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CONJUNCTIVITIS AND EYELID ECZEMA DUE TO HYPERSENSITIVENESS TO ADRENALIN SOLUTION EMPLOYED IN SPRAY-TREATMENT OF ASTHMA

By

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Ever since *Graeser* and *Rowe* (1934) began to use a spraying device for local adrenalin treatment of asthma, this method has become of great significance and extensive employment. It is not unusual, however, that in connection with this form of treatment, the patient is liable to get an attack of temporary palpitation of the heart, tremor, agitation and distress, which is often the result of too great and too frequent inhalation.

Hypersensitivity reactions to adrenalin have also occasionally been met with, as a rule, after injections.

Cohen and *Waterstone* (1940) observed two such cases which developed local necrosis, followed by pigmentary scars at the place of injection. The adrenalin used was not a preparation of the synthetic, but of suprarenal tissue. The authors were of the opinion that the changes were due to local anaphylaxis of the tissue.

Mitchell (1952) reports two cases with similar changes after injections. Here also the preparations were produced from suprarenal tissue and not from either synthetic or nor-adrenalin. *Mitchell* also holds the view that it is a question of a local allergic tissue reaction.

Rowe and Rowe (1948) tell of four cases with successive necrosis and pigmentary scars after injections with adrenalin extracted from animal tissue, while synthetic adrenalin gave no such results. They considered that the necrosis was due to cutaneous allergy (*Arthus'* phenomenon).

Dumm (1941) has described a case in which urticaria followed the application of extracted, but not of synthetic adrenalin.

Herxheimer (1951) gives an account of a patient who suffered from asthma bronchiale + urticaria. After injections with synthetic adrenalin the asthmatic trouble was certainly less, but the urticaria became more intense. On the other hand, noradrenalin did not produce urticaria.

Halle (1930) mentions a patient who was given injections of 2–3 ml. of a 5 % solution of procain to which was added one drop of adrenalin solution in dilution 1:1000. Local necrosis followed. The author looked upon the condition as hypersensitiveness to adrenalin.

A few places of manifestation other than the skin are also reported. In 1944 *Appelbaum* published two cases of temporary cerebrovascular disturbances with paresis, probably resulting from vasoconstriction of cerebral arteriolae, which occurred after the subcutaneous injection of 0.5 ml adrenalin hydrochloride at a dilution of 1:1000. The report does not state however, whether the adrenalin used was the synthetic or the one produced from animal tissue.

Leicher has described a number of cases of vasomotoric rhinitis caused by adrenalin which was employed in the local treatment of nasal mucous membrane for the purpose of reducing swelling. By performing different tests he came to the conclusion that the trouble lay in hypersensitivity-reaction to the adrenalin. Four patients reacted severely after being painted with synthetic adrenalin. Three of these also reacted strongly after suprarenal extract, while the reaction of the fourth was weaker. The reaction was equally severe whether the dilution was 1:1000 or 1:10,000. Eosinophilous cells were observed in the nasal secretion. On the other hand, no

vasomotoric symptoms appeared after subcutaneous adrenalin injections.

Thus, according to the literature, both the synthetic and adrenalin produced from animal tissue are sometimes liable to cause trouble which, at least in some cases, seems to be due to hypersensitiveness to adrenalin. As these cases are fortunately rare, and as correct interpretation is of importance to the treatment, we have considered it right to publish a case which has been under our observation.

In Jan. 1954, a woman aged 49 was admitted to the Med. Clin. II of St. Görans sjukhus (164/54). In Jan. 1953 she was taken ill with asthma bronchiale after an infection of the upper air-passage and was tended the immediately following time at the same department. The anamnesis disclosed that on two occasions earlier, a rash, among other things, resembling urticaria, had broken out in 1950 after partaking of butter and milk. Moreover, it was found that, during the patient's stay at the hospital, on one occasion when medicine containing iodine had been given an urticarial reaction occurred. Twenty-four hours after the medicine was discontinued, these changes disappeared.

The allergic investigation undertaken in connection with the patient's first hospital stay in 1953, gave no indications of any specific allergy, and for this reason she was dismissed with various symptomatica + hectalin spray, moreover, also treated as out-patient with injections of anti-catarrh vaccine. Since the dismissal in June 1953, the asthma had been so mild that no hospital care had been necessary.

The reason for admission in Feb. 1954 was not asthma bronchiale, but a troublesome itching in and around the eyes with intense conjunctivitis and edema of the eyelids, sometimes so severe that she could only see with difficulty. These troubles began the first time in Sept. 1953. They came with rather long intervals, and in accordance with the patient's observations were worse in connection with menstruation. Occasionally she was fairly trouble-free, but without any known cause, very severe eye troubles would make their appearance. She herself had not been able to find any reasonable cause.

In the autumn and winter of 1953-1954 the patient sought help from eye-specialists both diagnostically and therapeutically. She was given treatment with eye-drops and ointments, but without success. Finally, the illness was considered to be so disagreeable and inaccessible to customary therapy that a new allergic investigation was found desirable and the patient was readmitted to the hospital.

On admission nothing remarkable was found in the somatic status but moderate asthma bronchiale which involved the taking of asthma tablets and expectorantia as well as occasional use of the hectalin sprayer. There was also slight diabetes which, however, did not demand insulin. Redness and a somewhat edematous

skin, especially on the lower eyelids, showed on arrival, as also did pronounced conjunctivitis. During some days exacerbation with occasional, excessive eyelid-edema would occur particularly in the mornings, whereas the changes were considerably less on other days. The illness appeared during the first time of observation to be completely unsystematic and without any reasonable explanation.

However, it was soon obvious that being localized to the eyes and their surroundings, the trouble must derive and be conveyed from some exterior source. The patient was therefore again minutely questioned especially in regard to cosmetics, soaps, washing-material, and so on, but these articles could be excluded as causal. Epicutaneous tests with standardized extract and nail polish were found to be negative.

Then suddenly one morning, after some fairly free days, the trouble returned with renewed force. It was found that the patient had used nothing beyond the ordinary on the morning in question, except the hectalin sprayer. Epicutaneous tests were now performed with her spray-solution and the result was intense local reaction with irritation and itching of the eyes. The hectalin was now completely banned with the result that the eye changes entirely disappeared within a few days. Their easy reinducement also explains why the patient had more trouble in connection with the menstruation, when she used the spray to assuage the asthma, which augmented during these periods.

New epicutaneous tests were made with the different constituents of hectalin, each separately: chlorbutol 0.05 gr in spir. conc. 10, Natr. pyrosulph. 0.005 gr in aqua dest. 10, and adrenalin base (synthetic) dissolved in HCl (adr. base 1, HCl normale 5.6, aqua dest. ad 10). Repeated tests revealed that it was the adrenalin to which the patient was sensitive. The 10% adrenalin solution induced strong positive reaction. Controls with other asthmatic patients showed corresponding reaction negative. Epicutaneous tests with chlorbutol and natr. pyrosulph. gave negative results. Such tests were also made with weaker adrenalin solutions, namely, the above mentioned solution diluted 3, 10 and 100 times. The weakest of these always induced negative reaction, whereas the stronger gave weak positive. Adrenalin-injections caused the patient no trouble with the exception of local ischemia at the place of injection. It would seem that the explanation of this perhaps is, that the solution used is so much weaker than that employed for inhalation.

SUMMARY

A description is given of a case in which the inhalation of hectalin by means of a sprayer produced conjunctivitis and eyelid-eczema. Epicutaneous tests gave positive reaction with synthetic adrenalin whereas the reaction was negative among control persons with asthma. It would therefore seem reason-

able to believe that the case is one of allergy for adrenalin. When the patient discontinued the use of hectalin the trouble ceased also.

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