Further Section


Book Reviews

Money, J. (ed.) Bronchial Hyperreactivity Perspectives in Asthma 1 Academic Press, London 1982 274 pp.; E13.50 ISBN 0-12-506450-0 This volume contains the transactions of a symposium, held in June 1982. The Editor stresses in his preface that ‘susceptibility to spontaneous, or induced, changes in airway resistance is a characteristic feature of asthma’. The main subject of the symposium was to discuss if the enhanced reactivity of asthmatics to histamine, metacholine or prostaglandin F2a aerosols, exercise, cold air, infections, etc. is a prerequisite or consequence of the disease. In vivo and in vitro results were presented and discussed in an attempt to answer this basic question. This involved discussions of the mechanisms underlying allergic asthma and bronchial hyperreactivity and those which characterize the activity of prophylactic and therapeutic agents. Research workers and clinicians concerned with asthma will find the study of the papers presented at the symposium and the discussions rewarding. The main question, however, remained unanswered. Morley et al. investigated asthmatics, allergic to the house dust mite. Challenge with mite extract elicited in their patients an immediate asthmatic response and a late one, occurring 3-7 h post-allergen exposure. Administration of non-steroidal anti-inflammatory drugs, such as indomethacin or acetylsalicylic acid, which are potent inhibitors of prostaglandin synthetase (cyclooxygenase) did not prevent the immediate response, which implies, according to the authors, that prostaglandins are not involved in the immediate bronchospastic response. Pretreatment with NSIADs, however, prevented the occurrence of the late onset response, which is ascribed lipooxygenase products, such as leukotrienes (SRS-A). These interesting results clearly show that NSIADs do not direct arachidonic acid metabolism from the cyclooxygenase to the lipooxygenase pathway. Thus, aspirin intolerance cannot be explained by a ‘switch’ in arachidonic acid metabolism. According to Morley the effect of leukotrienes in vivo, and that of the lipooxygenase inhibitor benoxaprofen, are not impressive. For the critical reader the book offers many interesting and thought-provoking details. Paul Kallós, Helsingborg

Goran Möller (ed.) Immunological Reviews 70 HLA and Disease Susceptibility Munksgaard, Copenhagen 1983 218 pp.; DKr. 234.25 ISBN 87-16-09480-8 The human major histocompatibility complex, HLA, is located at the short arm of the sixth chromosome. Apart from the originally described three loci, A, B and C, the genes of which code
for surface antigens present on all nucleated cells and thrombocytes (Class 1 factors), a number of further loci have been detected, such as the D/DR locus, which codes for Class 2 factors, expressed on lymphocytes and/or macrophages. Moreover, between the B and D/DR locus genes are located, which code for the complement components C2, C4A, C4B and Bf (Class 3 factors or complotypes) and for the enzyme 21-hydroxylase. Statistical associations between Class 1 factors and susceptibility for certain diseases (e.g. B27 and ankylosing spondylitis) have been detected in the early stage of research. The identification of new loci and better methods for the detection of HLA-surface factors and the connection between them and the complotypes, made rapid progress feasible. As usual in these volumes, the recent developments are accounted for in excellent reviews by leading experts. To readers not very well acquainted with the extensive literature and the complicated terminology in this area, I recommend to read the last review first, a superb contribution by Svejgaard et al. entitled ‘HLA and Disease Susceptibility 1982’. It emerges clearly from this and the other reviews that the association between HLA and disease susceptibility is not only statistical. Definite functional relations between products of the D/DR-region genes and certain diseases could be detected. This region represents the ‘immune response area’ of the MHC, similar to that known in the MHC of mice and guinea pigs. For instance, the susceptibility for autoallergic and allergic (pollinosis) diseases is governed by immunosuppressor (Is) genes located within this area. The genetically determined lack of antigen-specific Leu 2a+ 3a” suppressor T lymphocytes leads to susceptibility and to high responsiveness for certain antigens, such as streptococcal cell wall antigen [Susazukiet al.]. This is but one of the exciting discoveries described in the present stimulating volume by Dawkins et al., Geczy et al., Scholz and Albert, Serjeantsop, Stastny et al., Winchester et al., and Hors and Dausset. The volume is warmly recommended.

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G. Möller (ed.)
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Allogeneic Bone Marrow Transplantation
Munksgaard, Copenhagen 1983 121 pp.; DKr. 130.55 ISBN 87-16-09504-9
The indication for allogeneic bone marrow transplantation (BMT) has been considerably widened during the past decade. After successful treatment of a few cases of severe combined immunodeficiency (SCID), cases with other forms of immunodeficiency, with aplastic anemia, leukemia and genetic disorders of hematopoiesis were treated with BMT. There were two main problems to consider: the acceptance of the graft in cases with full or partial immunocompetence and the possibility of a graft-versus-host reaction (GvHR), due to immunocompetent T cells in the grafted marrow. In their review, Korngold and Spreng discuss the results of their animal experiments, which showed that even if recipient and marrow donor shared all major histocompatibility antigens, GvHR could occur across minor, not MHC coded, histocompatibility barriers. They stress that this can occur in clinical cases too, e.g. when the donor is a fully HLA-compatible sibling. Korngold and Spreng quote the recent work of Reinherz et al., who successfully transplanted to a child with SCID HLA-mismatched parental marrow. The marrow was pretreated with monoclonal antibody against the relevant T cells (T 12) and rabbit complement. It is apparent that the possibility of
depleting potentially harmful cells from the graft will considerably enhance the applicability, security and success rate of BMT. It is to be expected that T cells developing from the graft will be tolerant against host antigens. In the above-mentioned case, treated by Reinherz et al., a late GvHR occurred, probably due to remaining T 12 cells or to such cells developed from precursors beyond the stage of immaturity, which would allow tolerance. The GvHR has been terminated by injection of monoclonal anti-T 12 antibody. Von Melchner and Bartlett deal with the ‘Mechanisms of Early Allogeneic Marrow Rejection’, effected by immuno-competent T cells of the host. A few imunocompetent T cells or precursors remained in lethally irradiated mice and were able to reject a marrow graft. Graft survival is also endangered by the allogeneic microenvironment. BMT leads to considerably elevated plasma IgE levels due to polyclonal B cell activation. Ringden et al. discuss in their contribution the significance of this phenomenon. Storb and Thomas show clearly in their review the great benefits which BMT can bring about in different extremely serious diseases. This review provides all relevant technical details of BMT. Tou-raine reviews the results of the treatment of 6 infants with SCID with BMT from fully HLA-compatible siblings. 3 of these were completely reconstituted and healthy 7-8 years after BMT. In a fourth case, recovery seemed to progress, the observation time was, however, too short for definite evaluation. 2 infants died of infections, already progressing at the time of grafting.

GvHR was no problem in these cases. In an attempt to overcome the barriers of histocompatibility and to widen the applicability of stem cell transplantation to patients with inborn errors of metabolism, Touraine and his team transplanted fetal liver and thymus cells (FLTT) from 8- to 14-week-old fetuses. There were two apparent drawbacks. The grafting had to be repeated with an interval of several months 3-6 times, before a definite engraftment could be established. In cases with SCID complete isolation in a germ-free environment (a ‘sterile bubble’) had to be maintained for up to 3.5 years, until immuno-competence has been achieved. 6 SCID cases were treated, 2 recovered completely, 1 is still under observation, but seems to progress well. 3 infants died: 1 of BCG infection, 1 of meningitis and the third of septicemia and GvHR. In the cases of metabolic disorders (3 cases with Fabry’s disease, 2 with fucosidosis, 1 with Niemann-Pick’s disease and 1 with Hurler’s syndrome) the signs and symptoms have been ameliorated and FLTT is probably beneficial. In these cases, which are immunocompetent, graft acceptance must be secured by immunosuppressive drugs, such as azathioprine and prednisone, a potentially hazardous treatment. In the reconstituted SCID cases, Touraine et al. noted a peculiar situation. These cases are chimeras, their T cells, developed from the mismatched graft, do not share any HLA haplotype with the host cells. According to the rule of Zinkernagel et al., helper, effector and probably also suppressor T cells are HLA restricted, i.e. are able to recognize foreign antigens (X) only when it is presented together with or coupled to a HLA antigen, which they also possess (self). This kind of dual recognition is not possible in the chimeric cases, all their immuno-logical functions were, however, normal. According to Touraine et al., an ‘allo-X’ recognition mechanism is operating in these exceptional cases instead of the normal ‘self-X’ recognition.

BMT poses many intriguing problems, the present volume will be helpful for future work in this important area.

Paul Kallós, Helsingborg
Molecular and Therapeutic Reviews Contemporary Immunology 2 Humana Press, Clifton 1982
All aspects of ‘cell-mediated immunity’ are thoroughly and expertly discussed in this informative and stimulating volume. Luderer and Harvey review present knowledge concerning the elusive T cell antigen receptor. Fathman discusses in an exhaustive chapter the regulation of the immune response. Immunosuppressive agents are reviewed in two contributions by Sigel et al. Keller et al. deal with the immunology of human non-Hodgkin’s lymphomas. Burek, Rose and Lillehoj treat in depth the clinically and theoretically equally important problems of cell-mediated allergic reactions in autoallergic diseases. Spector and Friedman discuss the role of T cells and their products in tumor rejection. Maziarz and Gottlieb review the role of the so called ‘transfer factor’ and other factors in leucocyte dialysates that affect cell-mediated immune reactions. Guarnotte and Parkhouse describe the recently developed important techniques for hybridization of lymphocytes and discuss their applications and the results achieved. Finally, Fudenberg et al. review the present standing of diagnosis and monitoring of defects in cell-mediated immunity. This is a masterfully written review of great clinical importance. Paul Kallós, Helsingborg