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Micromelia in Adult Fowl Caused by Manganese Deficiency During Embryonic Development.

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Byerly, Titus, Ellis and Landauer[1] and Landauer[2] reported the occurrence of micromelia of nutritional origin in chicken embryos and in newly hatched chicks. Later Lyons and Insko[3] observed micromelia in the embryos and newly hatched chicks of hens fed a diet deficient in manganese which was strikingly similar to that described by Byerly and associates and by Landauer. Lyons and Insko prevented the development of the abnormally shortened leg and wing bones by injecting manganese sulfate into the eggs just before placing them in the incubator.

Caskey, Gallup and Norris[4] prevented the development of the embryonic reduction in bone length due to manganese deficiency by feeding the hens manganous carbonate. They also showed that one of the chief symptoms of perosis, which develops in normal chicks fed a manganese-deficient diet, is a reduction in the length of the leg and wing bones. Caskey and Norris[5] found that perosis fails to develop when normal chicks fed a manganese-deficient diet are injected intraperitoneally with manganous chloride. Lyons and Insko[3] and Gallup and Norris[6] reported that the eggs of hens fed a manganese-deficient diet contain markedly less manganese than those of hens fed an adequate diet.

In further studies conducted at this laboratory it was found that frequently the chicks which hatched from the eggs of hens fed a low-manganese diet (0.00063% manganese) were ataxic. A group of 15 of these chicks, most of which were also micromelic, was placed in appropriate quarters for observation. During the first 8 weeks they were fed an adequate diet composed of 44.73% ground yellow corn, 20% degerminated yellow corn meal, 15% dried skim

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1 Byerly, T. C., Titus, H. W., Ellis, N. R., and Landauer, W., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1542.

2 Landauer, W., *Anat. Rec.*, 1936, **64**, 267.

3 Lyons, Malcolm, and Insko, W. M., Jr., *Ky. Agr. Exp. Sta. Bul.* 371, 1937, 61.

4 Caskey, C. D., Gallup, W. D., and Norris, L. C., *J. Nutr.*, 1939, **17**, 407.

5 Caskey, C. D., and Norris, L. C., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 590.

6 Gallup, W. D., and Norris, L. C., *Poul. Sci.*, 1939, **18**, 83.

milk, 10% meat scrap, 5% dehydrated alfalfa meal, 2.5% casein, 1.5% steamed bone meal, 0.5% calcium carbonate, 0.5% iodized salt, 0.25% cod liver oil (400 D per g) and 0.02% manganous carbonate. This diet contained 1.8% calcium, 0.95% phosphorus and 0.01% manganese. After 8 weeks the chicks were fed a somewhat similar diet containing 0.005% manganese.

Eleven of these chicks, 8 females and 3 males, attained maturity and were continued on experiment until approximately 16 months of age. Six of the surviving females and 2 of the males were markedly micromelic at the time of hatching. It was observed that the micromelic chicks at no time showed any apparent recovery from this condition.

Measurements of the shanks, the ulna sections of the wings and of the keels of the micromelic females were made at 11 months of age and compared with similar measurements of normal females of the same breeding and of approximately the same age and weight. No difference between the average lengths of the keels of these groups of hens was found but significant differences were revealed between the average lengths of the shanks and the average lengths of the ulna sections of the wings. A preliminary report of these results together with those on the ataxic condition has been made by Caskey and Norris.[7]

At the conclusion of the experiment the 6 micromelic females and 6 normal females of like breeding and of approximately the same age and weight were killed and their bones dissected and measured. The results of these measurements are given in Table I. A picture of one of the micromelic females is given in Fig. 1.

TABLE I.
Effect of an Embryonic Manganese Deficiency upon the Subsequent Bone Development of Chickens.

Bone measured	Length		Reduction in length, %	Significance of difference‡
	Normal* hens, cm	Micromelic† hens, cm		
Sternum	13.70	13.60	0.7	—
Femur	9.14	8.15	10.8	332:1
Tibia	12.90	10.96	15.0	1110:1
Tarso-metatarsus	8.42	6.87	18.4	4999:1
Humerus	7.84	7.30	6.9	124:1
Radius	7.08	6.30	11.0	587:1
Ulna	7.92	7.17	9.5	768:1
Metacarpus	4.24	3.90	8.0	8:1

*N.H. x R.I.R., avg age 17 mo and avg wt 2034 g.
†N.H. x R.I.R., avg age 16 mo and avg wt 2032 g.
‡Odds as determined by "Student's" method (Z test).

[7] Caskey, C. D., and Norris, L. C., *J. Nutr.*, 1939, **17**, (Supplement) 16.

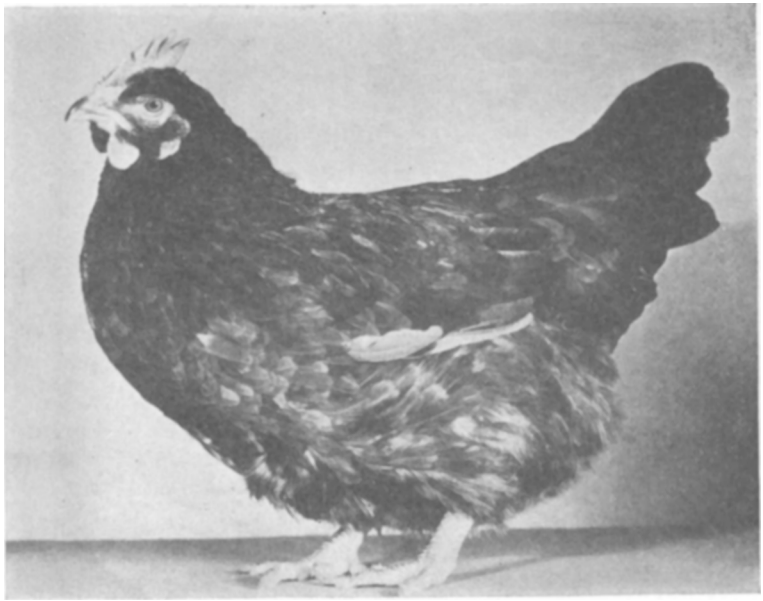

FIG. 1.
A typical micromelic hen.

The average length of the sterna of the micromelic females was only 0.7% less than that of the normal females. The difference in length was obviously of no significance. The difference between the average length of the metacarpi of the micromelic females and that of the normal females amounted to 8%, but it did not prove to be statistically significant when analyzed by "Student's" method (Z test). All the other differences in bone length proved to be highly significant statistically. The tibiae and the tarso-metatarsi showed the most marked retardation in development, the tibiae being 15% shorter than the normal bones and the tarso-metatarsi 18.4% shorter. The shortening was somewhat greater than that previously reported by Caskey, Gallup and Norris[4] in newly hatched chicks, but not as great as that reported by Landauer[2] or that reported by Lyons and Insko[3] for 21-day embryos and newly hatched chicks.

It is evident from these results that newly hatched chicks which become micromelic during embryonic development as a result of manganese deficiency do not recover from the micromelia when fed a diet containing an adequate amount of manganese during a period greatly in excess of that required for the attainment of maturity. No evidence was obtained, on the other hand, of a reduction in the

length of the sternum as a consequence of embryonic manganese deficiency. The difference in the effect of the embryonic manganese deficiency upon the bones of the legs and wings and upon the sternum may be related to the fact that the former undergo considerable calcification during the latter stages of embryonic development whereas the sternum is almost entirely uncalcified at the time of hatching.

Byerly and associates[1] reported that the anterior-posterior axis of the skulls of the micromelic chicken embryos which they examined was markedly shortened. Both this group of investigators and Landauer[2] observed that some of the affected embryos hatched but Landauer[2] stated that the head was always normal. It has been observed at this laboratory, however, that some of the newly hatched chicks rendered micromelic by manganese deficiency during embryonic development also possessed brachycephalic heads. Several of the micromelic females which were sacrificed at 16 months of age in order to study the reduction in bone length were still brachycephalic. This indicates that similar to the micromelia due to manganese deficiency the consumption of a diet adequate in manganese after hatching does not promote recovery from the brachycephalism.

Summary. Chicks which are rendered micromelic during embryonic development as a result of manganese deficiency do not recover from this condition when fed a diet adequate in manganese during a period of time greatly in excess of that required for the attainment of maturity.

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Rôle of Vitamin C in Addison's Disease.*

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The excretion of ascorbic acid in the urine of patients having Addison's disease has been studied by Siwe,[1] von Drigalski,[2] Geriola,[3] Wilkinson and Ashford.[4] Using the method of Harris and Ray,[5] all the aforementioned investigators found a state of vitamin C

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