

14.1.12

PW

THYMIC EPITHELIAL HYPERKERATOSIS, T-CELL DEFICIENCY AND IMMUNOLOGICAL DYSREGULATION IN MOUSE MUTANT "RHINO". H. Kawaji, R. Tsukuda and M. Takaoki. Biol. Res. Labs. Takeda Chem. Industries, Osaka 532, Japan

The rhino mice, an autosomal mutant, were known to have hairless and hyperkeratotic skin. In parallel with skin hyperkeratosis, extensive hyperplasia of Hassall's corpuscles with

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Medalia and C. Dugan. Div. Labs. Res., New York State Dept. of Health, Albany, N.Y. 12201, USA.

C57BL/6J mice do not express the IrZ gene and are unable to produce antibodies to a single dose of *Escherichia coli* β -D-galactosidase (Z), but mount memory. Priming-memory generation (PMG) predominates in the spleen of irradiated, spleen-cell transfused mice. Splenic erythropoiesis preceding a Z dose reduces frequency of PMG from 81 to 33% (90 mice/group, $p < 0.001$). This does not occur if: a) erythropoiesis is eradicated; b) Z is given before erythropoiesis stimulation, or later than 3 days after it; c) mice are not irradiated. In these, however, PMG frequency falls to 13% following transfusion of erythropoietic spleens (30-40% erythroblasts), as opposed to 81% in controls transfused with normal spleens (16 mice/group; $p < 0.001$). Similar effects are produced by 98% pure erythroblasts transfused into irradiated spleen cell reconstituted mice. Immunological disfunction thus occurs in genetic low responders when immunization coincides with erythropoiesis, at a critical time point during the latter process, within a restricted anatomical site such as the spleen.

14.1.14

P

AN ABNORMALITY IN THE EARLY STAGES OF IMMUNE COMPLEX KINETICS IN MURINE LUPUS. D. B. Magilavy and P. H. Plotz. N.I.H. Bethesda, MD., U.S.A.

To understand better the role of immune complex metabolism in the pathogenesis of autoimmune disease, we have studied immune complex uptake by the liver, the major organ responsible for clearance of complexes in the mouse. Livers were perfused in situ over 3-5 minutes with radio-labeled soluble immune complexes. In 3 non-autoimmune strains 60-72% of the complexes perfused were taken up and remained in the liver after 20 min of continuous perfusion with oxygenated Krebs-Henseleit buffer. In NZB and NZB/Wf₁ female mice, 66-78% of the complexes remained in the liver. To determine whether or not the bound complexes were internalized, we perfused unlabeled aggregated human gamma globulin in doses sufficient to saturate the liver. When such aggregates were perfused 7 minutes after radiolabeled complexes, $15.0 \pm 8.2\%$ (mean $\pm$ S.D.) of the complexes were displaced in the non-autoimmune strains, whereas $32.4 \pm 12.5\%$ were displaced from the liver in NZB and NZB/Wf₁ females ($p < 0.001$). Thus, although hepatic uptake of immune complexes in autoimmune mice appears to be normal or even enhanced, there may be impaired phagocytosis or weaker binding of complexes by the Kupffer cells. Such surface bound complexes remaining accessible to the circulation may contribute to the autoimmune process.

14.1.15

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ABNORMAL REGULATION OF THE IMMUNE RESPONSE IN PROTEIN-CALORIE DEFICIENT MICE. Inés Malavé & Marisol Pocino. IVIC, Aptdo. 1827, Caracas 101, Venezuela.

Spleen cells from C57BL/6 mice kept for 3 weeks on a low protein diet (D) leading to moderate protein calorie deficiency have increased antibody forming cell (AFC) sheep red blood cells (SRBC) after transfer to normal hosts or in Mishell-Dutton cultures. In spleen cells from donors immunized with doses of SRBC caused less suppression of AFC than in normally fed (N) recipients. The AFC response was also lower when splenic cells were cocultured with nonimmune cells from D than N donors indicating depletion of AFC to suppression by signals from antigen presenting cells in the D spleen. The delayed hyperimmune (DH) reaction induced by an optimal SRBC dose was lower in D and N mice but the response of DH was prolonged and not suppressed by high anti-DH in N animals. After lipopolysaccharide (LPS) reaction the number of AFC against bromelain or syngeneic mouse red blood cells was lower in D than N mice. It is concluded that acute protein calorie deficiency selectively affects immune response and allows the liberation of self reactive AFC.

PW

OF ANTI-IgG AUTOANTIBODIES BY THE MESENTERIC LYMPH NODE IN THE 129 MOUSE.

P.L. Masson & J.L. Van Snick, Unit of Experimental Medicine, ICP, Université Catholique de Louvain, B-1200 Brussels.

We have described IgA and IgM anti-IgG autoantibodies which appear with age in various strains of mice from certain colonies. The anti-IgG in the 129/Sv and 129/J strains are specific for the Fc region of IgG2a and do not cross-react with IgG from other species. These autoantibodies preferentially bind IgG2a that has been aggregated by heating or combined to its antigen. Their production is clearly related to an infectious agent but also depends on the genetic background of the animals. We have systematically investigated the in vitro production of anti-IgG by the various lymphoid tissues of 129/Sv and 129/J mice. During the first twenty weeks of life the production of IgM and IgA anti-IgG was restricted to the mesenteric and caudal lymph nodes. In older animals cells secreting anti-IgG were also present in the spleen and bone marrow, but not in lymph nodes other than those draining the intestinal tract.

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CONCENTRATION AND HETEROGENEITY OF SERUM IMMUNOGLOBULINS IN NUDE MICE. Mink, J.G., Radl, J., P. van den Berg and Benner, R. Dept. of Cell Biology & Genetics, Erasmus University Rotterdam, and Inst. for Exp. Gerontology, Rijswijk (ZH), The Netherlands.

The heterogeneity and concentration of the major serum Ig isotypes were investigated in 6, 40 and 110-week-old nu/nu and nu/+ mice. At 6 weeks IgM and IgG₁ were the most prominent serum Ig's in both groups of mice. At the age of 40 and 110 weeks most nu/nu mice had all Ig (sub) classes in their sera. The most striking differences between aged nu/nu and aged nu/+ mice were: (a) the generally decreased levels of IgG_{2a}, IgG_{2b}, and IgA; (b) the frequent occurrence of increased levels of IgG₁; and (c) the increased incidence of homogeneous Ig components (H-Ig) in the sera of nu/nu mice. The nu/+ mice also showed H-Ig but less than nu/nu mice. The onset and distribution of H-Ig of the various Ig (sub)classes was determined in a follow up study of nu/nu and nu/+ mice, and their background strains (BALB/c and CBA). The incidence of H-Ig in nu/+ mice was intermediate between the nu/nu mice and the background strains. BALB/c and CBA mice showed a later onset of H-Ig than nu/nu and nu/+ mice. The Ig heavy chain isotype distribution of 320 H-Ig of nude mice was 17, 43, 19, 8, 12 and 1% for IgM, IgG₁, IgG_{2a}, IgG_{2b}, IgG₃ and IgA, respectively.

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