

dim homogeneous background stain in preparations fixed in methanol, whilst in acetone fixed sections of the same material it was seen as a finely dispersed amorphous deposit. We did not consider this to be an artefact since apart from its absence from the controls there was a marked degree of uniformity in the strength of reaction between sections of the same tissue subjected to the 2 treatments¹³.

Zusammenfassung. Immunglobulin IgA wird beim Schwein immunochemisch im Darminhalt und immuno-fluoreszenzoptisch in der Mukose des gesamten Dünndarms nachgewiesen.

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Osseal Changes in Young Mice Undergoing Graft-versus-Host Reaction

The features of graft-versus-host (GVH) reaction are characterized by weight loss, lethargy, ruffled fur, hunched back posture, splenomegaly, the decrease of the absolute lymphocyte count and by impaired immunological reactivity with low level of circulating antibodies and immunoglobulins. Moreover the animals are generally retarded, and the progressive atrophic state is remarkable¹⁻⁸.

The purpose of this communication to discover the background of this general retardation of the growth and of the progressive atrophic state, which develops in young mice undergoing GVH reaction.

Materials and methods. GVH reaction was produced in (C57B1 \times A) F₁ hybrid mice, without regard of sex. The animals in experiment I were 2 weeks old, and in experiment II were 3 weeks old. The mice were injected i.p. with 150×10^6 spleen cells from adult C57B1 donors of both sexes (GVH groups). The mice of control groups received the same amount of isologous spleen cells. In both experiments, 3 weeks later following the injections, the establishment of the GVH reaction was confirmed by the significant decrease of the absolute number of circulating lymphocytes, and the decline of the body weight.

Radiographs of 10-10 animals with GVH reaction and 10-10 control mice were taken 3 weeks later, following the

spleen cells transfer in experiments I and II, simultaneously in pairs with controls by the same exposition time for radiomicrometric measurements⁹. The animals were then sacrificed and dissected. The splenomegaly with ascites and peripheral lymphonodular enlargement were confirmed macroscopically.

The distal end of femora were chosen for histological study; 4% formalin fixative, decalcification paraffin embedding and hematoxylin-eosin staining were used.

Results and discussion. The decrease of the absolute lymphocyte count and the decline of the body weight in experiments I and II are presented in Figure 1. In the radio-

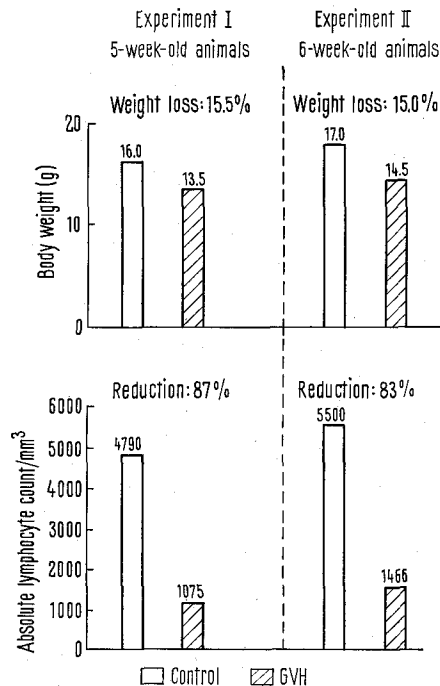


Fig. 1. The average body weight and absolute lymphocyte count in mice of GVH and of control groups.

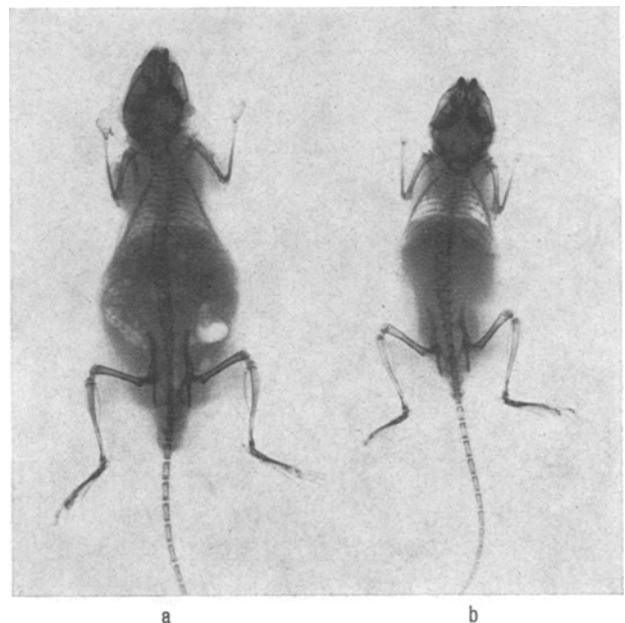


Fig. 2. Radiogram of a 6-week-old mouse undergoing GVH reaction (b) and a control littermate (a) from experiment II.

¹ E. E. BILLINGHAM, *Science* 130, 947 (1959).

² R. E. BILLINGHAM and L. BRENT, *Transplant Bull.* 4, 67 (1957).

³ M. KOLTAY, R. KINSKY and B. ARNASON, *Nature* 205, 509 (1965).

⁴ G. MATHÉ and J. L. AMIEL, *Rev. fr. Etud. clin. biol.* 8, 537 (1963).

⁵ N. W. NISBET and B. F. HESLOP, *Br. med. J.* 1, 129; 7, 206 (1962).

⁶ M. SIMONSEN, *Acta path. microbiol. scand.* 40, 480 (1957).

⁷ M. SIMONSEN, *Progr. Allergy* 6, 349 (1962).

⁸ M. SIMONSEN, in *Mechanism of cell and tissue damage produced by immune reactions*, II. Int. Symp. of Immunopathology (Eds. P. GRABAR and P. MIESCHER; Schwabe, Basel/Stuttgart 1962), p. 233.

⁹ L. BEREK, *Experientia* 25, 633 (1969).

graphs great differences between the mice of control groups and of the GVH groups were observed. These appeared to be particularly significant in long bones. The loss of bone minerals was also remarkable (Figure 2). The results of the radiomicrometric measurements are presented in Figure 3. In experiment I the retardation rate of the longitudinal growth amounted to 21%, of the diametric retardation 8.6% in the 5-week-old animals with GVH reaction; and in experiment II the longitudinal retardation of the growth amounted to 16% and the diametric 10.5% in the 6-week-old animals with GVH reaction. The most striking and remarkable changes could be seen in the decrease of the corticalis thicknesses of femoral midshaft. These represent in experiment I 37% and in experiment II 41% corticalis decreases in comparison with the controls (Figure 3). Taken together these data, the longitudinal, the diametric and cortical retardation with the loss of the bone minerals, represent a severe bone atrophy.

The normal structure may be seen in the microscopic sections from the control groups. The structure and thickness of the articular cartilage are normal. The epiphyseal plate shows the continuous enchondral ossification, besides the normal endo-, periosteal osteoblastic activity (Figure 4).

Similar histological sections from the bones of the mice undergoing GVH reaction in both experiments show remarkable phenomena. In the distal femoral epiphyses the articular cartilage became thin, the osseal trabeculae in the epimetaphyses are sparse and slightened at their side with little sign of osteoblastic activity. The growth plates are thin, the hyalin pillars rarefied and their ossification retarded. All diaphyseal cortices are strikingly thin, the endo-, periosteal osteoblastic activity markedly sparse (Figure 5).

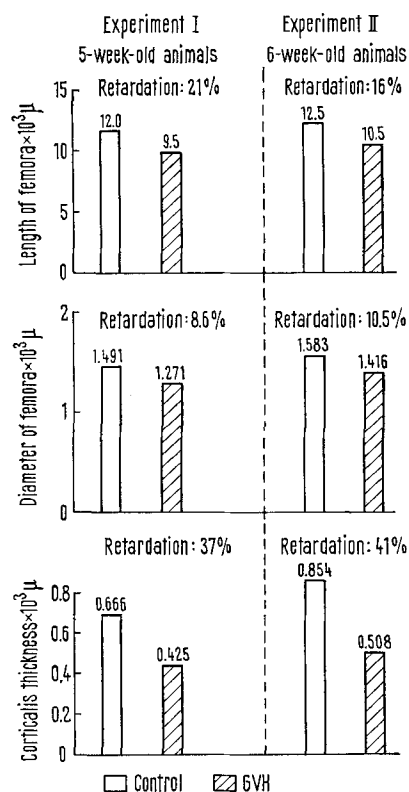


Fig. 3. The average length, diameter and cortical thickness of femora in mice of control and GVH groups.

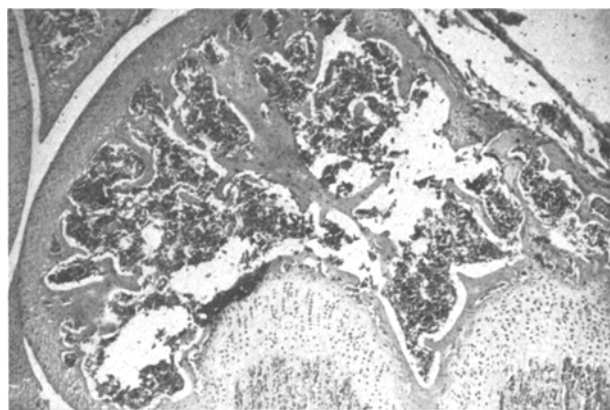


Fig. 4. Control microphotograph of the distal femoral end of 6-week-old littermates from experiment II. Hematoxylin-eosin staining. $\times 15$.

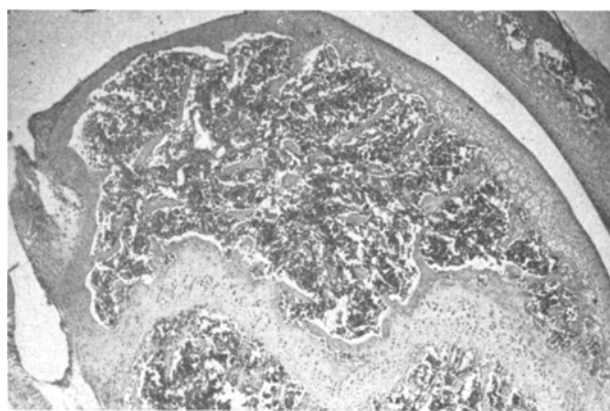


Fig. 5. Microphotograph of distal femoral end of a 6-week-old mouse of GVH group from experiment II. Hematoxylin-eosin staining. $\times 15$.

The observed alterations were demonstrable in all animals undergoing GVH reaction and the roentgenologic findings and histology were in good agreement with the clinical conditions.

These roentgenologic and histomorphological observations revealed a severe bone atrophy together with the retardation of the enchondral with the peri- and endosteal ossification as a background of the decreased development and the general retardation of growth in young mice undergoing GVH reaction.

The data presented revealed a symptom of graft-versus-host reaction undetected up to this point¹⁰.

Zusammenfassung. Immunpathologische Untersuchungen an Mäusen, welchen i.p. Milzzellen von Spender-tieren injiziert wurden. Röntgenologisch und histomorphologisch wurden Knochenatrophien festgestellt und es kam zu verzögerter Ossifikation sowie zu einer allgemeinen Wachstumsverzögerung.

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¹⁰ Acknowledgment. The authors wish to thank Miss I. ÁDÁMFIA, Miss M. BARBIE, Mrs. J. KOZMA and Mrs. S. OSZTAFIN for skilful technical assistance.