Clinical Immunology and Allergology

Editors:
C. Steffen & H. Ludwig

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CLINICAL IMMUNOLOGY AND ALLERGOLOGY

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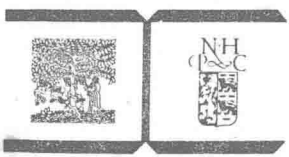

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Preface

Rapid progress in clinical immunology and allergology makes a timely presentation of recently gained scientific informations highly desirable. This was intended by the organizers of the XIth Congress of the European Academy of Allergology and Clinical Immunology. The present volume covers the lectures given by distinguished speakers in 10 symposia dealing with important topics of clinical immunology and allergology.

This book has been planned to review in detail present knowledge as well as future trends in clinical immunology and allergology. The topics were selected in order to arrive at a synthesis between basic research and clinical practice and also to review the clinical applicability of basic research.

The editors acknowledge with gratitude the cooperation of the contributors and hope that the information presented will be of interest to the reader.

The Editors

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Opening Address

First of all I would like to welcome you to this Congress. I do this as President of the European Academy of Allergology and Clinical Immunology. Its Council in their deliberations a few years ago when considering where the 1980 Congress should be held, decided that it should be in Austria. It should be noted that the European Academy of Allergology and Clinical Immunology holds a meeting every year. Two what we call small reunion meetings, are followed by a big meeting. This is such a meeting. It lasts all week and not just two or three days like the small meetings. The very numbers that are attending this meeting are an indication of the popularity of the venue for such a meeting but it is also, I hope, an indication that the scientific programme is of outstanding interest.

The scientific programme, as you will already have seen, is I think quite an amazing one. It has been thought out as the brain child, I believe, of Professor Dr. Steffen, the President, and also Dr. Ludwig, the Organising Secretary. I am sure they have had help from many of their committee members since the organisation has already been very efficient in the way it has sent out its preliminary programmes and arranged the social and scientific meetings. The Council may choose the country but it gives no help at all to run the meeting. A succesful meeting is due to the local efforts that have brought this about.

It is not an appropiate time to discuss at all what allergists will be discussing during this Congress. Immunology is expanding every year and impinges on so many branches of medicine and surgery. We are also looking more and more at the complex changes that take place inside and at cell surfaces. It is I think unfortunate that so many studies in the past have considered the experimental animal and not enough have involved suffering man.

I am not sure, how you manged to persuade such outstanding speakers as Dr. Jean Dausset and Dr. Philipp Norman to come and tell us of their knowledge. It is invidious of me to mention only two names when so many should be mentioned. I might mention also

that two of my allergy friends from Australia were also determined to come to this meeting. Indeed Austria and allergology are now very much on the scientific map.

May I, before I close, be allowed to say one more thing - almost my swan song! What I have to say is for those who among us treat patients. A doctor can be competent only when he has acquired the basic knowledge and technical skills of his speciality but he must also keep abreast of the advances of his own speciality and indeed this is why he attends such a Congress as this. But more than just confidence is required of a doctor who deals with patients. Doctors are members of a learned and caring profession. Their responsibility is manifest in an intensely personal relationship, a unique bond between them and those whom it is their privilege to serve. Patient and doctor may well hold different beliefs or, in their absence, philosophies of life. There are good and less good priests and teachers in every religion, as there are good and less good doctors. But the doctor must realise that he belongs to a team who cares for the sick. Doctors are unwise if they do not recognise this. Therefore doctors must remember the moral attributes of belief, compassion, understanding and tender loving care. They are fundamental to the best medical practice. Doctors are dealing with individual patients rather than with a disease which might be, for example, allergy.

Now I formally declare the Congress open.

Dr. A.W. Frankland
President of the European Academy of
Allergology and Clinical Immunology

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CLINICAL IMMUNOLOGY AND ALLERGOLOGY

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AUTOIMMUNITY

Clinical Immunology and Allergology
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PRESENT STATE OF KNOWLEDGE ABOUT MECHANISMS OF AUTOIMMUNITY*

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In 1900, Ehrlich and Morgenroth[1] formulated their famous horror autotoxicus rule stating that a healthy man or animal refuses to form autoantibodies which could inflict damage, self-poisoning, to the tissues of the antibody producer.

The popular and by and large still tenable explanation for the lack of autoantibody formation was given by Burnet[2] in his clonal selection theory, where he postulated that clones of lymphoid cells engaged in autoimmune responses are destroyed in embryonal life as a result of contact with overwhelming amounts of autologous antigens. This is followed by self-recognition or self-tolerance, i.e., unresponsiveness to self.

Interestingly, the exceptions to the horror autotoxicus rule were noticed within a few years after it was postulated. In 1903, Uhlenhuth[3] described the formation of tissue-specific antibodies by rabbits immunized with a homogenate of bovine lens. Most of these antibodies combined with rabbit lens and would also act upon the lens of the antibody producer; in this way they should be considered autoantibodies.

A year later, Donath and Landsteiner[4] showed that sera of patients suffering from cold paroxysmal hemoglobinuria contain a biphasic autohemolysin that combines with all human erythrocytes including those of the patient at low temperatures close to 0°C and induces complement-mediated lysis after the temperature is raised to 37°C. Interestingly, these antibodies were directed against two different types of antigens, frequently referred to as inaccessible and accessible antigens. The difference in autoantigenicity of these two types of antigens has been stressed repeatedly.

INACCESSIBLE ANTIGENS

The immune response to inaccessible antigens has been studied extensively since the above quoted discovery of Uhlenhuth[3]. A great deal of information about autoantibody formation to these antigens stemed from studies on thyroglobulin by Witebsky and Rose[5]. They showed that rabbits immunized intravenously with thyroglobulin of a foreign species origin would form thyroglobulin anti-

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bodies, some of which combined with autologous thyroglobulin, whereas rabbits injected with rabbit thyroglobulin would form no antibodies.

Attempts to explain this phenomenon were discussed in previous publications[6,7] in classic immunologic terms: "If thyroglobulin is injected into an animal of a foreign species it acts as a potent antigen with many active determinants. Apparently, the immune response to strong heteroantigenic determinants is eventually broadened by the response to weaker autoantigenic determinants. This situation is quite similar to combined immunization in which an immune response to a foreign protein conditions the response to an immunogenically weak hapten."[7]

Further extensive studies on the immunogenicity of thyroglobulin were conducted by Weigle and his associates[8-11]. These studies showed the immunization with thyroglobulin altered by coupling it with arsanilic or sulfanilic groups has a similar effect as immunization with thyroglobulin of a foreign species origin. The findings of Weigle may be interpreted as follows[10,12]: There exists only T but not B cell tolerance for autologous thyroglobulin. Characteristically, T cell tolerance is relatively weak. Once thyroglobulin is altered artificially by chemical manipulation or naturally by employing the protein of a foreign species origin, the T cells interact with these "non-self" moieties and present thyroglobulin to B cells. Since they are not tolerant, B cells may form antibodies to native configurations of thyroglobulin, including autoantigenic configurations.

It appears most likely that a similar situation occurs with many other sequestered tissue-specific antigens, including those of brain, adrenal and testicle. The autoantibody formation to all these antigens may be achieved in any healthy animal provided that proper immunization procedures are employed. One of the most frequently used procedures for autoimmunization is the application of Freund's adjuvant[13]. The way in which Freund's adjuvant promotes formation of autoantibodies has not been completely unraveled. Some investigators believe that this adjuvant exerts a non-specific stimulus on T cells after which they can participate in cooperation with B cells leading to formation of autoantibodies[14,15].

It has been demonstrated in animal experiments as well as by clinical experience that formation of autoantibodies to sequestered antigens does not have to be accompanied by any damage to the tissues. Still, in animal experiments, organ-specific autoimmune disease has been convincingly demonstrated after immunization along with Freund's adjuvant. Allergic encephalomyelitis[16,17] was produced by immunization with brain suspension, aspermatogenesis[13,18] by