

(From Oslo City Hospital, Norway, The Ear Nose and Throat Department.
Chief: Professor Truls Leegaard).

ON HISTOLOGICAL REACTIONS
IN ALLERGIC NASAL MUCOSA CAUSED
BY POLLEN

By

OLF STRÖMME, M.D.

Histological examinations have proved to be one of our best methods to enlarge our knowledge of allergic reactions. Particularly in connection with biological investigations this method has widened our idea in this as in other fields of medicine.

As to the tissue employed for such investigations the nasal mucosa appears to have been used comparatively seldom, considering the frequent role of this mucosa as an allergic shock organ, though investigations by Hansel (1936), Andersen (1943) and Berdal (1950, 1952) should be mentioned.

Subsequently the result of some histological investigations on the nasal mucosa of guinea pigs exposed to rye or birch-pollen as such or to extracts of these pollens, will be reported on. As to the methods of sensitization of animals and application of pollen or pollen extracts and the operative and histological technique is referred to a previous publication (1953).

In normal non-sensitized animals the cellular reaction to pollen and pollen-extract was insignificant mainly as a slight increase of histiocytes. This means that in normal nasal mucosa particles as pollen or colloidal solutions as pollen extracts are absorbed and pass through the mucosa with only a minimal foreign-body reaction.

In sensitized nasal mucosa the histological reactions were

conspicuous, and are termed (1) the immediate reaction, (2) the intermediate reaction, and (3) the late reaction.

The immediate reaction has a functional character and consists of a vasodilatation of terminal and larger vessels, increased permeability of the walls of the vessels with oedema of the tissue particularly localized to the loose connective tissue between the epithelium and the glandular layer.

The interfibrillary spaces become much larger and the epithelium appears much thicker than normal with many deeper lying epithelial cells surrounded by a non-staining halo.

The other main manifestation of the immediate reaction is a marked dilatation of the glandular layer. In normal mucosa the glands lie scattered in connective tissue. In allergic mucosa, especially over the inferior turbinate and during an allergic attack, the glands form a homogenous layer between the subepithelial connective tissue and the vascular pre-perichondrial tissue. The profuse secretion during an allergic attack is partly due to glandular secretion, partly to a trans-epithelial exsudation. The secretion during an allergic attack is obviously to rinse out the allergen just absorbed. Relatively much of the dissolvable antigen employed was often found around the glands. The impression was gained that the glands, after taking hold of absorbed dissolvable allergen, try to get rid of it again as quickly as possible, and for this reason start a secretion that is troublesome to the patient, but serves the purpose to rid the body from a harmful agent. The renovatory function of the nasal glands may be listed as an important duty of the nasal mucosa.

The manifestations of the immediate reaction, both the secretion and the vasodilatation, as well as sneezing, so often found in allergy, must be provoked as the result of a nervous reflex over regional and other ganglia.

The immediate reaction lasts more or less unabated for about one hour and then subsides quickly when a liquid allergen as pollen extract is the provocative agent, very slowly when a particulate allergen as pollen is employed. Obviously a liquid allergen is easier and more quickly destroyed or

transported away, compared with a solid particulate matter that slowly and continuously may give off to the tissue around an allergenic component.

The intermediate and late reactions both are cellular ones. During the first half-hour after application of pollen or pollen extract an increasing number of leucocytes appeared in the vessels. Among these were some few eosinophiles, but only in the second half-hour a massive invasion of eosinophiles was observed, firstly in the blood vessels, and later in the tissue around. Diapedesis of leucocytes into the tissue is a characteristic and impressive feature during this second stage of the allergic reaction. This observation supports Erlich's theory of the myelogenous origin of the eosinophil cells, contrary to the theory of the histiogenic origin as advocated by Ringoen (1921), Cooke (1932), Hansel (1936) and others. An eosinophil cellular reaction is not a constant feature with pollen as allergen, but when it occurs it is always most pronounced in the subepithelial connective tissue, where the oedema is also most marked. Especially around an absorbed allergen as pollen, the eosinophils were numerous in this layer, but when the pollen grains were brought further towards the periost the eosinophils did not follow, but kept stationary until they disappeared partly at least through the epithelium. In the olfactory nasal mucosa eosinophils were never observed, nor was absorbed allergen. At the abrupt transition between respiratory and olfactory mucosa, the eosinophils stopped on the respiratory side.

The duration of the eosinophil reaction depended on the kind of allergen that was absorbed. If a pollen extract had been used as allergen, the eosinophil reaction was short with a maximum after about one hour. But when pollen as such was absorbed in the mucosa, the eosinophil reaction was prolonged and strong for 24 hours or longer. Obviously the duration of the eosinophil reaction depends on the stay of an allergen in the tissue.

The late reaction now to be described seems very significant. When the nasal mucosa was removed for histological

examination from the first to the eighth day after the test-dose of pollen had been inhaled, this examination showed that until the fourth day there appeared an increasing number of large and medium-sized lymphoid cells, initially showing in the blood vessels, later in the surrounding tissue, like the eosinophiles previously.

The lymphoid cells first gathered subepithelially where the oedema and the eosinophilic reaction appeared most strongly, but unlike the eosinophil cells, the lymphoid cells gradually spread to the deeper layers of the mucosa.

These lymphoid cells by some investigators are called lymphocytes by others plasma cells. The present findings are in support of earlier investigations by Keuning and van der Slikke (1950), and reveal the cells in question, in casu in the nasal mucosa, to be large immature lymphoid cells gradually maturing into plasma cells and further into smaller lymphocytes. The cells initially appearing in the subepithelial vessels and tissue during the first few days are large and medium-sized cells with a basophilic cytoplasm and large bright nuclei. On the third day the cells to appear first had matured into plasma cells, some even into small lymphocytes as they wandered from the subepithelial layer towards the perichondrium, as had previously been the trend of the allergen.

On the fourth day this cellular reaction with lymphoid cells, plasma cells and lymphocytes was so strong that nearly all general tissue structure was effaced. On the fifth day the relative amount of plasma cells increased, especially in the deeper layers, whereas the amount of large and medium-sized cells was on the decrease, and as a whole the cellular reaction was diminishing. This tendency was clearer on the next day, until the histological picture on the seventh and eighth day was approaching the normal.

In degree parallel to the lymphoid reaction a number of mitotic cell-divisions was seen just under the epithelium. Such amounts of mitoses suggest a strongly increased cellular activity, and again direct our attention to the narrow strip of subepithelial tissue as a particularly active area in allergy.

Other investigators have observed in lymphatic glands and in the spleen, a close connection between these large and medium-sized lymphoid cells and plasma cells and the presence and amount of antibodies in the tissue and in serum (Dougherty, Chase and White 1944, Fagraeus 1948, Keuning and van der Slikke 1950).

The present findings of a strong cellular activity and a rich accumulation of accepted antibody-producing cells in the sensitized nasal mucosa in connection with absorption of allergens, point to the nasal mucosa as an important producer of antibodies. An immune-biological activity may be a particularly important function of the nasal mucosa.

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