

culature of the forelegs of one animal and a rare lesion in the abdominal musculature of the second.

Many of the animals, particularly the older ones, whether control or experimental, exhibited varied degrees of weakness and some incoördination towards the latter part of the experimental period. The central and peripheral nervous systems were not examined. As might be expected the alpha-tocopherol had no effect upon either the extent or character of the characteristic lesions of vitamin A deficiency present in all animals, and testicular atrophy occurred as readily in the experimental as in the control animals. Focal areas of interstitial myocardial infiltration occurred as frequently in the one as in the other.

Conclusions. Muscular lesions hitherto described in vitamin A deficiency in rats can be prevented by the administration of alpha-tocopherol and hence are not related to the vitamin A-deficient state. Vitamin E or alpha-tocopherol should form a part of the basal diet used to produce vitamin A deficiency in rats.

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Histamine in the Rabbit Skin.

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Using the trypan blue test we have shown¹ that histamine injected intradermally in the very young rabbit does not cause a seepage into the injected area of the dye injected intravenously. This fact is consistent with an observation described by Feldberg and Kellaway² on the pharmacological effect of histamine on the cat. Very young cats are very resistant to the injection of histamine. In particular, the pressure in the pulmonary artery is only slightly altered by the intravenous injection of histamine in young cats, while the same dose injected into old cats may produce marked changes. By determining the histamine content of the lungs in cats varying in weights from 0.5 to 6 kg, they have shown a parallelism between the increasing amount of histamine in the lung tissue and the pharma-

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¹ Rocha e Silva, M., *Nature*, 1940, **145**, 591.

² Feldberg, W., and Kellaway, C. H., *Aust. J. Exp. Biol. and Med. Sc.*, 1937, **15**, 81.

cological effects produced by the drug when injected into the vein. This work was undertaken to ascertain whether a parallelism exists between the histamine content of the skin and the response to the trypan blue test.

Experimental. We have determined (41 rabbits) the amount of histamine in rabbit skin by employing the Barsoum and Gaddum method³ as modified by Code.⁴ A technic devised by us⁵ was used to reduce the volume of the extract, when desirable. All figures regarding histamine refer to histamine dihydrochloride which was used in the assays. Simultaneously with the collection of the fragment of skin for extraction we determined the area of the skin slices. A rectangle of the skin surface was drawn against cellophane paper and the area measured over millimetered paper. Then the skin fragment was cut out with sharp scissors, the subcutaneous connective tissue carefully dissected and the rectangle of the skin weighed. The skin fragments were removed from the skin of the abdomen near the midline; in the newborn the skin from the side of the abdomen was included. The weights of the fragments extracted ranged from 0.3 to 6.0 g and the areas from 10 to 60 sq cm.

For depilation of the area of the skin, the use of chemicals commonly employed has been avoided by using scissors to cut the hair close to the skin surface. Perhaps this practice explains the fact that our figures are lower than those appearing in previous publications.^{6, 7, 8}

Results. The data in Fig. 1 show that immediately after birth the skin thickens and then becomes thinner and thinner until the body weight attains 300 to 600 g. In the adult rabbit (over 1500 g body weight) the skin is maximally thick. The variation in the histamine content is less since it decreases regularly from young rabbits to adult ones (Fig. 2). The determination of the curve of thickness of the skin as related to the body weight was necessary since one might be induced to interpret this decrease in the histamine content by assuming that the same quantity of histamine would be connected with a certain area and not with a certain weight of the skin. It may be seen, however, that very young rabbits, whose skin is as thick as that of adult rabbits, have large amounts of histamine in each gram of skin tissue.

³ Barsoum, G. S., and Gaddum, J. H., *J. Physiol.*, 1935, **85**, 1.

⁴ Code, C. F., *J. Physiol.*, 1937, **89**, 257.

⁵ Rocha e Silva, M., *Nature*, 1939, **144**, 252.

⁶ Tarras-Wahlberg, B., *Klin. Wochenschr.*, 1937, **16**, 958.

⁷ Riesser, O., *Arch. f. exp. Path. u. Pharm.*, 1937, **187**, 1.

⁸ Rocha e Silva, M., and Bier, O., *Arq. Inst. Biol.*, 1938, **9**, 133; *Compt. Rend. Soc. de Biol.*, 1938, **129**, 1140.

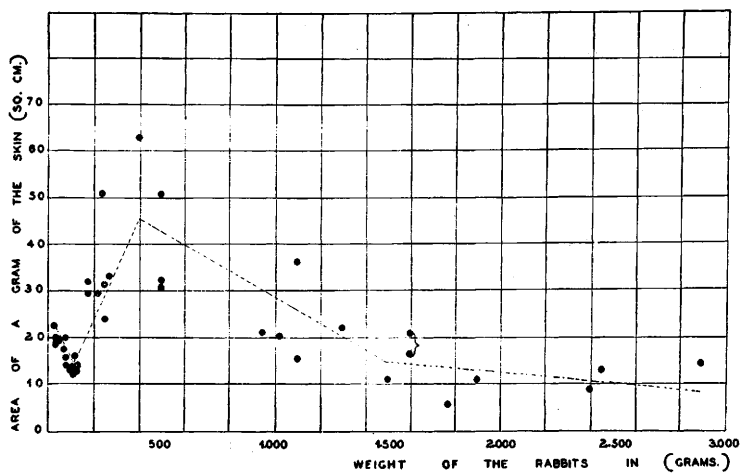


FIG. 1.

Curve of thickness of the skin of rabbits of different weights.

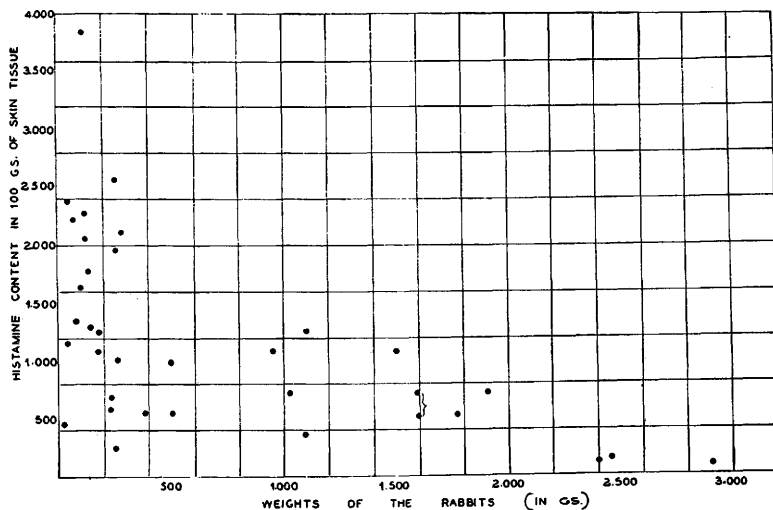


FIG. 2.

Histamine content of the skin in rabbits of different weights.

Hence, it is clear that the parallelism found by Feldberg and Kel-laway² between the pharmacological action of histamine and the amount of histamine present in the lung tissue does not hold in the case of rabbit skin. Adult rabbits, which react very well to histamine intradermally injected by showing a very beautiful blue spot after intravenous injection of trypan blue, have per gram weight of skin a very low histamine content in their skin, while the histamine content is sometimes exceptionally high in the skin of very young

rabbits which react poorly or not at all to the intradermal injection of histamine.

Whether this high amount of histamine in the skin of very young rabbits bears some relationship to the physiology of the skin is an open question.

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Influence of Nutritional Intake Upon Concentration of Vitamin A in Body Tissues.

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Batchelder's finding¹ that systematically increased intakes of vitamin A resulted in progressively more vigorous offspring even beyond the level at which the parents had reached the plateau of outwardly apparent wellbeing, suggests that liberality of intake of vitamin A may be a significantly influential factor in the body's internal environment, and adds importance to the question how generally the concentration levels in the body are influenced by the level of intake.

That the vitamin A content of the liver varies widely with the level of intake has been universally recognized since the quantitative work of Baumann, Riising, and Steenbock.² More recently Steininger, Roberts, and Brenner³ have investigated the fluctuations of the vitamin A concentration in the blood. Are there corresponding fluctuations in the muscles? Conclusive experimental demonstration is difficult because the concentration of vitamin A in the muscles is so low. Boynton's bioassays⁴ indicated that muscle contained only 0.25% to 0.5% of the concentration of vitamin A found in the livers of the same animals. Baumann, Riising, and Steenbock² reported "negative results" from their tests for vitamin A in the blood and muscles of normally nourished rats, but also spoke of their findings as in harmony with those of Boynton.

¹ Batchelder, E. L., *Am. J. Physiol.*, 1934, **109**, 430.

² Baumann, C. A., Riising, B. M., and Steenbock, H., *J. Biol. Chem.*, 1934, **107**, 705.

³ Steininger, G., Roberts, L. J., and Brenner, S., *J. Am. Med. Assn.*, 1939, **113**, 2381.

⁴ Sherman, H. C., and Boynton, L. C., *J. Am. Chem. Soc.*, 1925, **47**, 1646.