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SOME EXAMINATIONS IN CONNECTION WITH A CASE OF HYPERSENSITIVENESS TO COTTON-SEED

By

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It has long been known that cotton-seed contains substances with allergenic properties. Definite cases of manifest hypersensitiveness to cotton are, however, of rare occurrence, at all events in Sweden. As we have had such a case at the Allergy Department of St. Göran's Hospital, an account of the same will be given here below.

Case: A. K. L. ♀ journal number 2058-50. 43-year-old housewife without known heredity for allergic complaints. Had scarlatina as a child, but otherwise no illnesses worth mentioning during childhood and adolescence. In 1938, when the patient was 21 years old, she developed asthmatic trouble after an angina tonsillaritis. Since then sporadic asthma with rather short attacks and long symptomfree intervals. The attacks have not been seasonal and have frequently been preceded by an acute infection of the upper respiratory tracts. During the years 1943-48 the patient had scarcely any trouble at all. In the course of the years she had on several occasions been treated in hospital, where she was as a rule admitted in status asthmaticus. No allergic tests had been undertaken.

On the 2.II.50 the patient was admitted to the Allergy Department after having had moderately severe asthmatic trouble for about a week. She had status asthmaticus on admittance. On the occasion of the examination made at that time no anamnestic disclosures of importance were made over and above the case-history sketched above. At first glance the anamnesis yielded

no evidence pointing to specific hypersensitiveness. Physical examination showed, besides signs of slight emphysema, nothing worth mentioning. The usual focal examination gave neg. result. Sedimentation rate was normal, as were also serological titers. The skin-test was performed on the 8.11.50 with our standard series of allergenic extracts, consisting of about fifty different allergens. The test was carried out in the usual way with intracutaneous wheals on the back. Some minutes after the last wheal had been inflicted the patient developed severe dyspnea, violent feelings of anxiety, became pronouncedly cyanotic and collapsed unconscious. 0.7 ml 0.1 % adrenalin-solution was immediately administered subcutaneously, as well as oxygen-gas with mask and artificial respiration. As during the next few minutes the patient's condition rapidly became worse, respiration stopped and the heart-sounds could not be heard, a further 1.0 ml 0.1 % adrenalin-solution (diluted with 9 ml physiological (NaCl)-salt solution) was supplied slowly intravenously. This was followed by 10 ml theophyllamine intravenously. The respiration thereupon recommenced and the cyanosis gradually receded. The patient regained consciousness after

TABLE I
Skin-tests on november 8th, 1950.

Control —	Wheat +
Sheep's wool +	Rye —
Feathers ±	Barley ± (after 6 hrs +)
House-dust I ±	Oats ±
„ II ±	Maize ±
„ III +	Timothy-pollen +
„ IV +	Tree-pollen +++
Histamin ++	Pollen from ox-eye-daisy +
Fish ±	Reed-pollen —
Meat ±	Orange —
Vegetables +	Hazelnut ++ (after 6 hrs +)
Dog's hair —	Moulds +
Cat's hair —	House-dust +
Horse's hair ++	Cotton-seed cake +++ (after 6 hrs
Cow's hair +	++++++)
Cooked milk ++	Spices —
Uncooked milk ±	Birch-pollen +++ (after 6 hrs ++)
Cooked white of egg ±	Pine-pollen —
„ yolk +	Concentrated house dust +
Uncooked white of egg ±	
„ yolk ±	
Lycopode +	
Crustaceous animal +	
Cacao —	

about 15 minutes. Her condition then improved successively. After about an hour, however, the patient developed a brick-red erythema over the entire body, felt nausea and entered a state resembling peripheral shock with scarcely palpable pulse, tachycardia etc. She was given energetic treatment with oxygen-gas and oxedrin, and soon recovered. The erythema remained for twelve hours.

The skin-test on the 8.11.50 gave the results shown in table I.

The skin-test thus gave several positive reactions, and a particularly strong reaction was obtained with extract of cotton-seed cake. The suspicion immediately arose that the shock was caused by the last-mentioned allergen, and it was evident that this particular hypersensitiveness had not been disclosed on the occasion of the anamnestic examination. When the anamnesis was further penetrated it emerged that on several occasions when knitting with candle-wick yarn the patient had developed dyspnea and a whistling in the chest. She also remembered that she had had a severe attack of asthma when on one occasion she had applied a compress with cotton wool, and also on another occasion when she was stuffing a cushion with kapok.

In order to ascertain which of the positive reactions observed in the skin-test were of clinical significance, skin-titration and provocation-tests were carried out with the following results:

TABLE II

Allergen	Skin tit	Provocation test	Remarks
Sheep's wool	1 : 10 mill.	Neg.	Sniffed sheep's wool for 1 hour
House-dust	1 : 1000	Neg.	Inhal. of 1.0 ml extract 1 : 10
Wheat	1 : 100000	Neg.	Snuffing of flour
Timothy pollen	1 : 100000	Neg.	Snuffing of pollen
Pollen from oxeye daisy	1 : 10000	Neg.	Snuffing of pollen
Birch pollen	1 : 1 mill.	Neg.	Snuffing of pollen
Cotton-seed cake	1 : 1000 mill.	Pos.	Inhal. of 1.0 ml extract 1 : 1 mill. provoked asthma and coryza

The examination thus showed that the patient was manifestly hypersensitive to cotton seed and that other positive reactions in the skin-test were an expression for latent allergies. The shock on the occasion of the skin-test was certainly released by the extract of cotton seed.

Cotton is constituted by the seminal hairs of different species of the genus *Gossypium*. The seeds of this bush are

provided with long, white fibres and shorter fluff (linters). In the process of preparation for commercial use the fibres are separated from the seed. Even the shorter fluff is kept, separated from the seeds and used for wadding, stuffing for furniture etc. Small parts of the seed may in spite of the separation still remain in the finished product. Spies et al. (1946) have shown that the cotton allergen occurs chiefly in the seed, and hypersensitive reactions are therefore as a rule not provoked by highly purified cotton products, but by more impure products which contain parts of the seed, e.g. wadding, candlewick yarn etc. It may also be mentioned that the kapok-tree and the cotton-bush, which are botanically related, also contain closely related allergens (Coca and Grove 1925). Cohen and co-workers (1935) have shown, in some very interesting studies, that it is possible to extract from pure fibres of cotton and kapok that have aged in a sterile milieu without supply of air an allergen which gives strongly positive skin-reactions in patients hypersensitive to dust. It has not been possible to extract any such allergen from fresh fibres. Cohen has from these investigations wished to draw the conclusion that the active substances in house-dust consist to a large extent of disintegration products of different textile fibres.

In American surveys it is stated that positive skin-reactions to extract of cotton-seed occur in 2-5 % of cases of allergy (Aaron Brown, G. T. Brown, Samuel J. Taub, Feinberg, Mitchell). In our material from the years 1949 and 1950 we found in 19 of 769 skin-tested patients moderately strong positive reactions to extract of cotton-seed cake. Only in the above-described case was there any evidence of manifest hypersensitiveness. Several American writers have given accounts of definite cases of manifest hypersensitiveness to cotton.

In the discussion of the clinical assessment of positive skin-reactions it has frequently been stated that so-called refractory phases occur in the hypersensitiveness. It has also been observed in experiments on animals that after massive

allergic shocks the animal has occasionally become "deallergized" (Urbach). It seemed to us that the present case might be interesting to study with reference to the possible effect of the shock upon skin-titer and the result of provocation-tests. During the weeks following the shock we therefore performed daily skin-titrations and provocation-tests. In order to ascertain whether ACTH had any affect upon skin-titer and upon the threshold-value in provocation-tests, we administered ACTH for 4 days in somewhat varying doses and distributed over 3-10 injections every twenty-four hours. The patient was not aware of what was being injected, and during the days preceding and following the ACTH-period she was given blind-injections of physiological salt solutions. The results of these tests may be seen in table III.

The results of the investigation show that the day after the allergic shock and during the whole of the subsequent observation period the patient had strongly positive skin-reaction to the allergen in question. The titration-limit for the reaction was during the last 10 days of the observation-period higher by a potency of 10. The difference is too small, however, to allow of any definite conclusions concerning the effect of the shock upon the skin-titer. The ACTH treatment had no effect upon the skin-titer. Provocation-test were carried out according to the method proposed by B. Arner (1948). At the beginning of the tests the patient was thus free of symptoms, and the tests were regularly begun with inhalations of control-solution, which in all the tests gave a negative result. After this the patient was made to inhale cotton-seed extract in increasing concentrations. The amounts and concentrations of the extract that provoked objective symptoms are given in the table. The provocation-tests were positive the day after the allergic shock and daily throughout the whole period of observation. It was not possible to observe any changes worth mentioning in the threshold-value for the appearance of the symptoms. ACTH had no remarkable effect in this respect.

TABLE III
Skin titers, provocation tests etc. in the days after the allergic shock.

Date	Results of titration in the skin with cotton-seed-cake-extract				Results of provocation test (inhalac. of extract of cotton-seed-cake)			Total number of eosinophils in blood/ml.	ACTH mg/24 hours
	1:100 mill.	1:1000 mill.	1:10000 mill.	1:100000 mill.	Result	Dosis	Koncentrat.		
9.11.50	+	—	—	—	±	1.0 ml	1:1 mill.	1818	Placebo.
10.11.	+	±	—	—	±	1.0 ml	1:1 mill.	1020	"
11.11.	+	±	—	—	+	1.0 ml	1:1 mill.	1043	65 mg
12.11.	+	—	—	—	+	0.5 ml	1:1 mill.	10	40 mg
13.11.	+	±	—	—	+	0.4 ml	1:1 mill.	6	30 mg
14.11.	+	—	—	—	+	0.5 ml	1:1 mill.	3	15 mg
15.11.	+	±	—	—	±	1.0 ml	1:10 mill.	1818	Placebo.
16.11.	+	±	—	—	+	1.0 ml	1:1 mill.	1020	"
17.11.	+	±	—	—	+	1.0 ml	1:1 mill.	1043	65 mg
18.11.	+	—	—	—	+	0.8 ml	1:100,000	10	40 mg
19.11.	+	±	—	—	+	0.9 ml	1:100,000	6	30 mg
20.11.	++	+	—	—	+	0.9 ml	1:100,000	3	15 mg
21.11.	++	+	—	—	+	0.3 ml	1:100,000	733	Placebo.
22.11.	++	+	—	—	+	0.3 ml	1:100,000	1913	"
23.11.	++	+	—	—	+	0.2 ml	1:100,000	2253	"
24.11.	++	+	+	—	+	0.7 ml	1:1 mill.	2173	"
25.11.	+	+	—	—	+	0.7 ml	1:100,000	3020	"
26.11.	+	—	—	—	+	0.7 ml	1:100,000	1342	"
27.11.	++	+	±	—	+	0.3 ml	1:100,000	1202	"
28.11.	+	+	+	—	+	0.8 ml	1:100,000	1380	"
29.11.	++	++	±	—	+	0.4 ml	1:100,000	2128	"
30.11.	++	+	±	—	+	1.0 ml	1:1 mill.	1194	"

SUMMARY

The authors give an account of a case of allergy to cotton-seed, where on the occasion of the skin-examination the patient got a severe allergic shock. During a period of 22 days after this the patient was examined daily in respect of skin-titer and sensitiveness to provocation by inhalation of the specific allergen. The examination did not show any definite reduction of the skin-titer or the bronchial hypersensitiveness after the shock. During the period of observation the patient was given ACTH during a 4-day period, which did not lead to any remarkable changes in the sensitiveness of the patient's skin or bronchial mucous membrane. The case described did not provide any evidence for the occurrence of refractory periods in the hypersensitiveness after an allergic shock.

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