this medium its multiplication is sufficient to produce measurable quantities of hemagglutinin in the supernatant fluid even when small inocula are employed. It is therefore possible within certain limits to estimate with ease the capacity of the virus to multiply under these conditions. It has also been determined that Influenza A virus (PR8 strain) increases in this type of medium to a level at which its hemagglutinating property can also be readily assayed.

The development of measurable amounts of hemagglutinin in tissue cultures is of significance, since it provides a swift and convenient means of following the rate and degree of multiplication of the mumps and influenza viruses in a system which, compared with a medium such as the chick embryo or the mouse, is far less complex. The technic, therefore, might be applied profitably to the study of many problems, for example, the effect of various chemical compounds in accelerating or inhibiting the growth of these viruses.

It is noteworthy that the rate of multiplication of influenza A virus was found to be much more rapid than that of mumps. This difference has been previously observed in experiments with infected chick embryos and would seem, as Ginsberg, Goebel and Horsfall[8] have indicated, to reflect a basic difference in the biologic properties of the two agents.

Conclusions. 1. An egg-adapted strain of mumps virus has been cultivated in suspended cell tissue cultures. 2. In such media the mumps virus as well as Influenza A virus (PR8 strain) produce measurable quantities of hemagglutinin.

[8] Ginsberg, H. S., Goebel, W. F., and Horsfall, F. L., *J. Exp. Med.*, 1948, **87**, 385.

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Magnesium Deficiency in the Sexually Mature Rat.*

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That the young rat requires an adequate dietary intake of magnesium for normal life processes was first established by Kruse, Orent, and McCollum.[1] As shown by Tufts and Greenberg, two phases seem to be observed in magnesium deficiency in young rats.[2] The first is marked by vasodilatation, hyperemia, and hyperexcitability. The second phase is characterized by nutritive failure, cachexia, and kidney damage. There have been controversial reports as to the pathological involvement of the skin in magnesium deficiency in rats. Kruse and his co-workers reported definite trophic changes in the skin and nails of young animals on a diet deficient in magnesium. Likewise, other workers reported skin lesions in animals deprived of magnesium.[3,4] On the contrary, Tufts and Greenberg and others did not observe disturbances in the skin of young animals raised on diets deficient in magnesium.[5,6] Greenberg suggested that the trophic conditions observed by several workers were due to the experimental animals not receiving various constituents of the vitamin B complex in sufficient quantities.[7]

* Aided by a grant from the Dow Chemical Company, Freeport, Texas, through the Texas A & M Research Foundation.

[1] Kruse, H. D., Orent, E. R., and McCollum, E. V., *J. Biol. Chem.*, 1932, **96**, 519.

[2] Tufts, E. V., and Greenberg, D. M., *J. Biol. Chem.*, 1938, **122**, 693.

[3] Watchorn, E., and McCance, R. A., *Biochem. J.*, 1937, **31**, 1379.

[4] Shrader, G. A., Prickett, C. O., and Salmon, W. D., *J. Nutrition*, 1937, **14**, 85.

[5] Brookfield, R. W., *Brit. Med. J.*, 1934, **1**, 848.

TABLE I.
Effect of Magnesium on the Weights of Sexually Mature Rats.

Dietary treatment Mg	No. of animals	Initial wt g	Final wt g	Gain per wk g
+	3	156	337*	13.9
—	3	147	249	7.7
+	3	311	385†	14.2
—	8	311	346	7.0
+	4	215	283†	13.6
—	7	209	245	7.0

* Weight after a period of 8 weeks.
† Weight after a period of 5 weeks.

Though the manifestations of magnesium deficiency in the young rat have been well established, the specific effect of magnesium deprivation in the older rat is still questionable. The experiments reported here were designed to determine the effect of insufficient dietary magnesium on sexually mature rats.

Experimental. The composition of the diets used has been reported in a previous paper.[8] The magnesium low diet contained less than 1.0 mg of magnesium per 100 g, while the control diets contained approximately 30 mg per 100 g. Three different series of rats were used with average beginning weights of 152, 311, and 212 g respectively.

Vasodilatation and hyperemia were not outstanding symptoms in the sexually mature rats on the magnesium-deficient diet. In several animals none was observed at all, but in most instances these symptoms made their appearances 14 to 19 days following the start of the experiment. The vividness of the red color of the ears and extremities during this period was not pronounced, but the slight reddening of these areas was easily detected and usually was observed for 5 to 6 days with a gradual fading towards the end of this period. This increased length of time before vasodilatation and hyperemia could be observed and the lack of marked vasodilatation are differences between the young animals and the sexually mature animals. It has been shown that young rats on a magnesium-deficient diet show vivid reddening of the ears and extremities within 3 to 5 days after being restricted to the deficient diet.

The animals on the magnesium-deficient diet showed only a slight degree of nervousness and apprehensiveness during the period of vasodilatation and hyperemia, but increased nervousness was noticed 4 to 7 days after vasodilatation had subsided. No cases of spontaneous convulsions were observed.

Significant differences in the average weight gains of the experimental and control animals were noted as early as the second week. By the end of the 5th week the control animals had an average gain of almost twice that of the experimental animals. After 8 weeks on the regimens for the first series and 5 weeks for the second and third series some of the animals on the deficient diet were transferred to the magnesium-supplemented diet. These animals showed an immediate response in rate of gain in weight while those on the deficient diet made only slight gains or lost weight.

After approximately 3 weeks on the experimental diets, edema was observed in the nasal regions of the animals on the deficient diet. The hair became sticky, stiff, and lusterless. Occasionally a sticky, reddish exudate was seen on the feet, noses and ears. Erythematous changes in the skin began to appear between the 23rd and 28th day after the experiment had started. The erythematous changes were characterized by small circular areas on the dorsum of the back or neck in

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[7] Greenberg, D. M., *Ann. Rev. Biochem.*, 1939, **8**, 269.

[8] Kunkel, H. O., and Pearson, P. B., *Arch. Biochem.*, 1948, **18**, 461.

most of the animals. This skin condition appeared to become progressively worse with time, and erythema was noticed around the scrotal area in the males, on the abdomen, and on the sides and under the jaws of animals of both sexes. Following the erythema, purpural skin hemorrhages were observed in the areas which had shown erythema. Extensive eschar formation followed the purpura. Usually the eschars were hard and dry, and the escharotic tissue was confined to small circumscribed areas. Exfoliation followed the escharotic stage, and there was a loss of hair around the areas previously occupied by the eschars. In some cases, ulceration followed exfoliation. When this occurred eschars were usually reformed, and exfoliation generally followed.

Those animals that were transferred to the control diet showed rapid improvement and recovery from the skin lesions. In cases where eschars were present, exfoliation and healing took place rapidly. Denuded areas began to show hair growth in 7 to 10 days, and these areas could not be detected at the close of the experimental period without close examination which would reveal numerous short hairs. Edema subsided within a week after the animals received the increased dietary magnesium, and the animals appeared in good condition by the close of the experiment.

Summary. Sexually mature rats maintained on a magnesium-deficient diet develop lesions of the skin characterized by erythema, purpural hemorrhages and eschars. The addition of magnesium to the diet results in recovery from the skin lesions. Other symptoms observed are essentially the same as in the immature animal deprived of magnesium. The increased length of time before the appearance of symptoms in older animals probably reflects increased body stores of magnesium with an increment in the time required to deplete the tissues of this element.

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Effect of Aminophyllin on the Coagulation of Human Blood.*

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Aminophyllin (theophyllin-ethylenediamine) is commonly used in the treatment of patients with heart disease, particularly when the coronary arteries are involved. Recently, emphasis has been put on the importance of intravascular coagulation of the blood on the course and prognosis following coronary occlusion. Observations have been published ascribing to aminophyllin a thromboplastic action. Because of the serious therapeutic implications of this finding, if confirmed, the present study was undertaken. Field, Larson, Spero, and Link[1] in reviewing the literature, found that a number of authors were of the opinion that the methylxanthines had an accelerating action on blood coagulation. They also reported that single oral doses of a number of methylxanthines produced hyperprothrombinemia and a decreased sensitivity to the action of 3,3′-methylenebis-4-hydroxycoumarin. In view of these findings they believed it possible that use of these drugs in man might produce a tendency toward thrombus formation. Link[2] again emphasized

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1 Field, J. B., Larsen, E. G., Spero, L., and Link, K. P., *J. Biol. Chem.*, 1944, **156**, 725.

2 Link, K. P., *Harvey Lectures*, 1943-44, **39**, 126.