Depressive Reactions in Hypertensive Patients
A Comparison of Those Treated with Rauwolfia and Those Receiving No Specific Antihypertensive Treatment

By Richard M. Quetsch, M.D., Richard W. P. Achor, M.D., Edward M. Litin, M.D., and Robert L. Faucett, M.D.

Because of reports that derivatives of Rauwolfia serpentina may cause severe mental depression when used in the treatment of hypertension, the depressive reactions and possible contributing factors were studied in a group of 387 hypertensive patients. Some of the patients received no specific antihypertensive medication; some were treated with Rauwolfia derivatives alone and some with Rauwolfia and other antihypertensive drugs. Of the patients receiving Rauwolfia, alone or with other drugs, 26 per cent experienced depressive reactions whereas only 5 per cent of the others had them.

Since 1954 reports have indicated that derivatives of Rauwolfia serpentina may cause serious mental depression when used in the treatment of patients with arterial hypertension. Freis\(^1\) reported mental depression in 5 hypertensive patients following several months of treatment with reserpine in doses as low as 0.25 mg. a day. Wallace\(^2\) in a study of several different antihypertensive programs, noted depression in 4 of 44 patients taking reserpine with or without pentolinium, and in only one of 88 patients treated without Rauwolfia. Additional reports\(^3\)-\(^10\) in succeeding years have furnished more examples of depression occurring among hypertensive patients treated with Rauwolfia, and therefore have added weight to the suggestion that caution is needed in the use of these preparations.

Usually it has been stated that depressive reactions occur more frequently among hypertensive persons treated with Rauwolfia who had experienced some previous psychologic difficulty. However, it is not clear from these reports whether previous psychiatric problems are more frequent in those patients who become depressed as contrasted with those who do not. Wallace\(^2\) and Lemieux and associates\(^3\) compared the frequency of depressive reactions among their hypertensive patients treated with Rauwolfia with the infrequency of such reactions in patients treated with other antihypertensive drugs. We are not aware of any reports on the frequency with which depression may be expected among hypertensive patients not taking such medicaments. Also, the two reports cited do not make it clear whether the patients treated with Rauwolfia compounds were closely comparable as a group to the other patients studied, nor whether any particular features distinguish those who suffered a depressive reaction from those who did not.

The present study was undertaken to determine whether there are any factors that may contribute to the occurrence of depression in hypertensive patients, whether Rauwolfia drugs actually do enhance the production of such reactions, and whether it is possible to predict which patients may be especially susceptible to a depressive reaction.

Methods

Records were reviewed of all residents of Rochester, Minnesota, who were seen at the Mayo Clinic during the 2 years from January 1, 1954, through December 31, 1955, for whom a diagnosis of hypertension was recorded. Of 863 patients given this diagnosis, 391 were selected for further study because there was good evidence that their blood pressure levels were well sustained at values
The 391 patients were divided into groups on the basis of treatment that had been given for the hypertension. The first group received no specific antihypertensive medication. For the purpose of this study, sedatives, including barbiturates, were not considered to be specific antihypertensive medications. The second group received no specific antihypertensive medication other than some form of Rauwolfia serpentina. The third group was given some form of Rauwolfia medication and, for at least part of the period studied, some additional antihypertensive drug. Four persons received specific antihypertensive drugs exclusive of Rauwolfia. This number was too small for comparative purposes, and consequently data on this group are not included in this report. The details presented, then, concern 387 patients. Although some patients in the 3 groups received other forms of medication for a variety of co-existing conditions, these drugs were not considered in the present study.

Within the 3 groups studied, the patients were classified as to whether they had shown no evidence of depression, or evidence of mild, moderately severe, or severe depression. Mild depression was arbitrarily defined as a subjectively sad or depressed feeling noted by the patient, or a reaction which the clinician described as “depression” without additional amplifying information. For example, it was not uncommon to find a note, without any clue as to the specific symptoms, that merely stated, “Has been a little depressed the past two weeks; discontinue reserpine.” Such cases were classified as mild depression. Moderately severe depression was defined as any depressive reaction characterized by the addition of one or more of the following symptoms: anorexia, loss of weight, frequent crying spells, early morning awakening, preoccupation with death, psychomotor retardation or agitation not requiring hospital treatment, and suicidal thoughts or desires not accompanied by any real intent of committing suicide. We also classified as moderately severe any depression which led the physician to advise psychiatric consultation. Severe depression was defined as any depression requiring hospitalization or resulting in an attempt to commit suicide.

In addition certain basic factors were studied (table 1).

Although rescinnamine, deserpidine, and Rauwolfia alkaloids other than reserpine are reported to have appreciable hypotensive activity, there is good evidence that the major active principle in the whole root and alseroxylon preparations of...
Rauwolfia serpentina is reserpine. Therefore, in order to facilitate analysis of results, we converted all drug forms to an equivalent dose of reserpine on the basis of 1,000 units of whole root extract or 10 units of the alseroxylon fraction as representing the equivalent of 1 unit of reserpine. Therefore, unless otherwise specifically stated, the term Rauwolfia is used to include all of these preparations, and the dosage is expressed as the equivalent dose of reserpine.

**RESULTS**

Information on the basic factors concerning the patients selected for study is summarized in table 1.

**Depressive Reactions among Patients Receiving No Specific Antihypertensive Medication.** This group consisted of 185 patients, of whom 9 (5 per cent) experienced some depressive reaction (table 2). All of the depressed patients were women; three of the reactions were mild, three moderately severe, and three severe.

The patients in this group were somewhat older than those in the treated groups and this may have been one reason why they were not treated more vigorously. The pretreatment blood pressure and the frequency of severe changes in the ocular fundi in this group of patients were comparable to those treated with Rauwolfia alone, but less severe than in the group treated with a combination of Rauwolfia and other antihypertensive drugs. Many of the patients in this "untreated" group were seen only sporadically, so that it was not possible to correlate the occurrence of depressions with changes in blood pressure.

*Some reports suggest that 20 mg. of alseroxylon fraction may be more nearly equivalent to 1 mg. of reserpine."

**Table 2.** Patients Depressed During Two-Year Period of Study

<table>
<thead>
<tr>
<th>No specific treatment (185 patients)</th>
<th>Rauwolfia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild depression</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Per cent</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>All types of depressions</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Per cent</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
</tr>
</tbody>
</table>

**Depressive Reactions among Patients Receiving Rauwolfia Only.** The patients in this group were of about the same average age as those treated with a combination of drugs, but they had a lower average blood pressure and fewer had severe changes in the ocular fundi. This "Rauwolfia alone" group consisted of 154 patients, 43 (28 per cent) of whom became depressed (table 2). In 28 the depressive reactions were mild, in 8 moderately severe, and in 7 severe. Depressive reactions occurred in substantial numbers regardless of which preparation of Rauwolfia was used: 5 depressions were noted among 9 patients who were given only the whole root extract; 6 reactions among 31 persons who received solely the alseroxylon fraction; 21 depressions among 70 patients treated only with reserpine; and 11 of 44 persons who received more than one of these preparations during the period studied also showed some mental depression. Similar results have been reported previously in regard to whole root and reserpine.

**Depressive Reactions among Patients Receiving Rauwolfia Combined with Other Antihypertensive Therapy.** Rauwolfia preparations and in addition one or more other antihypertensive drugs were given to all patients in this group: veratrum preparations to 29; potassium thiocyanate to 6; ganglion-blocking agents to 21, and hydralazine to 12. The average duration of treatment with these additional preparations was 11 months and infrequently coincided exactly with the use of Rauwolfia. The average pretreatment blood pressure in patients in this group was higher and arteriolar changes in the fundi were more severe in more patients than in the other.
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2 groups, but the differences are not great (table 1).

The total number of patients in this "combined treatment" group was 48, of whom 10 (21 per cent) experienced depressive reactions. These were mild in 4, moderately severe in 5 and severe in 1 patient. The drugs taken in combination with Rauwolfia by these 10 depressed patients included pentolinum taken by 8, potassium thiocyanate by 6, veratrum preparations by 5, and hydralazine by 3. Except for Rauwolfia, no one drug or combination of drugs occurred sufficiently often to permit the conclusion that they had any tendency to enhance depression.

Combined Group. This grouping includes all patients who received Rauwolfia, whether alone or as part of combined therapy. Of the total of 202 patients, 53 (26 per cent) experienced a depressive reaction. This was mild in 32 (16 per cent), moderately severe in 13 (6 per cent), and severe in 8 (4 per cent) of the patients.

The Relation of Depression to Reduction of Blood Pressure. The nature of this study made it difficult to compare pretreatment and post-treatment blood pressure in some patients, because in many instances determinations were made infrequently and not under well-standardized conditions. The blood pressures therefore do not have the same validity as those derived from more closely controlled studies. Realizing these limitations, we attempted to determine whether any obvious correlation existed between depressive reactions and the degree of reduction of the blood pressure as a result of treatment. The results are shown in tables 3 and 4. There is a suggestion that the severely depressed patients had a greater average lowering of diastolic blood pressure than those who did not become depressed, but this is largely due to a great drop in both systolic and diastolic pressures on the part of 1 patient. We do not consider that there is any substantial relationship between the degree of lowering of the blood pressure and the occurrence of depressions, either in the treated or in the untreated group.

<table>
<thead>
<tr>
<th>Table 3.—Combined Group of 202 Patients Receiving Rauwolfia: Comparison of Depressed and Nondepressed Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No depression</strong></td>
</tr>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Average age (yrs.)</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Average known duration of hypertension (yrs.)</td>
</tr>
<tr>
<td>Average blood pressure (mm. Hg)</td>
</tr>
<tr>
<td>Before treatment</td>
</tr>
<tr>
<td>During treatment</td>
</tr>
<tr>
<td>Past history of depression</td>
</tr>
<tr>
<td>8 (5%)</td>
</tr>
<tr>
<td>Arteriolar changes in ocular fundi*</td>
</tr>
<tr>
<td>Group 1-2</td>
</tr>
<tr>
<td>Group 3-4</td>
</tr>
<tr>
<td>Complicating disease</td>
</tr>
<tr>
<td>Cardiac</td>
</tr>
<tr>
<td>Renal</td>
</tr>
<tr>
<td>Cerebral</td>
</tr>
</tbody>
</table>

*Grouping according to Keith-Wagener-Barker classification. Data not available for some patients.

Funduscopic Groupings. Severe (groups 3 and 4) hypertensive changes in the ocular fundi were reported in 4 (8 per cent) of the 53 patients who experienced depression while taking Rauwolfia and in 13 (9 per cent) of the 149 patients who did not become depressed. The frequency of various degrees of hypertensive changes in the ocular fundi for each degree of severity of depression among Rauwolfia-treated patients is shown in table 4. The severity of hypertension, as judged by this particular index, does not appear to have an appreciable effect on the occurrence of depression among patients treated with Rauwolfia. Among the untreated patients, severe changes in the ocular fundi were so infrequent that no conclusions were possible.

Cardiac Complications. Cardiac abnormalities, varying from severe congestive failure and myocardial infarctions to minimal electrocardiographic evidence of left ventricular
hypertrophy, were present in 110 of the 202 patients who received Rauwolfia. The distribution of these complications among the depressed and nondepressed patients is shown in tables 3 and 4. The presence or absence of cardiac disease did not appear to be a factor influencing the development of a depressive reaction.

Cerebral Complications. A history of hypertensive crises, definite cerebral infarction, or clinical evidence of cerebral arterial insufficiency was classified as a cerebral complication. Such findings were present in 13 (25 per cent) of those patients who became depressed while taking Rauwolfia and in 40 (27 per cent) of those who did not become depressed while taking such drugs (tables 3 and 4). Among those patients who were not given Rauwolfia, similar complications existed in 4 (44 per cent) of those who became depressed and in 34 (19 per cent) of those who did not experience depression. Thus it seems that there was no distinct relation-

ship between cerebral vascular disease and mental depression among the Rauwolfia-treated patients. On the other hand, such disease may have been an influencing factor in some of the depressive reactions that developed among the group of patients not receiving Rauwolfia.

Renal Complications. Disturbance in renal function of varying degree was noted clinically in 17 (9 per cent) of the 185 patients who did not receive Rauwolfia, but none occurred among the 9 patients in this group who became depressed. The occurrence of renal disease in patients who took Rauwolfia is shown in tables 3 and 4. Our study revealed no apparent relationship between renal complications and depressive reactions.

Age. The average age of patients who became depressed while taking Rauwolfia was about 1 year more than that of patients who did not experience a depression, with the range of age extending from 46 to 80 for men and 36 to 78 for women (table 5). There-
before age appeared to be of no importance in attempting to determine which patients were most vulnerable to a depression. However, among those patients not taking Rauwolfia the depressions did seem to occur chiefly in the older patients.

_Sex_ (Table 6). In the untreated group none of the men, as opposed to 6 per cent of the women, became depressed, while in the groups treated with Rauwolfia, depressive reactions developed about as frequently in men as in the women.

_History of Depression._ Of the 202 patients who received Rauwolfia, 19 had a history of mental depression prior to the use of Rauwolfia and 11 (58 per cent) of these 19 exhibited a depressive reaction during treatment. In 4 of these the history of a previous depression was obtained only after they became depressed while using Rauwolfia. Five patients still had a suggestion of depression at the time they started taking Rauwolfia, and 4 (80 per cent) of these 5 became more depressed while taking the drug. Of the other 14, 7 (50 per cent) became depressed. If all 19 of the patients with a past history of depression are omitted from the consideration, this would reduce the number of those who became depressed to 42 (23 per cent of the remaining 183 patients treated with Rauwolfia). Among the 42 are all of the 8 patients who had the most severe depressive reactions. Thus the absence of a history of depression did not lower remarkably the incidence of depressive reactions during the use of Rauwolfia.

Because of the type of material being analyzed, no attempt was made to correlate the incidence of depression with personality problems other than with a clear-cut history of depression.

These data justify 2 important conclusions: (1) that persons with a prior history of depressive reactions are likely to have such reactions while taking Rauwolfia, and (2) that a substantial number of persons who have no apparent past or present history of depression may still experience severe depression while under treatment with Rauwolfia.

**Table 5.—Correlation of Average Age in Years and Depression**

<table>
<thead>
<tr>
<th>Depression, all patients</th>
<th>No specific anti-hypertensive medication (186 patients)</th>
<th>All patients receiving Rauwolfia (202 patients)</th>
<th>All groups (587 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No depression</td>
<td>65.6</td>
<td>60.3</td>
<td>63.2</td>
</tr>
<tr>
<td>Depression, all</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>70.2</td>
<td>61.2</td>
<td>62.5</td>
</tr>
<tr>
<td>Severe</td>
<td>68.7</td>
<td>63.3</td>
<td>63.7</td>
</tr>
<tr>
<td>Severe</td>
<td>81.3</td>
<td>57.1</td>
<td>61.6</td>
</tr>
<tr>
<td>Severe</td>
<td>60.7</td>
<td>59.5</td>
<td>59.8</td>
</tr>
</tbody>
</table>

_Dose of Rauwolfia._ The average daily dose of Rauwolfia, expressed as milligrams of reserpine, was 0.53 mg. for those patients receiving only Rauwolfia, 0.65 mg. for those on combined treatment, and 0.55 mg. for the entire number of patients who received Rauwolfia (table 7). The average dose given to the patients who became severely depressed was a little higher (0.62 mg.). However, many patients took much larger doses for many months without becoming depressed, and no patient in this study became depressed while taking less than 0.2 mg. a day.

Although there is great individual variation in tolerance of Rauwolfia, for long-term treatment the dose should be not more than 0.25 to 0.5 mg. a day. This is in accord with the recommendations of many others but is lower than that recommended by Lemieux and associates.3

_Duration of Treatment with Rauwolfia._ The duration of treatment with Rauwolfia varied from a few days to 24 months, the average being 8 months for those patients who experienced depression and 10 months for those who did not. The onset of depression was often insidious, and Rauwolfia was not always discontinued at the time of the first symptoms. The average duration of treatment with Rauwolfia before the onset of depressive symptoms was only 5 months. Thirty-two (60 per cent) of the depressions occurred within the first 6 months of treatment, 15 (28 per cent) during the interval from 6 to
12 months, and only 6 (11 per cent) came on after 1 year.

More important than the average duration of treatment, however, is the great variation encountered. One patient became depressed in less than 1 month on a dose of 0.5 mg. a day. Another individual took 2.0 mg. daily for 20 months during the period studied without becoming depressed, only to become depressed 6 months later while taking the same dose. Although it appears that most depressive reactions will be manifest within the first 6 months of treatment, no patient taking Rauwolfia should ever be considered safe from the risk of depression, no matter how long he may have tolerated the drug. The physician, the patient, and the patient’s family should continue to be constantly alert for signs of depression in any person receiving Rauwolfia.

**Symptomatology.** The gross clinical features of the depressions that occurred in patients taking Rauwolfia were not particularly distinctive. Sometimes symptoms cleared up while patients continued to take substantial doses of the same Rauwolfia preparation. Most of the mild and some of the moderately severe depressions cleared promptly, after treatment with Rauwolfia was discontinued. Many of the moderately severe depressions, however, required additional medical therapy as well as some form of psychotherapy. The depressions cleared gradually in most cases, so that it was not possible to determine the average length of time that a depressive reaction lasted following cessation of the use of Rauwolfia.

Of the 8 patients with severe depression, some displayed chiefly agitation while others were retarded; 1 person made homicidal threats and there were 2 attempts at suicide, 1 of which was successfully carried out. Five of these 8 patients required electroconvulsive therapy to treat the depression adequately.

Nightmares were mentioned by many patients, and these were usually unpleasant, although 1 patient even enjoyed her exciting dreams. Many patients who otherwise tolerated the drug well had nightmares, and these seemed to have no relationship to depressive reactions.

**Comment**

It was not surprising that mental depressions were found more frequently among patients treated with preparations of Rauwolfia serpentina than among those who did not receive this drug. However, it was disconcerting to find that depressive reactions were 5 times more frequent in the Rauwolfia group and occurred in 26 per cent of all patients who received this drug. The implications of these observations are sufficiently important to warrant further consideration regarding their validity.
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By using a level of blood pressure that was definitely hypertensive and by including only local residents who could return for observation as needed, it seems to us that the persons selected compose groups that are comparable in most respects. Although the "untreated" hypertensive patients were somewhat older than those given Rauwolfia preparations, the two groups do not differ significantly with respect to number of patients, sex distribution, known duration of hypertension, degree of hypertension, or associated complicating disease. In addition, the same group of physicians treated all of the patients concurrently under similar circumstances, so that variations in approach to the patient were probably not a major consideration. Thus the group of patients who received no specific antihypertensive treatment and the groups of patients receiving Rauwolfia were closely comparable.

A factor that might have increased the number of depressions among patients treated with Rauwolfia is the possibility that this group was subjected to closer scrutiny for evidence of depression than those persons who received no specific treatment. As a result of such observation more mild depressions may have been recorded among the Rauwolfia-treated patients. However, this possibility seems unlikely for 2 reasons. 1. This study covered a 2-year period when the various preparations of Rauwolfia serpentina had been introduced into general use only rather recently. At that time there was little general knowledge that these medicaments frequently were associated with serious mental depression. Consequently, it is unlikely that many patients did not receive Rauwolfia because their physicians feared this complication. By the same token the physicians would not be particularly alerted for evidence of depression among patients receiving Rauwolfia. 2. The significance of mild depressions is debatable, and the frequency of their occurrence is variable. For this reason the depressive reactions were graded as mild, moderately severe, and severe. By eliminating the mild group we still found a 3-fold increase

in the moderately severe and severe depressive reactions among patients treated with Rauwolfia, and it is unlikely that such depressions would be overlooked or deemed unimportant in any patient. Under these circumstances the propensity of Rauwolfia for producing depression is still clearly evident.

The frequency of depression among patients receiving Rauwolfia could not be correlated with age, sex, known duration and severity of hypertension, nor with associated complicating disease or efficacy of therapy. However, in patients who have experienced a depressive reaction prior to beginning treatment, it seems possible to predict a greater than 50 per cent likelihood of depression occurring during the course of antihypertensive therapy with Rauwolfia. Although most depressions occurred during the first 6 months of treatment with Rauwolfia, a substantial number came on after 1 year. Consequently, constant close observation of the patient is essential during the entire period that Rauwolfia is being administered. While the relation of the dose to the depression was not striking, no depressions were observed among patients receiving 0.2 mg. of reserpine per day or less. However, it is possible that even this amount is not "safe" under all circumstances.

It is our belief that hypertensive patients with a prior history of mental depression almost certainly should not receive prolonged therapy with any preparation of Rauwolfia serpentina. In addition the risk of depression

| Table 7.—Relation of Dose* of Rauwolfia to Depressive Reactions |
|------------------|------------------|------------------|
|                  | Rauwolfia        |                  |
|                  | Alone            | Combined         | Entire group |
| No depression    | 0.52             | 0.68             | 0.56         |
| Depression       | 0.53             | 0.65             | 0.55         |
| Mild             | 0.56             | 0.56             | 0.56         |
| Moderately severe| 0.42             | 0.65             | 0.51         |
| Severe           | 0.57             | 1.00             | 0.62         |
| Average for group| 0.53             | 0.65             | 0.55         |

*Doses expressed as milligrams of reserpine or equivalent.
is sufficiently great among patients without such a history that the use of these drugs should be undertaken only after a careful evaluation of the patient's need for treatment and a thorough appraisal of his emotional status. Even then it is probable that, when other methods of antihypertensive therapy are available and control the blood pressure adequately without deleterious side effects, Rauwolfia preparations should not be used at all.

**Summary**

A review was made of 387 resident patients with arterial hypertension who were treated at the Mayo Clinic during the years 1954 and 1955. It was found that of 202 patients who were treated with some form of Rauwolfia serpentina, 53 (26 per cent) experienced a depressive reaction. This was moderately severe or severe in 21 persons (10 per cent). In contrast a comparable control group of 185 hypertensive patients who received no antihypertensive medication produced only 9 instances (5 per cent) of depression with 6 (3 per cent) being classed as moderately severe or severe. The evidence did not indicate any relationship of depression to severity of hypertension, to drugs other than Rauwolfia, or to the efficacy of treatment in lowering blood pressure. In addition no correlation could be found between depression and the age or sex of the patient, nor with any complicating disease.

Depression occurred in more than half of those persons who had a history of depression prior to beginning treatment with Rauwolfia and in almost a fourth of the patients without such a history. The dose of Rauwolfia tolerated by different individuals varied, but no depressions were observed in patients taking less than 0.2 mg. of reserpine daily. Although 32 (60 per cent) of the 53 depressive reactions occurred within the first 6 months after treatment with Rauwolfia was begun, 6 (11 per cent) came on after 1 year of treatment. Patients taking Rauwolfia serpentina, whether as whole root extract, alseroxyln fraction, or reserpine, require close observation indefinitely for any evidence of mental depression.

**QUETSCH, ACHOR, LITIN, FAUCETT**

In view of the frequency and severity of depressive reactions among hypertensive patients treated with Rauwolfia, the physician must evaluate the indications for use of this drug with extreme care and whenever possible avoid its use altogether.

**Summario in Interlingua**

Esseva facite un revista del casos de 387 residente patientes con hypertension arterial qui eseva trateate al Clinica Mayo durante le annos 1954 e 1955. Esseva trovate que le gruppo de 202 patientes trateate con le un o le alte forma de Rauwolfia serpentina includeva 53 (i.e. 26 pro cento) qui esperienciava un reaction depressori. Iste reaction eseva moderamente sever o sever in 21 casos (i.e. 10 pro cento). Per contrasto con isto, un comparabile gruppo de 185 patientes hypertensive recipiente nulle medication antihypertensive includeva solmente 9 casos de depression (i.e. 5 pro cento), e solmente 6 de istos (i.e. 3 pro cento) poteva esser classificate como moderamente sever o sever. Le datos non revela un relation inter depression e severitate del hypertension, inter depression e drogas altere que Rauwolfia, o inter depression e le efficacia del tractamento antihypertensive. In plus, nulle correlation eseva constatable inter depression e le etate o sexo del patiente o inter depression e le presentia de un morbo complicatori.

Depression occurriva in plus que un mediate del subjectos con un historia de depression ante le institution del tractamento con Rauwolfia e in quasi un quarto del patientes sin un tal historia. Le doses de Rauwolfia tolerate per differente individuos variava, sed nulle depression eseva observate in patientes qui recipeva minus que 0.2 mg de reserpina per die. Ben que 32 del 53 reactiones depressori (i.e. 60 pro cento) occurriva intra le prime 6 menses post le institution del tractamento con Rauwolfia, 6 (i.e. 11 pro cento) se declarava post un anno de tractamento. Patientes a qui Rauwolfia serpentina es administrate—non importa si in le forma de extracto ab le radice total, in le forma del fraction alseroxylna, o in le forma de reserpina—re-
DEPRESSIVE REACTIONS IN HYPERTENSIVE PATIENTS

quire le plus stricte observation—e isto in
definitemente—pro le presentia de manifesta-
tiones de depression mental.

Viste le frequentia e le severitate del reac-
tiones depressori in patientes hypertensive
tratacte con Rauwolfia, le medico debe evalu-
tar le indicaciones pro le uso de iste droga con
grande attention, e in tanto que possibile ille
debi evitar le uso del droga complemente.

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with large doses of reserpine. New Eng-
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