Proceedings of the Hungarian Scientific Council

The Hungarian Medical Trade Union and Hungarian Scientific Council held a symposium in the Biological Institute at Tihany on May 29–31, 1949, for discussion of the histamine problem. About 40 physicians and biochemists studying the subject had been invited to read papers of theoretical and clinical points of view.

Theoretical papers and discussions concentrated on the histamine-azo-benzole-azoprotein substance (Went-Kesztyüs). Coworkers of Issekutz spoke about histamine effects and histamine-antihistamine antagonism.

Clinical papers were read by K. Hajós, Rajka, Fekete. Histamine headaches were discussed by Eszenyi-Halasy, M. K. Hajós, L. Biró and Kajtor. The evaluation of antihistamine action in various therapeutical relationship was discussed by L. Biró and M. K. Hajós.

Went and Kesztyüs found a new histamine-azobenzole-azoprotein (Hap.) in which histamine was bound to bovine serum. Kesztyüs spoke about occurrence of free histamine in the tissues, circumstances of histamine formation, its accumulation and excretion in normal subjects. Finally described methods by which the new Hap-substance was synthetized. Went dealt with antihistamine effect of the same substance in animal-experiments, proving its species and chernospecificity. Toxic histamine doses failed to produce fall of temperature in anaphylactic guinea pigs, and passive protection could be obtained on isolated intestines and heart. Histamine and anaphylactic shock had been prevented at every occasion.

K. Hajós summarized clinical results after a 6 monthly follow-up in 31 asthmatic patients treated with the substance mentioned above. At first they were treated by the depot injection method, but as allergization of the skin proved to be insufficient, though the spread of cutaneous allergization could be demonstrated, later on subcutaneous treatment was followed by 25–30 cm³ of Hap. in 6–8 weeks. 18 felt better at the end of treatment, out of whom 12 proved to be remarkably well. Rajka first spoke about histamine and antihistamine action with regard on therapy in dermatological diseases. Only acute allergic conditions could be cured or temporarily influenced, even non-allergic itching could be suppressed. Further he gave results of treatment with Hap. adding corresponding clinical control reactions. The PK reaction with Hap. and the wheal inhibition test were positive in several cases.

Issekutz jun. spoke about analgetic effects of antihistamine, Nádor gave account of chemistry of pyribenzamine-like new substance, branded dehistin. L. Biró mentioned clinical application of antihistamines (antistin) in treatment of rheumatoid arthritis, peptic ulcer, headache, acute nephritis and scheduled histamine-treatment of gastric ulcers. In the ensuing discussion the question arose how success of histamine treatment of ulcers could be defined or satisfactorily compared to other treatments. The mentioned successful antihistamine therapy in acute nephritis would point to allergic origin, though K. Hajós emphasized that final cure should be determined by disappearance of hematuria and not normalization of blood pressure. M. K. Hajós delivered a paper on results with
a new Hungarian antihistamine-substance (RG960) resembling phenergan. Acute extrinsic allergic conditions mostly of dermatological origin could be cured, diseases of the respiratory tract remained unchanged.

Eszenyi-Halasy gave account of 100 cases of histamine headache, migraine, and similar symptoms treated with histamine, effect of it seemed to be satisfactory. Kajtor discussed neurological views on the subject, he found several cases of severe myositis following a few weeks’ histamine therapy. M. K. Hajós spoke further about treatment of headache combined with other allergic diseases, especially those appearing in allergic manifestations of the respiratory tract. Results were good for all histamine sensitive cases.

Miscellaneous papers. Fekete spoke about gynecological relationships of premenstrual histamine headaches. In nonconvulsive eclampsy smooth-muscle spasm of pulmonary precapillaries was probably evoked by histamine, whilst thyramine seemed to be responsible for spasm of preglomerular capillaries of the kidney in eclampsy. Toxicosis of pregnancy followed placentary hypoxemia by decreasing histaminase and increasing histamine production. In the following discussion it was unable to clean up mechanism of histamine effect nor to find basis of therapeutical success in histamine headache. Törö found that skin of rats became discoloured by Indian ink after local histamine treatment. Though endo-thel cells did not enter the capillaries, increase of permeability seemed to be responsible for the results. Histamine mobilized the endothel cells, the action being activated by Indian ink. Histamine is a tissue hormone activating tissue mobilization. Issekutz jun. discussed action and antagonism of histamine, novo-caine (procaine) and capsicine. Pataki spoke about action of thyroxine and histamine in creatinine metabolism. Lissák found free histamine in histaminergic nerves of the spinal cord; Frank discussed action of heparine in burns, and did not find histamine-heparine antagonism in surgical shocks. The paper of Herr-Porszász about histamine tachyphylaxy was followed by a long discussion of Went, Faragó, Rajka. Faragó tried to modify classification of allergic mechanism on immunobiological basis, this being discarded by Rajka. Went mentioned his theory about substitution of histamine by vasopressine substances in therapy.

Finally K. Hajós gave a summary of therapeutical evaluation in clinics. Bronchial asthma cannot be solved by histamine therapy because of various contributory factors determining paroxysms. Therapy could be successful only if all factors – psychosomatic, neurohormonal regulation and vegetative centers – were considered. He outlined methods of treatment of allergic diseases with special regard on histamine, histaminase, antihistamines and Hap. substance. For histaminase-treatment he recommended pregnant blood serum, as at end of pregnancy there is an increase in the blood histaminase level. M. K. Hajós added histamine treatment of allergic rhinitis, prevention and diagnosis of vasomotor rhinitis in industrial and occupational diseases.

At the end of the symposium teams were formed to continue research work in histamine-azoprotein-azobenzole, histamine headache, histamine-antihistamine therapy in peptic ulcer, nephritis, rheumatoid arthritis, and finding new histaminase substances as indicated in Hajós summary.

Summary of the latest meetings of the Hungarian Section of Allergists.

Febr. 16, 1949. Dr. Farkas spoke about allergic tissue reactions, pathological and biological changes at biopsy of patients died of bronchial asthma. As indicated by K. Hajós, he examined all organs beside the lungs, and found reactions similar to allergic inflammation in heart muscle, liver and the hypothalamus. In those, who had died in status asthmaticus the latter reactions had been most obvious.

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After discussions by Drs. Mosonyi and Preisach, Dr. Kahán spoke about the importance of antihistamines in ophthalmology, and found that as combined with privine they were useful in local therapy. Hajós emphasized that in ophthalmology and dermatology the antihistamines have better results than in bronchial asthma, where contributory factors beside histamine formation in the patho-mechanism had greater role and cannot be influenced by antihistamines.

June 7, 1949. Dr. Radnóti-Recht discussed intrinsic factors influencing childhood allergy, emphasizing own experiences and experiments in tuberculine allergy. Dr. Ladányi spoke about 10 % sodium citrate used in allergic conditions as based on rhinological investigations, giving for explanation, calcium and other electrolythic changes of the tissues. Mosonyi, Csefko, Simo, Sandelhausen discussed the papers. Hajós explained Ladányi’s treatment with the action of hyper-tonic injections used in allergic paroxysms.

Following questions are scheduled for discussion in the September meeting: Allergic occupational diseases (prevention, rehabilitation). The action of antibiotics in allergic diseases. Several papers about the role of the liver in allergic conditions.

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Undoubtedly, this new book is one of the most important medical publications of recent years. The brilliant and extensive experimental work of Hans Selye and his school covers many important fields and actual problems of physiology and pathology and is at the same time rich in new ideas, therefore a summarizing and authoritative interpretation of the results must be welcomed by all research workers and clinicians.

A. According to the conception of Selye anything which endangers life or disturbs vital functions in some way causes stress and adaptive responses. «Adapt-ability and resistance to stress are fundamental prerequisites for life and every vital organ function participates in them.» This statement by Selye outlines the extent of the field and the complexity of the matter. Selye and his school studied with most ingenious methods the effect of various stresses (i.e. infections poisoning exposure to cold or heat irradiations exercise fasting etc.) on the body of experimental animals and they described a number of characteristic systemic reactions the s.c. «general adaptation syndrome». This syndrome has three successive stages
the «alarm reaction» (shock and counter-shock)
the «stage of re-sistance» and the «stage of exhaustion». One of the most important effects of this syndrome is a change in the function of the adrenal cortex resulting in increased secretion of corticoids. This secretion starts through neuro-humoral mechanisms
a.o. through an increase of ACTH-production. Many of the symptoms of the general adaptation syndrome are effected through the hypophysis whose hormons affect the adrenal cortex. The hormons of the adrenal cortex (a.o. Cortisone) induce functions on which resistance is based. Resistance depends to a great extent on the secretion of gluco-corticotrophic hormones (for instance ACTH) and gluco-corticoids (i.e.
Cortisone). Selye and co-workers found that a number of the characteristic lesions which stresses of various kind produce in the tissues of animals can under certain circumstances be imitated by treatment of the animals with mineralo-corticoids such as desoxycorticosterone and desoxycortisone. In this way stresses not only induce adaptive processes but also through improper hormonal balance «diseases of adaptations a.o. rheumatic and allergic diseases.