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ON ANNULAR CUTANEOUS EFFLORESCENCES IN CONNECTION WITH TRANSFER TESTS OF THE PRAUSNITZ-KÜSTNER TYPE WITH STUDIES OF ANTIGEN MIGRATION IN THE ORGANISM

By

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A series of passive transfer tests were performed to study the effect of ACTH and cortisone on the antigen-antibody reaction using the Prausnitz-Küstner technique.

Certain patients who showed negative skin tests with the usual antigens were given injections of serum, from an asthmatic patient with pronounced specific hypersensitivity, both prior to and after the above preparations had been administered.

Four patients were subjected to the test. Like most authors who have carried out such experiments, it was found that the allergic urticarial reaction was not noticeably affected by the preparations.

On the provocation of the reactions however, observation was made of a chance occurrence, which may possibly contribute towards elucidating how certain ring-shaped cutaneous efflorescences arise, and how the expansion of the antigen in the organism is liable to be affected by allergic manifestations already in evidence. An account of the phenomenon would therefore seem to be justified.

Patient A. L., 2058/50 and 260/54, had among other things, a very high skin-titre for antigens, which are to be found in impure cotton-wool (C. Juhlin-

Dannfelt and collaborators 1953, for further details of the patient). The skin titration gave positive reaction with a conc. of 1:1.100 mill., and the inhalation of antigen solution provoked an asthmatic condition at a conc. of 1:1 mill., that is to say, a concentration which is 1.000 times weaker than the one generally employed for intracutaneous tests. The asthmatic patient had noticed that she was troubled by cotton-wool. As is known cotton-wool is composed of white thread-like fibres which surround the seeds of the *Gossypium* genus. During the refining process the fibres are separated from the seeds which, latter, contain antigen substances, as does the impure wool. But there are no such substances in refined cotton-wool.

As an example of the phenomenon previously referred to, an account might be given of the transfer-test which a patient underwent at the Rheumatic Clinic, Lund:

A girl, A. N. No. 74/51, aged 12, had been given treatment for rheumatic fever. Injections of serum from the patient A. L. and of serum mixed with salt solution were administered. The injections took place on 2.4.1951 in the manner illustrated by Fig. 1, where each injection of serum or diluted serum is marked with a circle. The concentration of the diluted serum is stated beside the circle. A cutaneous titration with cotton-seed cake gave a negative result 10^{-3} .

On 4.4.51, the reactions were provoked with a cotton-seed cake antigen dilution of $\frac{3}{4} \times 10^{-4}$. Six circles were injected whereas five were not. The former are indicated in Fig. 1 by a $\times$.

The injections were given at 11 o'clock. Control tests were simultaneously made on non-sensitised skin. These tests were negative.

Fig. 2 (coloured plate) shows the development of the allergic cutaneous reactions. Injections made at the various places are indicated on Fig. 1. The four pictures a-d were taken at the following times:

- a. at 11.20
- b. „ 11.28
- c. „ 11.35
- d. „ 11.48

The pictures a, b and c reveal all provoked reactions, while on d, only enlargements of the reactions A, B and C on Fig. 1 are seen.

As the pictures in Fig. 2 illustrate, there occurs severe wheal reaction of the usual type surrounded by marked erythema after the administration of antigen, at the place where undiluted serum was injected (A). This erythema does not expand however concentrically round the urticarial formation but develops in a direction towards the with serum injected skin places B and C. Between these and the row of

serum-dilutions D-K, the skin is pale, which indicates that this was not the point of departure for the antigen diffusion. At the two upper places B and C, where undiluted serum was earlier injected develop urticarial formations with raised margins and depressed centres. It is clearly seen that the eminences began to form at the under-edge of the places marked B and C, with subsequent gradual completion of the circle. (Thus at the places B and C antigen was never injected.)

The results were similar as regards the other patients even though the ring-formation was not always so apparent. A distinct formation of this kind would seem to depend upon a correct adjustment between the injected quantity of antigen and antibodies.

DISCUSSION

After the allergic reaction has begun to develop at A, non-neutralized antigen migrates to the periphery. At places where the antigen encounters fixed antibodies there occurs a new allergic reaction. Should there be a marked edema, continued antigen expansion in this direction would seem to be arrested. This resistance in the form of increased tissue-pressure leads to further migration along the periphery of the first urticarial formation, which acts as an obstacle like a breakwater for the waves. Pursuing its course thus, the antigen reacts with fixed antibodies and an arch-like eminence arises, which finally closes and assumes the shape of a circle. These raised margins serving as obstructions prevent the antigen from entering the centres where the antibody concentration is the highest.

The circumstances pertinent to circular cutaneous efflorescences have been reviewed by Haxthausen (1949) and Sulzberger (1940). The investigation by Menkin (1938) concerning the role of inflammation in immunity is also of interest in these problems.

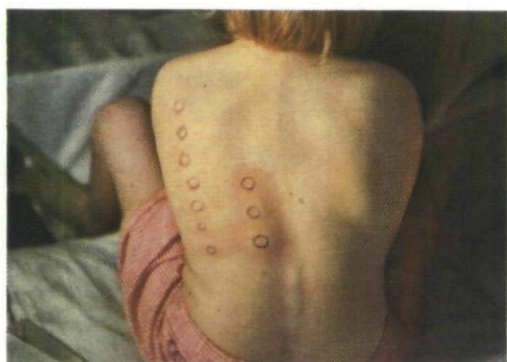
In his work on allergy in skin diseases (1949), Haxthausen maintains that in some of these, allergic factors are



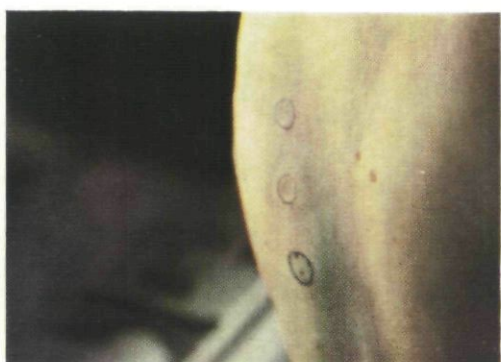
a



b



c



d

Fig. 2.

liable to affect the clinical picture. It is in this way that circular formations, among other things, may come into existence.

Circular formations imply a distinct difference between centre and periphery. According to Haxthausen these formations generally appear in cutaneous diseases on a peripheral migration of an efflorescence which develops retrogressively in the centre. Some authors explain this as being due to the disappearance of the cause of the disease from the centre and to its wandering outwards. Haxthausen, however, considers the explanation to be inadequate, as it implies that the disease-agent is only able to migrate in a peripheral direction. Nor is the explanation in agreement with what occurs when two rings meet. Haxthausen writes: "If the mere presence of the agent were decisive on the picture of the lesion, we would expect the rings simply to overlap each other. But, as is well known this is not what happens. As soon as two rings meet, they open and the place of contact takes on the character of the two central areas. This phenomenon can only be explained as attributable to the circumstance that the skin area encompassed by a ring has become insusceptible to the agent, or at any rate it has changed its reaction to the agent. In other words, an allergic state of the skin has been established in the centre of the rings, most often characterized by more or less complete immunity".

In addition to Haxthausen's explanation that if two circles meet, the mutual parts of the rings disappear it would seem reasonable to count with another possibility—judging from observations included in the present work, namely, that the antigen supply to those parts of two rings which are in common is either suspended or reduced.

The local allergic process with edema can be of use from the standpoint of the organism by hindering the antigen from penetrating further into the organism to places where allergic reaction would be more hazardous for the organism on the whole, than would be the local preventative allergic process. But the local reaction itself, by reason of its localization, is

Serum (diluted)		Serum (undiluted)
1:6561	○ K	
1:2187	⊗ J	
1:729	⊗ I	
1:243	⊗ H	
1:81	⊗ G	
1:27	⊗ F	○ C
1:9	○ E	○ B
1:3	○ D	⊗ A
		×

Fig. 1.

- Place where serum or diluted serum was injected on 2.4.51.
 × Place where antigen was injected on 4.4.51.

The concentration of the diluted serum is stated beside the circles.

liable to cause serious consequences due, for instance, to space-limitation in the bronchi where the local reaction gives rise to asthma.

SUMMARY

A phenomenon which was observed in transfer tests performed according to Prausnitz-Küstner technique is described. Circular formations of urticarial type developed under certain conditions. The importance of the observation in reference to understanding the circumstantial origin of cutaneous efflorescence of the ring-type is discussed. The observations would suggest that the allergic reaction already in evidence may affect the continuance of antigen migration.

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