm. Hg or more (table 1).

# DISCUSSION

It may be disputed that the home recordings of blood pressure do not represent the therapeutic effect of the drug but rather the expected difference between home and office blood pressure levels regardless of whether the patient was under treatment or not. This argument is somewhat beside the point, since the aim of the treatment was to maintain the average level of blood pressure in a range which the therapist considered to be satisfactory. In the majority of patients the home recordings indicated that this was the case, while the office recordings did not.

Another interpretation of the above data is that the home recordings more accurately reflected the therapeutic effects of the drug, whereas the office recordings represented an "escape" from the hypotensive effect of the drug occasioned by the apprehension associated with the visit to the doctor's office or clinic. There is much collateral evidence to support this interpretation. First, the cases in this series were selected on the basis of being so-called "fixed" types of hypertensive patients. They failed to show reductions of blood pressure below 180/ 110 mm. Hg after being hospitalized for 1 week or longer. Second, the administration of therapeutic doses of pentapyrrolidinium was associated with a significant reduction of blood pressure while the patient was in the hospital, and this level was maintained in the home recordings following discharge from the hospital. Third, home recordings, particularly in the first month of treatment, disclosed varying degrees of postural hypotension which undoubtedly were drug-induced. Fourth, home recordings often disclosed dips of blood pressure to the normal range even in the patients with malignant hypertension. Fifth, it frequently was necessary to decrease the patient's dosage, because home pressures disclosed periods of low blood pressure associated with symptoms of weakness and faintness which disappeared when the dosage was reduced. Sixth, in the patients with malignant hypertension obvious objective improvement, such as disappearance of papilledema and clearing of hemorrhages and exudates in the optic fundi, continued after discharge from the hospital, and in the cardiac patients the degree of heart failure was markedly reduced or cleared completely as compared to the pre-treatment state. In brief, symptoms, sideeffects and objective improvement correlated in a credible and rational way with the home recordings of blood pressure, whereas there was no, or very poor correlation of these collateral observations with the office blood pressure values in many instances.

That certain emotional stimuli counteract the hypotensive effects of the ganglionic-blocking agents has been documented by Smirk.<sup>4</sup> He showed that when these drugs are given by continuous intravenous infusion it is possible to reduce the blood pressure to a selected level and maintain this under quiet conditions with little alteration. However, conversations with the patient involving emotional topics still raised the blood pressure considerably. This observation has repeatedly been corroborated in this clinic under hospital control conditions. It has been shown both in animals<sup>5</sup> and in man<sup>6</sup> that the ganglionic-blocking agents potentiate the pressor effects of circulating epinephrine and norepinephrine. Whether epinephrine release or some other mechanism is responsible is unknown, but there seems to be ample evidence that the patient can escape from the hypotensive effects of the ganglionic-blocking agents under psychic stress.

Other investigators who have had extensive experience with the ganglionic-blocking drugs in treating hypertensive patients also emphasize the importance of utilizing some other method than doctor's office recordings of blood pressure in regulating dosages. For example, Smirk<sup>7</sup> states, "Casual blood pressures are taken, but they are of very little use in the control of dosage. Quite high blood pressures may be encountered in outpatients whose blood pressure is satisfactory under home conditions." Schroeder,<sup>8</sup> in discussing the control of patients out of the hospital, states, "The patient (or a member of the family) is instructed in the use of the sphygmomanometer, and measures his own blood pressure before each dose, checking the readings frequently with an experienced observer."

The objection frequently is raised that by recording blood pressure in the home undue emphasis is placed on blood pressure per se, and so may fix a neurotic obsession. Those who claim this have made few or no personal observations of the effects of home pressure recordings. Their opinion has been a reasonable assumption rather than a verified scientific fact. By the same reasoning one might expect that diabetic patients would develop neurotic fixations concerning their disease, since they record their urine sugar concentrations at home several times daily. Most physicians would agree that if this method of managing diabetes induces a neurotic obsession it is not necessarily harmful to the patient.

Many so-called "problem" cases of hypertension are referred to this clinic. Frequently the patient is a middle-aged woman referred because of extremely high levels of blood pressure. Examination, however, discloses little or no organic damage. Such patients usually are extremely apprehensive about their blood pressures, and, even in those cases in which the readings have been hidden from the patient, questioning often reveals that the patient is aware of the fact that her office levels are dangerously high. Unless the patient is already neurotic, such problems have been solved satisfactorily by lending the patient a manometer for a short period in order to obtain a record of the home pressures. In most instances the home recordings are found to be normal or nearly so, or, if not, will respond readily to hypotensive medication. In our experience, therefore, if we are not dealing with a basically unstable or neurotic personality, home recordings provide greater reassurance than any other therapeutic procedure. That which was mysterious and threatening to the patient becomes straightforward and matter-of-fact.

It is not to be implied that all patients with hypertension require home blood pressure recording. The apparatus is expensive and the procedure time-consuming. More important, many cases of hypertension are benign, and there is no need to focus the patient's attention so frequently on his disorder. However, in the problem cases and in the patients under treatment with the ganglionic-blocking drugs, such as pentapyrrolidinium, home recordings have been of great value, and did not seem to produce an unhealthy mental reaction in our patients.

It is important to know whether the ganglionic-blocking agents protect the patients at all times or only when they are at rest in the home or hospital. Approximately one third of the present series obtained occasional readings while at work, and in no instance were the readings higher than those obtained at home. Moderate physical exercise also was without effect, and heavy physical work while under treatment with pentapyrrolidinium was more apt to reduce rather than raise the blood pressure. Emotional situations associated with anxiety and apprehension, whether at home or at work, seemed to be the principal pressor stimuli. The patient who records his own pressure quickly learns to recognize and avoid the situations which will raise his blood pressure.

Finally, home recordings of blood pressure have done much to insure the patient's coöperation in the treatment regimen. There is a human tendency to "forget" to take dosages and to modify the physician's instructions. When these lapses occur the patient finds the results of his indiscretion reflected in a rise of blood pressure. He also learns to recognize the side-effects associated with hypotension and the need for modifying dosage. He can supply the physician with precise information as to the relation of

side-effects and blood pressure readings so that the therapist is not left in doubt as to whether to raise or lower the dosages.

# SUMMARY AND CONCLUSIONS

A series of 32 hypertensive patients were hospitalized and treated with pentapyrrolidinium. During the follow-up period blood pressure recordings were obtained at home as well as in the office or clinic and compared to the pre-treatment hospital control blood pressures.

1. In all except 1 patient the average, posttreatment systolic home pressure was 30 mm. Hg or more lower than the pre-treatment hospital pressure. However, in only 10 patients was the average, systolic office pressure 30 mm. Hg or more lower than the pretreatment, hospital pressure.

2. The average post-treatment, home diastolic pressure was 20 mm. Hg or more lower than the mean pre-treatment, hospital reading in 27 patients, whereas the average, post-treatment office recording was 20 mm. Hg or more lower than the pre-treatment reading in only 6 patients.

3. Evidence is presented to support the conclusion that the excessively high office pressures while under treatment are due to "escape" from the hypotensive effects of the drug during the time the patient visits the office or clinic.

It is concluded that the majority of hypertensive patients under treatment with ganglionicblocking agents require daily recording of blood pressure in the home during the period of dosage adjustment in order to prevent overdosage and consequent undesirable side-effects.

## BIBLIOGRAPHY

- SMIRK, F. H.: Action of a new methonium compound in arterial hypertension, Pentamethylene 1:5 bis-N-(Nmethyl-pyrrolidinium bitartrate) M&B2050A). Lancet, 1953, 1, 457.
- FREIS, E. D., PARTENOPE, E. A., LILIENFIELD, L. S., AND ROSE, J. C.: Clinical appraisal of pentapyrrolidinium (M&B 2050) in hypertensive patients. Circulation, 1954.
  9, 540.

- 3. KEITH, N. M., WAGENER, H. P., AND BARKER, N. W.: Some different types of essential hypertension: their course and prognosis. Am. J. M. Sc., 1939, 197, 332.
- SMIRK, F. H., AND ALSTAD, K. S.: Treatment of arterial hypertension by penta- and hexamethonium salts based on 150 tests on hypertensives of varied etiology and 53 patients treated for periods of 2 to 14 months. Brit. M. J., 1951, 1, 1217.
- 5. MOE, G. K.: Potentiation of pressor action of epinephrine by tetraethylammonium. J.A.M.A., 1948, 137, 1115.
- FREIS, E. D., MACKAY, J. C., AND OLIVER, W. F.: Effect of "sympatholytic" drugs on cardiovascular responses to epinephrine and norepinephrine in man. Circulation, 1951, 3, 254.
- 7. SMIRK, F. H.: Results of methonium treatment of hypertensive patients. Brit. M. J., 1954, 1, 717.
- SCHROEDER, H. A.: Hypertension; method of treatment, in Conn, H. F., editor: 1954 Current Therapy. Philadelphia: Saunders, 1954.