Antihistamines in the Treatment of the Common Cold: A Preliminary Report*

JOHN W. MIDDLETON, M.D. and J. ALFRED RIDER, M.D.
Galveston, Texas

So far as we can determine only three reports on the use of antihistamine drugs in the treatment of the common cold have appeared.1,2,4 Our interest in them in the treatment of the common cold was stimulated by the report of Brewster in 1947 on the effect of diphenylamine hydrochloride (Benadryl) in over one hundred cases. Although at first we used various antihistamine drugs casually and without statistical analysis, we soon got the impression that in many patients the symptoms were modified and in a few instances the cold could be terminated within a few hours.

The present study was undertaken in an effort to carefully analyze the effect of these drugs. The patients were primarily medical students and student nurses on whom it was possible to maintain adequate observation and “follow-up.” Because it was desired to interfere as little as possible with normal activity and work, and in order to best insure continuation of therapy, drugs known from previous experience to have few severe side effects were selected. A further element in the choice of drugs was to have tablets of approximately the same size and color.

Method of Study

Pyranisamine maleate (Neo Antergan†), and phenindamine (Thephorin‡) were used in the study. Pyranisamine was given in 50 mgm. doses, phenindamine in 25 mgm. doses four times daily for three days. In some instances where rapid relief was obtained, patients found it unnecessary to complete a full course of therapy.

At first every other, later every third, patient was given placebo tablets which were of the same shape and color as the test drugs but without medicinal effects. They were given according to the same dosage schedule as the antihistamines. Patients receiving these tablets were used as controls.

The drugs and placebos were furnished in paper envelopes bearing only the dosage instructions and a code number. No patient was informed as to the drug or placebo that was used in his case.

*From the Department of Internal Medicine, University of Texas Medical Branch, Galveston, Texas.
†Brand of pyranisamine maleate, supplied by Merck and Company.
‡Brand of phenindamine, supplied by Hoffmann-La Roche, Inc.
## TABLE I

<table>
<thead>
<tr>
<th></th>
<th>PYRAMISAMINE</th>
<th>PHENINDAMINE</th>
<th>TOTAL</th>
<th>CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Cases</td>
<td>Number Treated</td>
<td>Number Benefited</td>
<td>Per cent Benefited</td>
</tr>
<tr>
<td>Common Cold without Allergy</td>
<td>65</td>
<td>30</td>
<td>22</td>
<td>73</td>
</tr>
<tr>
<td>Symptoms less than 12 hours</td>
<td>24</td>
<td>9</td>
<td>6</td>
<td>67</td>
</tr>
<tr>
<td>Symptoms 12-24 hours</td>
<td>16</td>
<td>9</td>
<td>7*</td>
<td>78</td>
</tr>
<tr>
<td>Symptoms more than 24 hours</td>
<td>25</td>
<td>12</td>
<td>9†</td>
<td>75</td>
</tr>
<tr>
<td>Common Cold with Allergies (history)</td>
<td>27</td>
<td>6</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>Symptoms less than 12 hours</td>
<td>11</td>
<td>3</td>
<td>3†</td>
<td>100</td>
</tr>
<tr>
<td>Symptoms 12-24 hours</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Symptoms more than 24 hours</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>92</strong></td>
<td><strong>36</strong></td>
<td><strong>28</strong></td>
<td><strong>78</strong></td>
</tr>
</tbody>
</table>

* 1 case "aborted"   † 2 cases "aborted"
The drugs and placebos were assigned in the order in which the patients presented themselves for treatment. Only those who came in complaining of a cold, with some symptoms of rhinitis: i.e. nasal congestion, nasal discharge, sneezing, burning, or itching of the nasal mucosa were accepted for the study. Although it is known that in many instances the first symptom of a cold may be a sore throat, patients with this only were excluded from the report. We felt that too many other conditions may be so manifested. However, a few of the patients were given one or another of the drugs with reported benefit.

Each patient filled out a form listing symptoms and their duration, the average number of colds per year and their average duration in the past, and any allergy history. In most cases the oral temperature and the appearance of the nasal and pharyngeal mucosa were recorded. Each patient was asked to return in 48 or 72 hours for further observation. The few that did not voluntarily return in the allotted time were seen the following day through the Student Health Service. At the time of return the forms were completed. This consisted in recording the time when relief of symptoms (if any) was obtained, the duration of symptoms, the time of treatment, and a subjective comparison of the present cold with previous ones as to severity and duration. Side effects attributed to the drug were noted. The nose and throat were usually not inspected if the patient was symptom free.

No attempt was made to interpret the statements made by patients comparing the duration and severity of their present cold with previous colds, since this was based upon subjective impressions and memory.

Results

A summary of the results obtained is given in Table I. For the purposes of evaluation, patients with histories of allergy were tabulated separately. Of the total treated with antihistamines 76 per cent were benefitted with partial or complete relief of symptoms, whereas only 45 per cent of the control group reported such benefit. The type of benefit afforded was primarily disappearance of, or a decrease in, nasal congestion and/or nasal discharge. Others noted relief from cough, sore throat, sneezing, etc., but we did not consider these in the benefitted group unless their nasal symptoms improved also.

Eighty-eight per cent of patients with history of allergy were benefitted, as compared with 72 per cent of the non-allergy group. However, this was a small group, and the apparent difference may not be of real significance. Further, it was still impossible to predict which patient with allergies might be benefitted. Finally,
it is in this group that there is the greatest difficulty in differentiating an acute cold from allergic rhinitis, and the results may be subject to some question on that account.

Colds were considered to be "aborted" only if symptoms were entirely relieved within 12 hours after the start of therapy and remained absent after treatment was discontinued. On this basis only seven colds could be considered as "aborted." Although a number of other patients stated that their colds were "aborted," some symptoms had persisted and therefore they were not included. Of the seven "aborted" colds, two had had symptoms for less than 12 hours, four from 12 to 24 hours, and one for a longer period.

Since we felt that it was extremely difficult, if not impossible, to determine the presence of a cold in patients whose symptoms were of less than three hours' duration, treatment was not given where symptoms had been present for a lesser period. At the other extreme, was the group who had had symptoms for more than 24 hours; in only a few of these were symptoms present for more than 48 hours. Two cases in this group were excluded from the tabulation because it was not possible to determine whether the clearing of symptoms was due to the effect of the drug or to the natural course of the cold. All other cases treated are included in this report.

There was no definite correlation between duration of symptoms prior to therapy and effectiveness of therapy, either as to relief of symptoms or number of colds aborted. A greater percentage with symptoms of 12 to 24 hours' duration were relieved than either of the other groups, but here again this series was small, and statistical significance may be lacking. Further breakdown of the small group (20) whose symptoms had been present less than 12 hours likewise showed no correlation between results of treatment and duration of symptoms.

<table>
<thead>
<tr>
<th>TABLE II</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drowsiness</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Pyranisamine maleate</td>
<td>6</td>
</tr>
<tr>
<td>Phenindamine</td>
<td>1</td>
</tr>
<tr>
<td>Controls</td>
<td>1</td>
</tr>
</tbody>
</table>

* More than one side effect reported by one patient.
The principal side effects reported for each drug are recorded in Table II. Only one patient complained of more than one side effect. It is of interest to note that one patient receiving a placebo complained of numbness and tingling in the hands. For the most part the side effects were not severe, and in no instance was a drug discontinued because of them.

Discussion

The results reported here show a much smaller percentage of patients benefited than in the series reported by Brewster,2 or Gordon.4 Although treatment was not initiated in any case with symptoms for less than three hours, we did not observe any definite correlation between duration of symptoms and benefits obtained, including “aborted colds.” Patients with a history of allergy of some type were benefited in a higher percentage than the others.

There was no significant difference between results from pyranisamine maleate and phenindamine. Although the former gave a higher percentage of side effects, none was severe enough to interfere with therapy. Results in the control group, although small in number, were similar to those obtained in other investigations of the common cold, particularly efforts to prevent colds, such as those of Cowan, Diehl and Baker.3

Although our results are not startling, it appears that there was a definite and significant difference in the percentage of cases benefited with antihistamine therapy, as compared to the control group. While no attempt at analysis was made, it may be that those cases that fail to benefit, or those that have a recurrence of symptoms after therapy is stopped, should be re-evaluated, particularly with reference to possibility of infection of the paranasal sinuses.

We do not claim, as a result of this investigation, that there is an altered response to viral or bacterial infection, but rather that there may be a modification of symptoms. A possible rationale for the use of the antihistamines in the manner here reported is suggested by the report of Troescher-Elam5 and co-workers, who noted the presence of a histamine-like substance in nasal secretions from patients with the common cold, in quantities at least equal to that from patients with allergic rhinitis.

SUMMARY AND CONCLUSIONS

1) Sixty-three cases of the common cold were treated with antihistamines and 29 with placebos as a control.
2) There appeared to be a definite and significant percentage of cases benefited by the antihistamines.
3) Few colds seemed to be truly “aborted” by this therapy.
4) Neither duration of symptoms of a cold nor a history of allergy is any indication of the amount of benefit that may be expected.
5) The results obtained in this small series warrant further critical investigation and study.

SUMARIO Y CONCLUSIONES
1) Sesenta y tres casos de catarro común fueron tratados con antihistaminas y 29 con “placebos” como testigos.
2) Parece que hay un porcentaje definido y significante de casos beneficiados por los antihistamínicos.
3) Pocos catarros parecen haber sido verdaderamente “abortados” por esta terapéutica.
4) Ni la duración de los síntomas, ni los antecedentes de alergia en un caso de catarro común, son indicadores del grado de beneficio que es de esperarse.
5) Los resultados obtenidos en esta pequeña serie autorizan a una investigación ulterior y estudio crítico.

REFERENCES