

Final remarks

H. H. Naumann, München, West-Germany

Will there be any therapeutic consequences from what we heard today? Furthermore we have to question if the immunological and biochemical factors which recently have been detected could offer new starting points for practical therapy. From the special standpoint of rhinology it should be stated that injuries of the mucosa cannot be expected only coming from the outside, from the environment, like in the sense of an infection or of a physical and/or chemical damage (dust, heat, posttraumatic conditions etc.). Also simultaneously occurring other disturbances of the organism may cause an impairment of the mucosa. May I remind you of diseases of the circulation, the heart, the liver or the endocrine system? Let us think further of the various side-effects of the drugs that may also irreversibly influence the ciliar apparatus, the microcirculation, the glandular activity and the conditions of secretion and mucosa!

It is therefore necessary that at the beginning of a rhinological therapy one should try, first of all, to identify and, if possible, even to eliminate all these direct or indirect endogenous causes of irritation or damage. Included are here, if needed, operative corrections of patho-anatomical intranasal changes which are supporting the disease. Only after elimination of these factors one should investigate, whether the defence-mechanisms of the mucosa are working correctly and sufficiently or - if not - whether it is possible and feasible to influence their functions therapeutically.

Let us go through the list of groups of factors which we have discussed today:

1. *The mucociliar apparatus*: Prof. Toremalin has already pointed out in detail the practical therapeutic consequences of disturbances of this protective system. I don't want to repeat them.

2. *The immunological reactions*: Hyperactivity as well as hypofunction lead to illness. A very frequent clinical manifestation of hyperfunction is the atopic allergy of the mucous membrane of the nose (i.e. the immediate type like pollinosis). Hereby, the available possibilities for the symptomatic as well as the causal therapy are quite well established. I do not necessarily have to go into further details before this audience.

However, conditions are different in those allergoses of the mucosa which do not belong to the immediate but to the delayed type (for instance in the so-called infection-allergy). In this group, it is, so far, mostly not possible to identify the

responsible allergen or allergens. For the time being we are in this particular field still largely dependent on assumptions and hypotheses: We cannot treat causally but only symptomatically. Our hopes are based here on research of the near future. A broad, systematic serial examination of both the mucosal tissue and the secretions should actually enable us to recognize the real causes in such cases and - by that - to find also an efficient causal treatment.

The hypofunction of the immunological system of the mucosa exhibits all degrees from the clinically unobtrusive subnormal function to the manifestation of the most dangerous primary - frequently inherited - immunological defects. In the field of the humoral immunity minus-variations, so far, have been relatively well-known. This concerns activities of the serum-antibodies, respectively immunoglobulins, which act - among others - very efficiently against encapsulated pyogenic bacteria. In the case of a deficiency of serum antibodies (for instance in the case of a hypogammaglobulinemia) a substitution therapy with immunoglobulins may have, according to our impression, a lasting favourable influence against a susceptibility to infections.

The IgA-deficiency is the most frequent clinical immunodeficiency syndrom. It can be obviously proven in one person among 600 and the IgA deficiency belongs then to both the serum and the secretion. Only in 20%, however, is the rate of infection in these persons significantly elevated and clinically apparent. Till now it is not yet clear, whether a substitution therapy with IgA is an efficient and recommendable treatment or not.

At the time being, in the field of cell-mediated immunity we are confronted with a much more complicated situation. The cell-mediated immunity - as concerns the mucous membrane, is responsible and indispensable for the control of many types of bacteria, but also of most viruses, fungi and protozoa. Essentially it is more complicated and doubtful to prove a lacking protective power in the cell-mediated immunosystem than in an immunoglobulin deficiency. In this group of diseases therapeutic measures are also more uncertain and apparently less efficient. Attempts with vaccines for the activation of cell-mediated immunity are estimated today quite controversial as to their efficiency.

However, there is justified hope that with a better knowledge and understanding of the several factors which are particularly of importance for the cell-mediated immunity we will succeed to create an effective causal therapy by direct stimulation of these factors.

3. *Protective enzymes and inhibitors:* So far, our clinical experience has not been convincing with a substitution of Lysozym (in form of tablets or spray). According to our findings during the analysis of the secretions, the lacking of Lysozym and a herewith connected deficiency syndrom could not be proven in the field of the nasal mucous membrane.

Interferon, as a most effective antiviral principle, till now could not be evaluated diagnostically by us in the secretion, because of technical reasons. The spectacular but also very specific and therefore limited effect of the group of interferons on viruses is sufficiently known. To this date, a broad therapeutical application of interferon (as a substitution where a deficiency of interferon was assumed) failed because of the enormous expenses. An activation or induction of the production of interferon in the diseased organism itself shows still some problems due to technical and toxicological reasons. Obviously, within the near future a change can be expected. It remains to be seen whether the application of interferon will provide considerable therapeutic benefits as a routine treatment especially in acute and serious diseases of the respiratory tract.

The situation is similar with the group of inhibitors which are present in both the mucosa and the secretion: It seems as if, in future, there might be a possibility to strengthen the defence-potential of the diseased mucosa by a substitute in case of an inhibitor-deficiency syndrome.

The formation of immunogenic decomposition-products by means of phagocyte-proteases is discussed today strongly. This mechanism could offer an explanation, why acute inflammations pass over so often into a chronic course. In other words: An autoimmun-principle or mechanism would be - at least partly - responsible for the chronicity of an inflammation - if this hypothesis can be proven!

In this connection, of course, also the immunosuppressive function of the protease-inhibitors could get an increasing clinical interest. Prof. Hochstraßer pointed this out in his paper.

So far the comment on the actual therapeutic consequences of the papers we have heard today. I confess, that the harvest is still small as far as the new detections are concerned.

Apparently many of these new observations and results are not yet ripe for a practical transposition into clinical application.

I'm convinced, however, that these biochemical investigations and their results will get an increasing importance also for our practical work- and already in the next future.

Prof. Dr. med. H. H. Naumann
Univ. HNO-Klinik
Marchioninistrasse 15
8 München 70
West-Germany