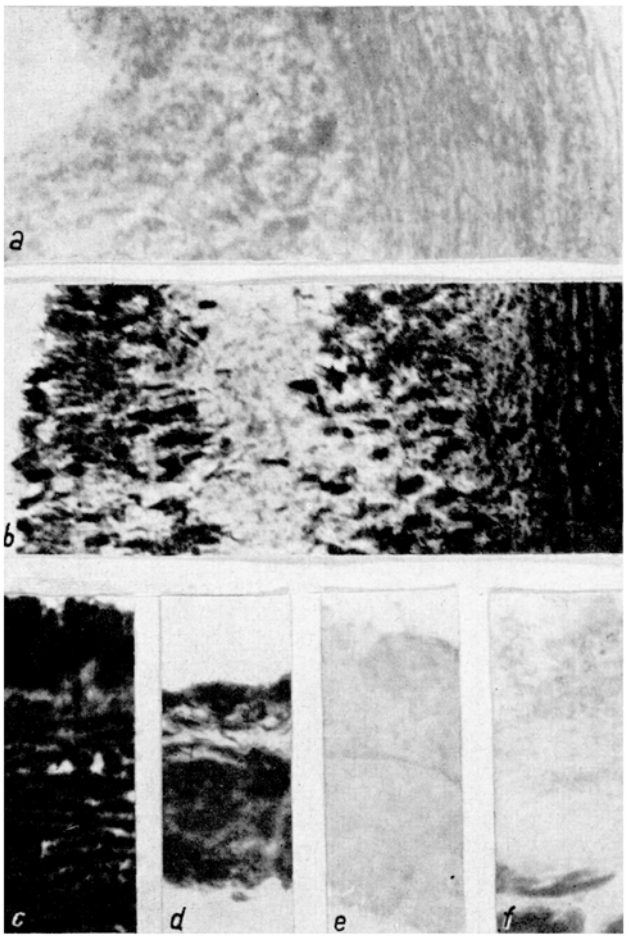

All microphotographies refer to the aortae of atherosclerotic rabbits. a) Succinic dehydrogenase. Slight positive reaction in muscle cells of media (right half of the Figure) and in the macrophages (lipophages) and fibrocytes (left half of the Figure) of intima. b) DPN-diaphorase. Strong positive reaction in macrophages and fibrocytes on surface of the plaque (left quarter) and in muscle cells of media (right quarter). In the center of the plaque (second quarter) negligible reaction. c) Lactic dehydrogenase. Intense reaction in the plaque (top) and in muscle cells of media. d) Lactic dehydrogenase in the plaque (bottom) on the semilunar valve (compare with Fig. c). e) Glutamic dehydrogenase. Reaction is almost negative. f) Glucoso-6-phosphate dehydrogenase. Weakly positive reaction in some cellular elements of the plaque, a stronger one in adjacent myocardium (bottom).

in favour of the concept of relatively high metabolic activity of the intima in the initial stage of the atheromatous lesions.

Z. Lojda and V. Felt

Embryological Institute, Medical Faculty, Charles University and Research Institute for Endocrinology, Prague (CSR). June 15, 1960.

Zusammenfassung

In Aorten von Kaninchen mit experimenteller Atherosklerose wurden die folgenden Dehydrogenasen untersucht: DPN-Diaphorase, Lactat- und Malat-Dehydrogenase, TPN-Diaphorase, Succinat-, Glucoso-6-phosphat- und Glutamat-Dehydrogenase. Die Aktivität der fünf erstgenannten war in den Endothelien, Makrophagen (Lipophagen) und Fibrozyten der verdickten Intima und kleiner atherosklerotischer Beete deutlich erhöht. Die Befunde stehen im Einklang mit der Ansicht, dass die Stoffwechselaktivität der Intima am Anfang der experimentellen Atherogenesis erhöht ist.

The Effect of Litter Rank on the Development of Mouse Lymph Nodes

Evidence has been obtained that maternal age influences the occurrence of mongolism in human beings[1] and that the incidence of spontaneous[2-4] and induced[5] tumors in mice varies with litter rank. The mechanism by which these effects are produced is unknown. The present studies, however, indicate that in young mice of certain strains lymph node size changes significantly in successive litters. Since lymphatic tissue is an important part of host defense, the possibility exists that the influence of litter rank in tumor growth might be mediated through an alteration in lymph node development.

Female mice were used throughout. They were weaned at 5 weeks, thereafter housed 5–12/cage, kept on racks in an air-conditioned room, and fed water, and Purina Laboratory Chow *ad libitum*. At sacrifice, by cervical dislocation, two elbow and two inguinal nodes were removed, trimmed of extraneous tissues, blotted, and the combined weights determined on a Roller-Smith torsion balance.

In the first experiment the lymph node and body weights of 6–7 $^1/_2$ week old second and fourth litter low-tumor C57BL/Sp mice were compared. Mean body and lymph node weights (standard error in parentheses) for 7 second litter mice were 15·9 (0·3) g and 11·6 (0·6) mg respectively, while those for 7 fourth litter mice were 14·0 (0·5) g and 8·3 (0·5) mg respectively. Highly significant ($P < 0{\cdot}01$) decreases in both body and lymph node weights of fourth litter C57BL/Sp mice were observed. On the other hand, similar measurements on first and fourth litter low-tumor $C3H_f$/AnSp mice showed no significant litter rank difference.

In the second experiment (Table I) body and lymph node growth were investigated in C57BL/Sp mice of first through fourth litters by comparing their weights in mice 3 and 6 weeks of age. No significant differences were observed at 3 weeks. Significantly lower body and lymph node weights of mice of the third and fourth litters were found at 6 weeks ($P < 0{\cdot}001$ and $< 0{\cdot}05$ respectively). Smaller percent increases in lymph node weight during the 3–6-week interval were found in mice of second and third litters than in first litter mice. In marked contrast, no such trend was observed in the body growth of successive litters.

Recently[6] it was observed that in foster-nursing mice from strains characterized by large lymph nodes to mothers possessing small nodes the young developed smaller lymph nodes than non-foster-nursed controls. Conversely, foster-nursing mice with normally small nodes to mothers with large lymph nodes resulted in large nodes in the young. These results indicated that a maternal-infant relationship in mice during the nursing period, presumably mediated *via* the milk, is important in lymph node development.

Acknowledgment. This investigation was supported in part by research grant No. C-2151 from the National Cancer Institute, Public Health Service and in part by an institutional grant to the Detroit Institute of Cancer Research from the United Foundation of Greater Detroit through the Michigan Cancer Foundation.

[1] L. S. Penrose, Sci. Month. *52*, 359 (1941).

[2] J. J. Bittner, A. A. A. S. Res. Conference on Cancer (1949), p. 63.

[3] O. Muhlbock, J. Nat. Cancer Inst. *12*, 819 (1952).

[4] E. C. MacDowell, J. S. Potter, M. J. Taylor, E. U. Ward, and T. Laanes, *Mouse Genetics* (Annual Report Dept. of Genetics, Carnegie Inst. of Washington 1943), p. 126.

[5] L. C. Strong, J. Gerontology *6*, 340 (1951).

[6] S. Albert and R. M. Johnson, Cancer Res. *20*, 55 (1960).

[7] T. D. Luckey, Texas Rep. Biol. Med. *14*, 482 (1956).

Tab. I. The effect of litter rank on lymph node development in C57BL/Sp mice[a]

Age weeks	No. of mice	Body weight g	Lymph node weight mg
		First litter	
3	14	6·2 (0·4)	6·0 (0·5)
6	12	15·1 (0·3)	13·9 (1·0)
Increase – %		144	132
		Second litter	
3	26	6·8 (0·3)	6·2 (0·5)
6	27	14·5 (0·3)	13·1 (0·7)
Increase – %		113	111
		Third litter	
3	12	5·8 (0·4)	5·3 (0·7)
6	29	13·1 (0·4)	9·3 (0·7)
Increase – %		126	76
		Fourth litter	
6	9	12·2 (1·2)	9·9 (1·4)

[a] Values are means and their standard errors.

Tab. II. The effect of litter rank on lymph nodes of C3H/AnSp and AKR/Jax mice[a]

Strain	No. of mice	Body weight g	Lymph node weight mg
		First litter	
C3H	12	15·3 (0·5)	21·1 (1·3)
AKR	10	14·1 (0·7)	10·7 (0·6)
		Second litter	
C3H	7	13·2 (0·6)	17·2 (1·1)
AKR	9	14·9 (0·6)	14·6 (1·7)

[a] Values are means and their standard errors.

Work with germ-free animals[7] has indicated that in the absence of an outside stimulus lymphatic tissue fails to develop to an appreciable extent. The present experiments suggest that some maternal stimulus in C57BL/Sp mice apparently diminishes with the age of the mother and/or the number of litters raised.

The effect of litter rank on spontaneous tumor incidence has not been found to be uniform. Bittner[2] observed that mammary tumor incidence was increased in advanced litters. On the other hand, MacDowell *et al.*[4] found a decrease in leukemia incidence in later litters. Preliminary experiments (Table II) indicated that the effect of litter rank on nodes from mice with a high incidence of either spontaneous mammary cancer (C3H/AnSp) or leukemia (AKR/JaxSp) was likewise not uniform. Lymph nodes from 6–$7^1/_2$-week old second litter C3H/AnSp mice were smaller than those of age matched first litter mice; while nodes from 6–$7^1/_2$-week old second litter AKR/JaxSp mice were larger than those of age matched first litter mice. These differences were significant at the 5 percent level. These preliminary findings suggest the possibility that alteration in the quantity of the lymphatic component of host defense may be involved in the alteration of spontaneous tumor incidence by litter seriation.

S. Albert

Detroit Institute of Cancer Research and Wayne State University College of Medicine, Detroit (Michigan), March 21, 1960.

Zusammenfassung

Das Gewicht der Lymphknoten von 6–$7^1/_2$ Wochen alten C57BL- und C3H-Mäusen sank in aufeinanderfolgenden Würfen ab. Umgekehrte Verhältnisse fanden sich bei AKR-Mäusen. Verzögertes Wachstum war für die kleinen Lymphknoten der späteren Würfe bei drei und sechs Wochen alten C57BL-Tieren verantwortlich.

DISPUTANDUM

The Stereochemistry of Reduction by Complex Metal Hydrides

It has been concluded that two effects operate to determine the stereochemistry of an alcohol obtained by hydride reduction of an asymmetric cyclohexanone: the ease of formation of the complex between the carbonyl group and the complex hydride (steric approach control); and the relative energetics of the formation of the products once the initial complex is produced (product development control)[1]. While there is some disagreement over the exact proportions of epimeric alcohols obtained in the reductions[2,3], it seems clear that as Dauben *et al.* originally reported, use of sodium borohydride as reducing agent tends to lead to a greater proportion of the unstable epimeric alcohol than does the use of lithium aluminum hydride. Dauben suggests that this difference in the composition of products is due to the greater effective size of the borohydride species as compared with lithium aluminum hydride.

Although this hypothesis appears to have been generally accepted[4], there are difficulties associated with it. The B-H bond length in borohydride is 1.25 A[5] and it has also been found from measurements of force constants that the Al-H bond length in the aluminum hydride ion is 1.66 A[6]. These bond-length values show that the correctness of Dauben's suggestion depends on the borohydride ion in methanol or pyridine being solvated to a greater extent than the aluminum hydride ion in ether or tetrahydrofuran.

While the theory of ion-solvent interactions is not yet in an entirely satisfactory state, it is thought that monovalent anions which have a crystal radius of 1.80 A or greater are not solvated in water or methanol[7]. The crystal radius of the borohydride ion is 2.03 A[8] and the

We thank Dr. D. J. Royer of the Georgia Institute of Technology, Dr. W. R. Gilkerson of the University of South Carolina, and Dr. R. H. Harris of the University of Nebraska for many helpful discussions concerning the physical and inorganic chemistry of the complex metal hydrides.

[1] W. G. Dauben, G. J. Fonken, and D. S. Noyce, J. Amer. chem. Soc. *78*, 2579 (1956). – W. G. Dauben, E. J. Blanz, J. Jiu, and R. A. Micheli, J. Amer. chem. Soc. *78*, 3752 (1956).

[2] W. G. Dauben and R. E. Bozak, J. org. Chem. *24*, 1596 (1959).

[3] K. D. Hardy and R. J. Wicker, J. Amer. chem. Soc. *80*, 640 (1958).

[4] L. F. Fieser and M. Fieser, *Steroids* (Reinhold, New York 1959), p. 268.

[5] P. T. Ford and R. E. Richards Disc. Faraday Soc. *19*, 230 (1955).

[6] H. L. Roberts and L. A. Woodward, Trans. Faraday Soc. *52*, 1458 (1956). – Cf. D. A. Brown, J. chem. Phys. *29*, 451 (1958).

[7] R. A. Robinson and R. H. Stokes, *Electrolyte Solutions* (Butterworths, London 1955), p. 51–62, 117, and 162.

[8] S. G. Abrahams and J. Kalnajs, J. chem. Phys. *22*, 434 (1954).