

Clinica otorinolaringologica della Università di Milano
(Direttore: Prof. L. Pietrantoni)

ADRENAL CORTEX RESPONSE AFTER INTRA- VENOUS INJECTION OF ACTH IN SEASONAL HAY-FEVER PATIENTS BEFORE AND AFTER A PROVOKED NASAL CRISIS¹

By

L. TESEO, E. CLERICI and G. CAPUANI

It is well known that adrenalectomized animals show anaphylactic shock more often than controls. Clinical use of ACTH and cortisone has shown the importance of adrenal hormones in allergic diseases. Recent works of many authors on adrenal function in allergic patients report contrasting results, but it is now generally believed that subjects suffering from allergy should have a lowering of adrenal function particularly of the glycoactive fraction. One can say that these subjects show an insufficient metabolism of adrenal hormones. Some authors consider allergic diseases are due to poor adaptation and Selye thinks that the crisis is due to shock and believes the period between the crisis to be due to fatigue.

The aims of our research were to study: 1) adrenal response in hay-fever patients not in the acute period when compared with normal ones, 2) adrenal response in hay-fever patients immediately after a provoked crisis when compared to rest periods, 3) adrenal response after a provoked crisis in hay-fever patients after treatment with ACTH, 4) the possible difference of eosinophile count in peripheral blood when compared with blood taken from the shock organ after provoked crisis treated by ACTH.

¹ *ACTHormon* (Richter, Milano) has been used in these experiments.

The methods used have been: I) Thorn test. We altered this test by giving the patients 2 mg. of ACTH intravenously instead of 25 mg. intramuscularly. This modification has already been used by Gordon et al. and Serafini et al. The intravenous way has been chosen as we thought it would give more exact results. As a matter of fact comparison between subcutaneous or intramuscular and intravenous doses shows that the same therapeutic effect can be obtained by administering intravenously a dose one-tenth of the intramuscular one (Melli). This may be due to the fact that the hormone given subcutaneously is easily destroyed and that only a little non ascertainable part of it gets used. Furthermore eosinophil counts can be done after the same interval used in the old Thorn test, as there seems to be no difference between the time of appearance of the eosinophil fall whatever method of injection is used (Melli). We choose the 2 mg. dose considered by other authors (Serafini) to be the most suitable to stimulate the adrenal cortex. Eosinophile cells have been stained using the technique of Pilot and Cecil and counted by Fuch's and Rosenthal's method. Blood samples were taken from the inferior turbinal and the cubital vein before giving ACTH and four hours later. White cells count was made to be sure that there were no general modifications of these cells. Local anaesthesia without adrenaline was used and it was strictly confined to the zone of the inferior turbinate where we wanted to take the blood sample. This technique was used to avoid stress which could have altered the results.

II) Provoking of the allergic crisis by using a constant dose of pollen to which the patient had shown positive cutaneous reactions. When the patient was sensitized to more than one pollen we used the most active. A little glass stick whose end was pan-like shaped was charged with pollen and placed successively in both nares asking the patient to inhale it. Sneezing, rhinorrhea and tears appeared after about two minutes and lasted for a period varying from two hours to a whole day. Before and after this crisis, cubital and turbinal

blood samples were taken and an eosinophile count using the previously mentioned methods was made. We didn't think it useful to investigate the quantity of uric acid and creatinine in urines as most authors believe them to be of no importance.

Using the above technique we have carried out the following researches:

I) Modified Thorn test in the morning was used for ten normal resting and fasting patients. These subjects had no allergic disease nor any identifiable allergic condition nor did they have any adrenal disorder. Eosinophil counts were made in these patients using the technique already described on nasal and peripheral blood samples.

II) Modified Thorn test in ten subjects suffering from seasonal hay fever whose allergen had been identified (mostly Graminae and Compositae) followed by an eosinophil count. This research was made in the months preceeding pollination when the patients showed no signs of illness.

III) An allergic crisis was started in the ten patients cited in point II by inhalation of samples of pollen using the technique already described. Count of eosinophils in nasal and peripheral blood was made before the test and 4 hours afterwards. This test was performed at least 5 days later than the preceeding one and under similar conditions.

IV) After a minimum of 5 days after the preceeding tests another eosinophil count was made on peripheral and nasal blood samples of these allergic patients. It was performed in the morning on the resting and fasting subjects. One hour later, a nasal crisis immediately followed by intravenous injection of 2 mg. ACTH, was started. 4 hours later another eosinophil count was made on peripheral and nasal blood samples.

Results of our researches are summarized in the following tables:

TABLE I

Modified Thorn test on nasal and peripheral blood samples of ten normal subjects.

Number	A		B		C	
	1	2	1	2	1	2
1	110	130	55	50	50 %	61 %
2	170	220	117	158	31 %	28 %
3	230	280	76	98	67 %	65 %
4	100	110	45	46	55 %	58 %
5	90	80	50	47	44 %	41 %
6	75	80	40	41	46 %	49 %
7	180	150	38	34	79 %	77 %
8	150	105	43	27	71 %	78 %
9	297	300	184	195	38 %	35 %
10	180	210	135	164	25 %	22 %

TABLE II

Eosinophil count in hay-fever patients after intravenous ACTH.

Number	A		B		C	
	1	2	1	2	1	2
1	140	120	22	25	84 %	79 %
2	170	220	60	60	65 %	72 %
3	200	110	150	100	25 %	9 %
4	210	310	100	50	76 %	67 %
5	270	150	50	30	70 %	80 %
6	120	100	35	30	70 %	70 %
7	121	204	100	40	17 %	80 %
8	170	200	88	80	48 %	54 %
9	1000	1100	500	500	50 %	54 %
10	900	800	500	500	44 %	37 %

Table I shows results of Thorn test on ten normal subjects. Column A indicates number of eosinophils before the test, column B after it, column C shows the percentage of difference between the two counts. Each column has been divided into two: the first gives values of peripheral blood, the second one those of blood taken from turbinates. The same

TABLE III
Eosinophil count in hay-fever patients after a provoked crisis.

Number	A		B		C	
	1	2	1	2	1	2
1	90	100	50	50	44 %	50 %
2	100	130	50	50	50 %	51 %
3	330	270	160	170	51 %	37 %
4	220	330	170	170	22 %	48 %
5	120	130	90	90	25 %	30 %
6	150	80	40	40	73 %	50 %
7	140	245	110	110	28 %	55 %
8	150	160	88	88	41 %	45 %
9	800	880	770	700	4 %	20 %
10	950	960	700	720	26 %	25 %

TABLE IV
Eosinophil count behaviour after crisis followed by ACTH.

Number	A		B		C	
	1	2	1	2	1	2
1	170	100	50	10	70 %	90 %
2	190	220	30	35	84 %	84 %
3	130	120	40	40	69 %	66 %
4	250	300	45	40	82 %	86 %
5	220	300	30	40	86 %	86 %
6	140	150	30	35	78 %	76 %
7	250	234	30	30	84 %	87 %
8	209	200	100	143	52 %	28 %
9	1000	1100	300	300	30 %	37 %
10	900	700	350	300	61 %	66 %

division as above has been used for the other tables. Table II shows eosinophil values in ten seasonal hay-fever patients. Table III handles values in the same subjects before and after inhaling pollen responsible for their symptomatology and Table IV before and after a crisis followed by ACTH injection. Considering these tables we may say that:-

I) Intravenous ACTH is followed generally by a fall in eosinophils both in normal and allergic patients. The mean percentage of fall in 50 % in normal and 55 % in allergic patients (these counts have been made on peripheral blood).

II) Provoked crisis in seasonal hay-fever patients by inhaling pollen responsible for their symptomatology causes a fall of blood eosinophils of about 36 % (peripheral blood samples).

III) If ACTH is given intravenously to allergic patients after a crisis provoked by inhaling of pollen the fall of eosinophils reaches 70 % in the peripheral blood.

IV) In normal patients a fall in eosinophils may be considered identical in peripheral and nasal blood (small variations are due to technical errors). In allergic subjects there is a small difference in fall of eosinophils after the crisis whether followed or not by ACTH injection. This difference is not always marked and the number may be higher or lower in peripheral blood when compared with nasal blood.

These researches are still going on in our Clinic. The following conclusions may now be drawn:

1) There is no clear difference of adrenocortical response to intravenous ACTH between normal and allergic subjects, we do not believe therefore that adrenal function as shown by our tests changes in hay-fever patients who are not having symptoms when compared to normal subjects.

2) Provoked nasal crisis may start an adrenocortical reaction shown by a fall in eosinophils. This fall appears to be lower than the one caused by intravenous injection of 2 mg. ACTH. It would seem that stress and allergic crisis are similar and act both through stimulation of the adrenals.

3) Immediately after a nasal crisis ACTH is able to cause a more intense adrenocortical response than during quiescence periods. A nasal crisis is therefore not likely to exhaust or lessen the cortical reaction and one could suppose it is even able to enhance the reaction to ACTH or that a summing of stimuli takes place.

4) It is not easy to explain the difference between eosino-

phils counts in peripheral and nasal blood after crisis or after ACTH injection as it appears to be more evident than in normal subjects, but the findings are too few and irregular. It is possible that a greater concentration of eosinophils in shock organs is followed by an irregular passing in the venous system of the turbinates.

SUMMARY

The authors have examined the adrenocortical reaction of ten hay-fever patients during rest periods by using the Thorn test (intravenous injection of 2 mg. ACTH) and examining afterwards the percentage fall of eosinophiles in peripheral and nasal blood samples. The test was performed after intravenous injection of 2 mg. ACTH, after provoking a nasal crisis and after combining the nasal crisis with ACTH treatment. It has been noted that:

1) There appears to be no difference in behaviour during the test in hay-fever patients when compared with normal subjects.

2) The provoked nasal crisis acts on the adrenals as a stressing agent.

3) The adrenal reaction to intravenous ACTH is present even after a provoked crisis.

4) There is no difference in percentage fall of eosinophils between peripheral and shock organ blood.

Ten normal subjects were used as controls.

ZUSAMMENFASSUNG

Die Verff. haben die Reaktion der Nebennierenrinde in 10 allergischen rhinopatischen Patienten ausserhalb der kritischen Jahreszeit untersucht. Eine Variante des Thorn Test's wurde verwendet (intravenöse Einspritzung von 2 mg. ACTH) und als Zeichen der Reaktivität wurde der Fall der eosinophilen Zellen in peripherischen und in Nasenblut studiert. Man machte den Test nach intravenöser Einspritzung

von 2 mg. ACTH, nach provizierter Nasenkrise, und nachdem man die Nasenkrise mit ACTH Verabreichung kombiniert hatte. Es wurde festgestellt dass:

1) Es keinen Unterschied in der Test Reaktion zwischen allergischen Subjekten ausserhalb der kritischen Jahreszeit und normalen Subjekten giebt.

2) Die provozierte Nasenkrise einen Nebennierenstress verursacht.

3) Die Nebennierenreaktion nach ACTH Verabreichung auch nach einer provozierten Krise noch eindeutig festgestellt werden kann.

4) Es keinen eindeutigen Unterschied zwischen dem Prozentsatz im Fall des Eosinophilkörper im peripherischen Blut und demjenigen in Nasenblut giebt.

10 normalen Personen dienten als Kontrolle.

RESUME

Les auteurs ont utilisé le test de Thorn modifié (injection intravéneuse de 2 mg. ACTH) pour examiner la réponse corticosurrénale évaluée comme pourcentage de chute des éosinophiles dans le sang périphérique et dans celui prélevé dans l'organe de shock en 10 subjects souffrant de rhinopathie allergique saisonale pendant la période de l'absence de symptômes. On a fait le test après une crise nasale provoquée, après une crise associée à injection de l'ACTH et après injection de 2 mg. d'ACTH. On a relevé que:

1) Il n'y a pas de différence dans la réponse au test entre les rhinopathiques allergiques et les sujets normaux.

2) La crise nasale provoquée agit sur la surrénale comme cause de stress.

3) La réponse surrénale à l'injection d'ACTH est encore évidente même après une crise provoquée.

4) Il n'y a pas de différences nettes entre les pourcentages de chute des éosinophiles prélevés dans le sang périphérique et ceux de l'organe de shock.

On a pris dix sujets normaux comme contrôles.

BIBLIOGRAPHY

- 1) *Gordon et al.*: Jour. Lab. Clin. Med., 36, 827, 1950.
- 2) *Sayers, Burm and Jager*: Journ. Clin. Endocrin., 9, 953, 1949.
- 3) *Z. Eriksson-Lihr and Forssell*: Acta Allergol. II, 1949.
- 4) *R. A. Cooke*: Allergy in Theory and Practice.
- 5) *Tuft*: Clinical Allergy.
- 6) *Gillespie*: Brit. Med. Jour. I, 1139, 1930.
- 7) *Serafini et al.*: La Clin. Terap. II, 1, 1952.
- 8) *Morbray and Bishop*: Brit. Med. Jour. January, 3, 1953.
- 9) *Cecil*: Brit. Med. Jour. Nov. 17, 1951.
- 10) *Aguirre, Arjona, Triguera*: Acta Allerg. III, 1950.
- 11) *Z. Eriksson-Lihr*: Acta Allerg. IV, 1951.
- 12) *White*: Jour. of Allergy 21, 4, 1950.
- 13) *M. Schwartz and Th. Castberg*: Acta Allergol. I, 272, 1948.
- 14) *Dragstadt et al.*: Jour. exp. Ther. 9, 359, 1937.
- 15) *Debré et al.*: Soc. de Biol. 123, 679, 1937.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.