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The Function of the Suprarenal Cortex in Allergic Diseases

By Z. Eriksson-Lihr

In 1948, before we in Finland had learned about the interesting work on ACTH, which was in progress in the U.S.A., a study of the function of the suprarenal cortex was started at the Hospital for Allergic Diseases in Helsingfors, Finland. It occurred to us that the clinical symptoms generally found in adreno-cortical insufficiency, such as adynamia, hypotonia, hypoglycemia, a sensitivity to histamine, to lack of oxygen and to infections, are also often seen in different kinds of allergic diseases. Our first studies were undertaken by the methods mainly used at this time in Europe for the determination of the function of the suprarenal cortex. For the study of the mineral metabolism we used the Robinson-Power-Kepler test and for the determination of the carbohydrate metabolism the glucose-, insulin- and adrenalin-tolerance tests. Later determinations of the 11-oxycorticosteroids were performed and finally a study of the eosinophilic response of the leucocytes to ACTH, cortisone and epinephrine was made using the so-called Thorn test. The purpose of this paper is to give a short review of the results obtained.

The Robinson-Power-Kepler test has been performed in 273 cases, children and adults, suffering from different allergic diseases, in many of them several times for control (table 1). 23 of the 135 children (17%)

Table 1
Kepler test 273 cases

Diagnosis	Children			Adults		
	Cases	Kepler +	%	Cases	Kepler +	%
Asthma	80	11	13,8	89	21	23,6
Eczema	25	3	12,0	27	4	14,8
A + E	22	6	27,2	6	2	33,3
Other Allergy	8	3	37,5	16	2	12,5
Total	135	23	17,0	138	29	21,0

Table 2
Insulin tolerance test. 215 cases

Diagnosis	Children					Adults				
	Cases	Latency time				Cases	Latency time			
		<3'	3-6'	6-9'	>9'		<3'	3-6'	6-9'	>9'
Asthma . . .	60	13	21	17	9	81	12	34	24	11
Eczema . . .	19	7	10	1	1	12	2	4	5	1
A + E . . .	18	4	12	2	0	5	2	1	1	1
Other allergy	7	0	4	3	0	13	1	5	4	3
Total . . .	104	24	47	23	10	111	17	44	34	16

and 29 of the adults (21%) showed a positive Kepler test, pointing to a disturbance in the water-mineral metabolism as it is mainly found in Addison's disease, due to an insufficiency of the desoxycorticosteroids of the suprarenal cortex.

The double glucose tolerance test by *Staub*, performed in 105 cases showed in almost all of them a normal absorption of the glucose from the intestines.

The Insulin tolerance test (0.1 units of insulin per kg body weight) was performed in 215 cases. In a normal person this small amount of insulin causes an approximate 30% decrease of the bloodsugar after a so-called latency period of about 6-8 minutes or more, which it takes for the bloodsugar to fall below the starting level. In about half an hour the bloodsugar value is again normalized. The normal subject shows almost no reaction to this test. In insufficiency of the suprarenal cortex, as in Addison's disease, the latency period in this test is short, the bloodsugar falls continuously and remains low for one to two hours. As is seen in fig. 1, the curve of the allergics follow closely the curve obtained in Addisonians. The reaction to the hypoglycemia in the allergic patients was remarkable. Many patients showed such severe preshock symptoms that the test had to be discontinued by oral administration of glucose in order to prevent a real shock. In spite of this, in some patients a major shock with unconsciousness and convulsions was seen.

In table 2 the latency times of our cases are given. In 68.1% of the children and 55% of the adults the latency time was less than 6 minutes.

In 206 cases both Kepler and insulin tolerance tests were performed (table 3). Of the 102 children only 12 showed at the same time a positive Kepler test and an insulin latency time less than 6 minutes. In only 5 of the children a positive Kepler test and an insulin latency time of less than 3 minutes was seen. In 104 adult allergics the results were respectively 8 and 3 cases. These results are rather interesting. They indicate,

Table 3
Kepler and Insulin test 206 cases

Diagnosis	Children					Adults				
	Cases	Kep-ler+	Ins.<3'	Kepl.+ Ins.<3'	Kepl.+ Ins.3-6'	Cases	Kep-ler+	Ins.<3'	Kepl.+ Ins.<3'	Kpl.+ Ins.3-6'
Asthma . . .	60	9	13	3	4	63	20	8	3	4
Eczema . . .	17	3	7	1	2	21	3	4	0	2
A+E . . .	17	5	3	1	5	4	2	0	0	0
Others . . .	8	3	0	0	1	16	2	1	0	2
Total . . .	102	20	23	5	12	104	27	13	3	8

it seems to me, that the insufficiency of the different suprarenal hormones is not always seen at the same time. Interesting also is the observation, that all the patients, who showed disturbances of both desoxycorticosteroids and 11-oxycorticosteroids, were very severe cases of allergy.

The adrenalin tolerance test was performed in 80 cases. The amount of epinephrine administered was 0.014 mg per kg body weight, given subcutaneously. This test is presumed to give a picture of the glycogen content of the liver. If the glycogen content of the liver is diminished, epinephrine is unable to mobilize it in comparative quantities and the increase of the bloodsugar is smaller than the normal (45-60 mg%). This happens in cortical insufficiency, in which case the glyconeogenesis is disturbed and the glycogen reserve of the liver is diminished. In only about 50% of our cases a normal increase of the bloodsugar curve was found, the other cases showed an average increase of only 25 mg%.

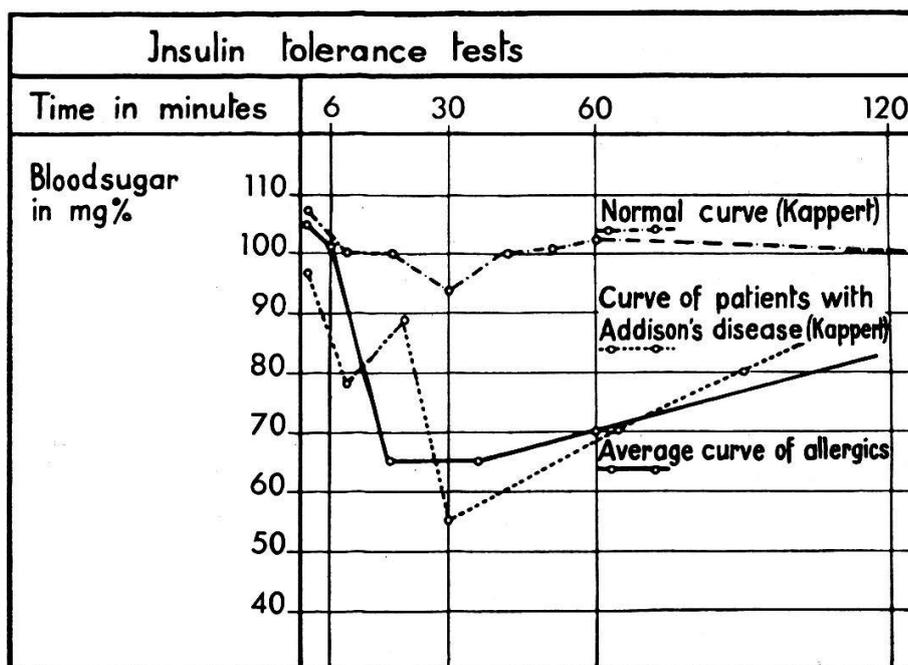


Fig. 1.

Table 4
11-Oxy-Corticosteroids. 57 cases

Diagnosis	Children			Adults		
	Cases	Norm.	Subnorm.	Cases	Norm.	Subnorm.
Asthma	16	4	12	20	5	15
Eczema	4	0	4	4	1	3
A + E	4	2	2	1	0	1
Other allergy	3	1	2	5	0	5
Total	27	7	20	30	6	24

Blood eosinophilia and lymphocytosis are considered as typical symptoms of insufficiency of the suprarenal cortex and are mostly observed in Addison's disease. In a study of the white blood count in 500 cases of different allergies in children and adults, without present signs of infection, a consistent tendency to lymphocytosis and, as is well known, to eosinophilia, was observed.

The excretion of the 17-ketosteroids in the 24 hours urine was measured in 96 allergic cases of different origin, using the Zimmermann-Callow method. In 24 of these low values were obtained, whereas 6 showed abnormally high values. As normal values were considered those determined by *Hamburger* for healthy Danish people, aged 2-102 years.

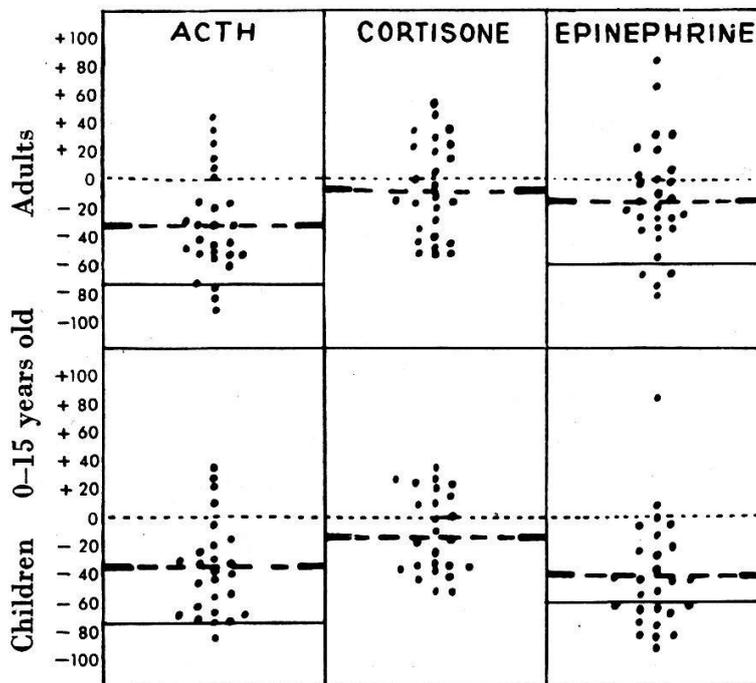


Fig. 2.

Thorn tests in allergies:

Thorn tests average in allergies - - - -
Thorn tests average in normals ———

Because of these results, showing in about 80% of the allergics a disturbance in the mineral or the carbohydrate metabolism, a direct determination of the 11-oxycorticosteroids in the 24-hours urine was undertaken in 57 cases by the method described by *Heard, Sobel* and *Venning*. Out of 27 children only 7 gave normal values, whereas 20, that is 75%, showed subnormal, often very low values. Of the adults, 6 gave normal and 24 (80%) low values.

Finally a study of the blood eosinophile response to ACTH (*Armour*), cortisone (*Merck*) and epinephrine was undertaken. *Recant* and *Hume, Forsham* and *Thorn* assume that 25 mg of ACTH reduces the amount of blood eosinophiles at least 50% within 4 hours, wherever the function of the suprarenal cortex is normal. The same result is seen by giving 0.2 to 0.3 mg epinephrine intramuscularly. Several objections to these tests have been expressed lately. Especially the results found in allergics, where the eosinophile count is mostly high, have been criticized. In spite of this, we felt it interesting to make a study of the *Thorn* test in allergics as, according to our theory, it could be possible that the eosinophiles are high in allergy because of an insufficiency of the suprarenal cortex hormones. These tests were performed in 30 children and as many adults. The results are seen in fig. 2.

The *Thorn* test with ACTH in normal adults as well as in children showed an average fall of the eosinophiles of about 80%. The allergics gave an average fall of only 33%. The *Thorn* test with epinephrine was 60% in normal subjects. In adult allergics an average decrease of not quite 20% was seen, whereas the allergic children gave a better response, a decrease of the eosinophiles of 40%.

As the 11-oxycorticosteroids are supposed to be the main cause of the eosinophile response in the *Thorn* test, our results with ACTH and epinephrine were compared with results obtained with 30 mg cortisone (*Merck*). As can be seen in the fig. 2, the decrease of the eosinophiles after cortisone was surprisingly small. If the decrease of the blood eosinophiles is due to the 11-oxycorticosteroids, one would expect the decrease of the eosinophiles to be normal after cortisone also in cases with low values of the 11-oxycorticosteroids, like our allergics. That this did not occur, points, I think, to the fact that the eosinophiles are also influenced by other causes, not by the 11-oxycorticosteroids alone. In adult allergics the poor response of the eosinophiles to epinephrine speaks for a more complicated, in these cases exhausted pathway for this reaction.

The results thus obtained, showing a disturbance of the mineral- or carbohydrate-metabolism and of the 11-oxycorticosteroids determined

in about 80% of allergics studied, point to an insufficiency of the hormones of the suprarenal cortex in the afore-mentioned cases.

In the light of these investigations we should still like to keep to the statement we made in 1949.

that we assume the Allergic Diseases to be a group of Diseases of Adaptation (Selye) due to a relative Insufficiency of the Suprarenal Cortex Hormones.

Studies now performed in our hospital of allergic cases before, during and after attacks also point in this direction.

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