

## HISTOLOGICAL CHANGES IN ALLERGIC-HYPERPLASTIC POLYPOUS RHINOPATHY

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For allergic, vascular and secretory changes of the nasal mucosa **Eckert-Möbius** and **Lüscher** have recommended the concept of "rhinopathy," in contradistinction to the numerous bacterial types of rhinitis and sinusitis. According to **Hörbst** it is difficult to determine whether there is an "allergic" — or "pathergic" — cause of the disease, since a diffuse hypersensitization of the nasal mucosa exists which does not derive from an antigen-antibody reaction, but from a "pathergic" basis.

When hypersensitization occurs, at first only discrete and mild reversible changes may appear in the nasal and sinus mucosa; however in some cases these lead to hyperplastic superfluous growths of the polyp type.

For some years we have made microscopic examinations of the mucosa of all our patients with hypertrophies of the nasal mucosa and nasal polyps. Special attention was directed to characteristics of the nasal mucosa in allergic diseases of the nose and sinuses. In recent years we have used the silver carbonate method according to **Jabonero** which generally yields the best results.

Of 76 cases reviewed by us of in part recurring nasal polyps in allergic rhinopathy and bronchial asthma we found granulomas (Fig. 1), which were identical with the nodular growths described by **Haslhofer** and **Riccabona**, in 23 cases in hematoxylin-eosin stained sections, as well as with silver impregnation. These nodules displayed characteristic features with silver impregnation. Thus a large cell granuloma immediately adjacent to capillaries contains distinctive silver positive polygonal cells with reticular dendrites, between these elements lympho- and plasmocytes as well as numerous eosinophiles. Such granulomas were also to be found subepithelialy, as well as in the depths of the polyp stroma. These notorious silver-positive cells which occur physiologically in the basal membrane of the mucosa and in the neighbourhood of the mucosa appear to multiply richly and quickly on the spot in allergic diseases.

In the silver impregnation specimen from the nasal polyp of a 57 year old female patient with bronchial asthma, the cell dendrites as well as the delicate veil-like structure of the protoplasm are brought out quite clearly with silver impregnation. In the network of the cellular dendrites as well as in the more distant surroundings of the silver cells plentiful eosinophiles and lymphocytes.

While we directed our main focus of attention to the cellular elements in these examinations, attention was later devoted primarily to changes in the area of the vascular nervous system. The vegetative nervous periphery is understood by **Feyrter** to be the termination of the sympathetic nerves in the form of a reticulum in the supplied tissue. The fibers of this reticulum consist of a plasmatic, nucleus-containing unmyelinated syncytium in which run fine, also reticular, anastomosing neurofibrils. **Jabonero** described these nervous

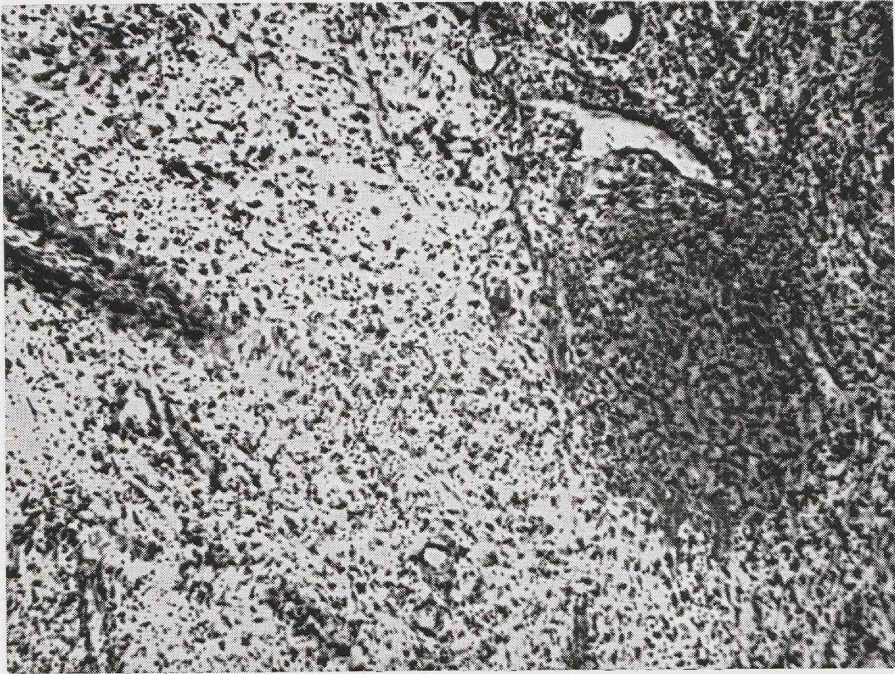


Fig. 1. Typical granuloma near a vessel in nasal polyps in allergic rhinopathy.  
Granulome typique au voisinage des vaisseaux dans les polypes allergiques du nez.

pathways leading from the ganglion cells of Dogiel II, as a vegetative terminal formation, which consists of a syncytium of interstitial cells. This ribbonlike syncytium forms fibrils, granules and vacuoles, and is the nervous distal part of the synapse (**Jabonero**).

With the silver impregnation method of Jabonero we could demonstrate such protoplasmic formations in nasal polyps with allergic rhinopathy and bronchial asthma which show differentiation into fibrils and partly contain vacuoles and nuclei.

In a 61 year old man with bronchial asthma we could show in an edematous nasal polyp a forklike protoplasmic vegetative formation with a few nuclei with in this neighbourhood numerous argentophile cells and between these some nervous protoplasmic terminal formations.

Probably a part of our argentophile dendritic cells are mastcells in near connection with the vegetative nervous terminal formations. After staining of our slides from nasal polyps with toluidin blue we could demonstrate typical mastcells corresponding to our argentophile dendritic cells with the beginning of the secretion in dendrites. In other slides there were many mastcells, partly degranulated, in the vicinity of blood vessels and glands.

In connection with these results we attempted to determine experimentally how far similar changes could be obtained in animals. For this purpose

we sensitized 10 guinea pigs with horse serum intraperitoneally; 14 days later we produced anaphylactic shock through horse serum inhalations in these animals in a glass cage. In intervals of two days each the guinea pigs were shocked a total of five times and killed during the fifth shock.

In this experimental series also we found beneath the epithelium, after silver impregnation according to Jabonero, rich amounts of silver positive cells with cell dendrites which form a dense network and appear to be interconnected by their offshoots. These cells correspond to the silver positive dendritic cells demonstrated by us in nasal polyps with allergic rhinopathy and bronchial asthma. In further sections in the guinea pig series we could demonstrate vegetative terminal formations whose protoplasm was partially damaged and whose fibrils were in a state of granular decomposition.

These findings in allergic rhinopathy, bronchial asthma, and in animal experiments after allergic shock are, in agreement with the works of the pathologists — **Zischka and Letterer** — indeed characteristic for allergic reactions but not to be designated as specific.

For examination of the effects of cortisone on the hyperplastic-polypous nasal mucosa we carried out, beside hematoxylin-eosin sections, also a silver impregnation stain according to Jabonero. In the series of nasal polyps with bronchial asthma which we examined we found, before cortisone therapy, numerous typical granulomatous nodules in the edematous polyp stroma. After cortisone therapy (prednisone) we could no longer demonstrate these characteristic groups of nodules.

Until now we have not been able to exhibit an amalgamation of the silver cells with the neural tissue in our polyps. We believe that perhaps these cellular growth in nasal polyps in allergic rhinopathy and bronchial asthma **owe their origin to a neurally regulated irritation effect**, whose target point is withdrawn upon operative removal of the polyp. Thus the same result is achieved as with the removal of a focus, assuming first that the removal is carried out early enough.

Until now histochemical examinations of polypous mucosa in comparison with normal mucosa have yielded characteristic findings only in part. The content and distribution of acid and alkali phosphatase, as well as unspecific esterases, in the various tissue constituents do not seem to vary basically, and this can be said as well about the plasmal reaction. The basal substance of the connective tissue is strikingly changed. The amorphous part, consisting of polysaccharide-protein complexes, is particularly affected, which naturally exerts great influence on the physicochemical state of the connective tissue fibers (degree of swelling). As a result of the disturbance in the hyaluronic acid-hyaluronidase system abnormal polymers of varying degree appear, most with high water combining capacity, as **Hlaváček** and **Lojda** have extensively demonstrated. Histologically even simple measures such as staining with 0.1% toluidin blue display a metachromatism particularly in the superficial parts of the basal substance near the epithelium which is lacking in the region of the normal mucosa; correspondingly the PAS reaction is intensified locally.

In respect to cellular content, we, like other investigators — **Hlaváček** and **Lojda** — have found a pronounced proliferation of eosinophiles in the tissue, as well as a variable amount of plasma cells with a plasma which is for the

most part intensively pyroninophile (rich in ribonucleic acid). Notable is also the large amount of PAS positive substances in leukocytes and cells of the histiocyte family. We found mast cells in greater numbers in those portions of the polyps where there was less edema, primarily in the subepithelium.

Within the frame of experimental allergy research, success has already been achieved in direct observation of the penetration and subsequent fate of a series of substances in the nasal mucosa. Great difficulties have appeared however in the quite important group of protein bodies, which due to lack of suitable, adequately specific, reactions can not be traced directly in animal experiments. We now believe we have found a suitable way of bringing nearer to clarification a series of undecided questions about this group of substances as well, concerning the penetration and subsequent fate of local antibody formation, etc., by coupling of suitable fluorescent stains with protein bodies as in immunohistology. Our investigations up to now however do not allow us to present a thorough discussion yet.

### SUMMARY

1. In nasal polyps in allergic rhinopathy we were able to demonstrate by silver impregnation (Bielschowsky-Gros, Jabonero) granuloma formations which consist chiefly of large silver positive dendritic cells in various forms and sizes.
2. In these elements frequent silver positive granules were demonstrable which we should like to interpret as the sign of a secretory state of these elements. Probably a part of our argentophile dendritic cells are mastcells. Also granular protoplasmic neural formations with fibril differentiation, which correspond to the vegetative terminal formations of Jabonero, could be recognized especially in the vicinity of blood vessels.
3. In accordance with our clinical findings with nasal polyps we were also able, in animal experiments, to discover a distinct proliferation of silver positive dendritic cells and injury to the vegetative terminal formation after multiple anaphylactic shocks.
4. In allergic nasal mucosa changes in bronchial asthma small granuloma-like nodules which were clearly demonstrable before cortisone therapy, disappeared **thereafter**. Tissue eosinophilia had receded completely in most cases simultaneously with the edema. The argentophile dendritic cells described by us were also demonstrable in small residual polyps.
5. Our histochemical examinations until now of polypous mucosa have not shown uniform characteristic findings.

### LES ALTERATIONS DANS LA RHINOPATHIE HYPERPLASIQUE-POLYPEUSE

1. Les muqueuses nasales montrent dans les rhinopathies allergiques un épithélium cilié pluristratifié doté de nombreuses cellules caliciformes et parfois de métaplasies épithéliales. La membrane basale est le plus souvent épaissie et hyalinisée. On trouve en outre un oedème tissulaire sous-épithélial important, dû à une perméabilité capillaire accrue, ainsi qu'une richesse en éosinophiles.

2. Dans les polypes du nez, on note fréquemment dans la couche sous-épithéliale et dans le stroma des formations granulomateuses, principalement périvasculaires, faites de fibroblastes, de substance intermédiaire avec des fibrilles épaissies, d'abondants éosinophiles, des lymphocytes et des cellules plasmatiques. A l'impregnation argentée, on voit au niveau de ces granulomes des cellules appendiculaires de différentes grandeur et grosseur.
3. Dans les cellules appendiculaires, on met fréquemment en évidence des granulations argentifères qui sont à interpréter comme le signe d'un état sécrétoire de ces éléments. Particulièrement au voisinage des vaisseaux, il est possible de mettre en évidence des éléments neuraux protoplasmiques, granulés et différenciés de façon fibrillaire; ils correspondent aux formations végétatives terminales de Jabonero.
4. En cas d'asthme bronchique, les nodules granulomateux de la muqueuse nasale allergique disparaissent après traitement à la cortisone. L'éosinophilie tissulaire et l'oedème régressent simultanément et complètement dans la plupart des cas. Après traitement à la cortisone, les cellules argentifères décrites étaient encore parfois visibles dans quelques petits polypes résiduels. L'histochimie montrait une tendance à la normalisation de la teneur de mucopolysaccharides.
5. L'expérimentation animale révèle après plusieurs chocs anaphylactiques une nette augmentation des cellules appendiculaires argentifères, avec des atteintes des formations végétatives terminales.
6. L'histochimie des muqueuses nasales montre certaines modifications dans la teneur en mucopolysaccharides et en ferments.
7. Ces modifications de la muqueuse nasale trouvées en cas de rhinopathie allergique sont à considérer comme caractéristiques pour une réaction allergique, mais non comme spécifiques.

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