On Epinephrine Tests in Skin Diseases. II

By

Masao Miura

(三浦 正男)

From the Department of Dermatology, Tohoku University, Sendai,

Director: Prof. M. Ito

(Received for publication, April 19, 1955)

I. Comparison of Results of ACTH- and Epinephrine Test

A comparison of the results of the two kinds of test effected on 37 cases at intervals of 2~3 days showed the following results:

Results -50% and above (+), and -49% or less (-)

a) 22 cases of uniform results (59.5%)
   (-) in both tests ........................... 5
   (+) in both tests ........................... 17

b) 15 cases of discrepant results (40.5%)
   (+) in ACTH test and (-) in epinephrine test........... 2
   (-) in ACTH test and (+) in epinephrine test........... 13

Lohmeyer and Husselman1) made both tests in 32 cases and obtained uniform results in 17 and discrepant results in 15, and were led to express very skeptic views on the clinical value of epinephrine tests. In Japan also, Ohmori2) and Abe observed similar results and has given their doubts on the reliability of epinephrine tests. The author's results seem to agree with the results obtained by Lohmeyer et al. at a glance, but upon more detailed examinations they can bring opposite conclusions. That is: 1) The rate of average decrease of the eosinophils in 37 cases amounted to -32% upon ACTH tests and to -40% following epinephrine tests, the latter being more marked. 2) The percentage of decrease upon epinephrine tests were below those upon ACTH tests in 8 cases only, in all the other 29 cases the epinephrine tests giving always higher ratio of decrease than that of ACTH. 3) Among the cases of discrepant results, only 2 cases showed (-) upon epinephrine test and (+) upon ACTH tests but in the other 13 cases showed normal values upon epinephrine tests but (+) upon ACTH tests. This, if the percentage of decrease of eosinophils alone is considered, epinephrine eosinopenia is more apparent than ACTH eosinopenia, it is generally safe to assume that cases showing (-) results upon epinephrine tests will give negative results upon ACTH tests too. From the above, it is
concluded that though, may be, epinephrine tests cannot entirely supersede ACTH tests, they are at least useful to some extent.

II. Relationship between Epinephrine Test Results and Clinical Process

The results of tests repeated 2~8 times each on 79 skin disease cases within a period of observation of 7 days to one year were as summarized in Table I.

### Table I

<table>
<thead>
<tr>
<th>Epinephrine test results ( Compared with initial value )</th>
<th>Clinical process</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improve (decrease more than 20%)</td>
<td>Improve</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Unchange</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Aggravate</td>
<td>0</td>
</tr>
<tr>
<td>Unchange (change within 20%)</td>
<td>Improve</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Unchange</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Aggravate</td>
<td>0</td>
</tr>
<tr>
<td>Aggravate (increase more than 20%)</td>
<td>Improve</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Unchange</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Aggravate</td>
<td>1</td>
</tr>
</tbody>
</table>

As to the relation of the progress of disease and the epinephrine test result, Ohmori et al. have observed agreement in 45% and in present study in 77 cases, parallel results were obtained in 52 cases (67.5%). So it may be said that epinephrine tests show the state of progress with considerable accuracy. We conducted implantation of cow's pituitary glands one to seven times each in alopecia areata in 24 cases, but little constancy was found in the relation between the progress of their diseases and the results of epinephrine tests, except in 3 cases who showed improved test results accompanying clinical improvements.

III. Variations of Epinephrine Test Results during continued Administration of Cortisone

Two cases of Addison's disease and one each of pemphigus vulgaris, erythema nodosum and mongolism cases were subjected to epinephrine tests before, during and after cortisone treatment and the changes in the results followed up.

Case No. 1. Male, 29 years, Additon's disease. The test result was −24% before the initiation of cortisone treatment, −40% on the 20th day of the treatment when the administered cortisone totaled 675 mg., and on the 57th day, when the total dose reached 1,145 mg., became
Case No. 2. Male, 40 years, Addison’s disease. Test result before treatment, \(-39\%\); on 89th day (total cortisone dose, 1,370 mg.), \(-51\%\).

Case No. 3. Male, 61 years, pemphigus vulgaris. Test result before treatment \(-44\%\); on 33rd day (total cortisone dose, 3,300 mg.), \(-56\%\); 34th day after discontinuation of treatment, \(-33\%\). This patient had a relapse of eruption soon after discontinuation of the treatment and though the eruption healed upon readministration of cortisone treatment, died of general marasm. Upon autopsy, frank atrophy and degeneration were apparent in the pituitary and adrenal cortex.

Case No. 4. Female, 30 years, erythema nodosum. Test result before treatment, \(13\%\); on the 10th day (total dose of cortisone, 1,000 mg.), \(-57\%\); 34th day after discontinuation of treatment, \(-33\%\).

Case No. 5. Female, 30 years, mongolism. Test result before treatment, \(15\%\); on the 24th day of treatment (total dose of cortisone, 1,370 mg.), \(-55\%\); 15th day after discontinuation of treatment, \(-36\%\).

Kark et al.\(^3\) and Waldenström\(^4\) have found normal values as epinephrine test results of surgical Addison’s disease who had their adrenal glands on both sides excised and had been treated with cortisone on account of prostate carcinoma, and expressed their doubts on the clinical value of this test, but in author’s cases, it was admitted that the test values normalize gradually during cortisone treatment and in Case No. 3 and 4, a relapse to the pretreatment values upon suspensino of the treatment. These improved results during cortisone-treatment apparently does not mean sheer improvement in the function of the pituitary-adrenocortical system, but we must take transitional effects of the administered cortisone into consideration. The mechanism leading to eosinopenia following epinephrine tests is not yet adequately explained, but a solution might be sought in the hypothesis by Walderström that epinephrine causes eosinopenia by release of the corticoid depots in the body. Now, since a continued administration of cortisone involved an accumulation in the body to some extent, the epinephrine in such cases, beside directly influencing the pituitary-adrenocortical system, may be supposed to effect a release of the depots of accumulated cortisone and thus enhance the resulting eosinopenia.

IV. Behavior of Circulating Eosinophils under Antigen Loading Test

The author have made the experiments described hereunder for the purpose of elucidating the influence of the allergic reaction on the pituitary-adrenocortical system in certain cases of allergic diseases with the changes of eosinophils in blood as index.
Description of cases and experimental method: One case each of dietetic urticaria and urticaria perstans papulosa and 2 cases each of drug exanthema and cold urticaria were subjected to epinephrine and antigen loading tests at 1~2 days intervals. Latter tests includes orally given one full meal or one dosis of the drug. The eosinophils were counted before and every one hour after the antigen administration.

Results. As shown in Figs. 1~6.
In all the 6 cases above, the decrease of circulating eosinophils showed the tendency of being emphasized in paralleled with the intensity of the
Fig. 3. Drugexanthema (PAS), male, 40 years. 30 min. after administration of 2 g. of PAS, exanthemes, developed all over the body and vomiting followed. No reaction observed upon administration of sodium salicylicum, aspirin etc.

Fig. 4. Drugexanthema (PAS), male, 38 years. Upon administration of 2 g. of PAS, slight itching was felt, but no exanthema was noted.

reaction i.e. the degree of eruption during antigen loading tests. Besides, when the curves of the circulating eosinophil counts as the time of epinephrine administration, at the time of antigen loading, at the time of administering non-antigen substances and the spontaneous fluctuation curve under no loading are compared, the author find generally a parallel lowering of the curves at the time of antigen loading and at the time of epinephrine administration. Also a general resemblance of the curve at the time of non-antigen substance administration and to that of spontaneous fluctuation under no loading is noticed. If this result is to be explained by the so-called general adaptation syndrom theory of Selye, it may be said to reflect the
Fig. 5 and 6. Cold urticaria, females, 15 and 18 years. One of the feet was immersed in cold water (11°C~13°C) for 30 min. each. Soon a frank urticaria developed, extending from the lower to the upper things.

requirement of strong endocrine adaptation against the antigen antibody reaction caused in the body by administration to subject with allergic disposition of certain drugs or food that would have no effect upon subjects with no allergic disposition. In this case, the reaction mechanism would be interpreted, as Selye says, as consisting in a chain reaction in the pituitary-adrenocortical system following of histamin or histamin-like substances produced by the allergic reaction with the antigen as stressor.

V. Relation of Epinephrine Test to Urinary Content of 17 Ketosteroid

The results of epinephrine tests and measurements of urinary 17 keto-
steroid content by Holtroff and Koch's method conducted on 25 skin disease cases were studied in comparison.

Results. As shown in Table II.

| TABLE II |
|-----------------|------|------|
| Urinary excretion of 17 K.S. | Epinephrine test results | Normal | Abnormal |
|-----------------|------|------|
| Normal          | 4    | 4    |
| Decrease        | 5    | 12   |

Many investigators have conducted epinephrine tests and 17 keto-steroid determinations in combination, but their results have not been constant, so that Posey et al.\(^5\) have declared the two as unrelated, but Miyake, Baba and others have seen a generally parallel relation between the two. In present study, the author have found in 16 cases (66.7%) among the total 25 cases a parallelism of the results.

Conclusion

1. The results of ACTH and epinephrine tests showed agreement in 60% of the tested cases. The latter test in superior to the former, and the subjects showing negative results in epinephrine tests may be without much error to give negative results in ACTH tests also.

2. The relation between the clinical progress and the results of epinephrine tests showed parallelism in about 70% of the tested cases. Thus epinephrine test may be presumed to indicate the state of illness with considerable accuracy.

3. Continued cortisone administration normalized the results of epinephrine tests in the majority of the cases.

4. The author succeeded in demonstrating that an internal introduction of antigen in allergic skin disease cases calls for an intense endocrine adaptation from the standpoint of the theory of general adaptation syndrome.

5. The results of epinephrine tests and measurement of the urinary content of 17 ketosteroid showed parallel changes in 70% of the tested cases.

References