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Precipitation of a Selenium Deficiency by High Dietary Levels of Copper and Zinc[1] (38754)

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The elements essential for animals are highly interrelated with both essential and nonessential elements and a high level of one element can induce a deficiency of another (1). Prior to the discovery of the essentiality of selenium, soluble salts of silver were shown to accentuate a Vitamin E deficiency in rats (2). Subsequent studies have shown that exudative diathesis produced in chicks by adding soluble salts of silver to either the drinking water or feed can be prevented by selenium (3, 4). Recently the toxic effects of including methylmercury in the drinking water of rats was shown to be counteracted by dietary selenium (5). Injection studies with rats have also demonstrated that selenium can counteract the toxicity of mercury or cadmium (6, 7). A selenium toxicity in chicks was partially alleviated by inclusion of mercuric chloride, cupric sulfate, or cadmium sulfate in the diet (8).

The present studies were conducted to determine if a selenium deficiency could be induced in chicks by including a high level of copper in the diet. The effect of zinc was also studied because this element is closely interrelated with copper in animals (9) and has similar chemical parameters.

Materials and Methods. Two experiments were conducted with Hubbard broiler chicks kept in electrically heated battery brooders with wire mesh floors. Two groups of 10 chicks were fed each of the experimental diets and feed and water were supplied *ad libitum*. Composition of the basal diet used in both experiments is shown in Table I. The diet analyzed (10) to contain approximately 0.2 ppm selenium. In experiment 1, levels of added copper from 0 to 1600 ppm were fed with and without 0.5 ppm selenium. In experiment 2, levels of added zinc from 0 to 4000 ppm were fed with and without 0.5 ppm selenium. The basal diet also contained 100 ppm added zinc. Copper was added as cupric sulfate, zinc as zinc sulfate and selenium as sodium selenite.

The chicks were fed the experimental diets for 4 wk. Total feed consumption and final mean body weight per pen was recorded. Mortality was noted during the experiments and all dead chicks and survivors were grossly examined for evidence of exudative diathesis or muscular dystrophy. The surviving chicks were killed at 4 wk of age and the epidermis over the abdomen and breast areas removed so that the presence of subcutaneous exudates and white striations in the breast muscle could be readily observed.

Results. When the diets were unsupplemented with selenium 800 or 1600 ppm added copper resulted in high mortality (Table II). Adding 0.5 ppm selenium prevented mortality. Both dead and surviving chicks had a high incidence of exudative diathesis and muscular dystrophy with the two highest copper levels without added selenium (Table II). The significantly depressed growth rate and feed consumption in chicks fed the two highest levels of supplemental copper was not alleviated by the added selenium.

High mortality and a high incidence of both exudative diathesis and muscular dystrophy were observed in chicks fed 2100 or 4100 ppm added zinc, when the diet contained no added selenium (Table III). Neither exudative diathesis nor muscular dystrophy was observed in chicks fed a diet supplemented with selenium. Growth rate was significantly depressed with 2100 ppm or more of added zinc. Although the growth rate was numerically higher for comparable zinc groups with added selenium, the differences were not statistically significant.

Discussion. These experiments demonstrate

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that a selenium deficiency can be induced in chicks by high levels of either copper or zinc. No selenium deficiency signs were observed in chicks fed the basal diet containing approximately 0.2 ppm selenium without high levels of copper or zinc. When the diet contained approximately 0.7 ppm total selenium no signs of a selenium deficiency were observed in any of the chicks regardless of the level of added copper or zinc.

The selenium content of diets fed to domestic animals ranges from less than 0.1 to over 1.0 ppm depending on the geographical origin of the ingredients. Whether or not a selenium deficiency will be observed in the presence of high levels of copper or zinc will depend upon dietary levels of selenium, copper and zinc in the diet. It is probable that considerably lower levels of copper or zinc than those observed in these experiments could induce a selenium deficiency if dietary selenium was below 0.1 ppm. Although added selenium completely prevented deficiency signs of selenium and markedly reduced mortality, selenium did not prevent the growth depression associated with the high levels of these elements. The toxic effects of copper and zinc, therefore, are not simply related to a selenium deficiency but involve disruption of other biochemical reactions in the body.

The mechanism by which copper or zinc interferes with selenium utilization in the chick is not revealed by these experiments. Evidence has been obtained that copper may interfere with selenium absorption as a reaction product of selenium dioxide with an equimolar amount of cupric sulfate was less toxic to chicks than an equivalent amount of unreacted selenium dioxide (8). Copper or zinc may react with selenium either in the alimentary tract or within the tissues of the animal to form compounds that reduce absorption of selenium and/or its availability for synthesis of selenium containing proteins in the body. Selenium is an integral part of

TABLE I. COMPOSITION OF DIET

Ingredient	%
Ground peas (pisum sativum)	60.4
Ground wheat	20
Torula yeast	10
Stabilized animal fat	6
Ground limestone	1.7
Dicalcium phosphate	1.0
Salt (iodized)	.3
D,L-Methionine	.3
Vitamin premix[a]	.25
Trace Mineral mix[b]	.05

[a] Vitamin premix supplied the following per kg. diet: Vitamin A, 11,000 IU; Vitamin D_3, 3300 ICU; Vitamin E, 8.8 IU; riboflavin, 6.6 mg.; niacin, 44 mg; Vitamin B_{12}, 22 mcg.; Ca pantothenate, 8.8 mg.; choline chloride, 1200 mg.; ethoxyquin, 125 mg.

[b] Trace mineral mix supplied the following per kg. diet: manganese, 75 mg.; zinc, 100 mg.; iodine, 0.5 mg.

TABLE II. EFFECT OF COPPER AND SELENIUM ON GROWTH AND INCIDENCE OF SELENIUM DEFICIENCY SIGNS IN CHICKS.

Added to diet (ppm)		Body weight[a] 4 wk (g)	Feed consumed/bird[a] 0–4 wk (g)	Mortality (%)	Incidence (%)	
Cu	Se				Exudative diathesis	Muscular dystrophy
0	0	507 AB	810 BC	0	0	0
200	0	505 AB	908 AB	0	0	0
400	0	546 A	971 A	0	0	0
800	0	384 E	597 D	50	50	30
1600	0	158 F	526 DE	60	75	88
0	0.5	451 CD	793 BC	0	0	0
200	0.5	476 BC	858 ABC	0	0	0
400	0.5	533 A	891 AB	0	0	0
800	0.5	408 DE	749 C	5	0	0
1600	0.5	186 F	451 E	0	0	0

[a] Values without a common letter are significantly different ($P < 0.05$).

TABLE III. EFFECT OF ZINC AND SELENIUM ON GROWTH AND INCIDENCE OF SELENIUM DEFICIENCY SIGNS IN CHICKS.

Added to diet[a] (ppm)		Body weight[b] 4 wk	Feed consumed/bird[b] 0–4 wk	Mortality	Incidence (%)	
Zn	Se	(g)	(g)	(%)	Exudative diathesis	Muscular dystrophy
0	0	512 A	987 A	0	0	0
1000	0	490 A	929 AB	0	0	0
2000	0	347 CB	754 CD	15	30	25
3000	0	242 D	626 E	45	55	80
4000	0	214 D	741 CDE	20	45	55
0	0.5	549 A	897 AB	0	0	0
1000	0.5	487 A	932 AB	5	0	0
2000	0.5	400 B	858 BC	0	0	0
3000	0.5	270 DC	701 DE	0	0	0
4000	0.5	262 DC	743 CDE	5	0	0

[a] Basal diet had 100 ppm zinc.

[b] Values without a common letter are significantly different ($P < 0.05$).

glutathione peroxidase which functions to prevent peroxidation of the tissues (11). The development of exudative diathesis in chicks is correlated with a reduction in glutathione peroxidase (12).

Exudative diathesis and muscular dystrophy were observed in chicks in these experiments even though 8.8 IU of Vitamin E were added per kilogram of diet and the diet contained an adequate level of sulfur amino acids (0.794%). Ordinarily muscular dystrophy is not observed in chicks receiving a diet adequate in sulfur amino acids. Cystine has a primary role in the prevention of muscular dystrophy and is more effective than methionine on an equi-sulfur basis (13). The basal diet used in these studies contained 0.202% cystine and 0.592% methionine on a calculated basis. Considerable conversion of methionine to cystine was necessary, therefore, to provide the needs of the chicks for growth and prevention of muscular dystrophy. Perhaps high levels of copper or zinc interfere with this conversion mechanism thereby resulting in a deficiency of cystine for prevention of muscular dystrophy. Previous studies have shown that selenium is ineffective in preventing muscular dystrophy in diets totally deficient in Vitamin E but will prevent it if combined with a small amount of Vitamin E (14). The latter dietary condition prevailed in these studies and supplemental selenium completely prevented muscular dystrophy.

Summary. High mortality and a high incidence of exudative diathesis and muscular dystrophy were observed in chicks fed a diet supplemented with either 800 or 1600 ppm copper. Adding 0.5 ppm selenium to a basal diet containing 0.2 ppm prevented mortality and selenium deficiency signs. Dietary zinc levels of 2100 to 4100 ppm also resulted in high mortality, exudative diathesis, and muscular dystrophy. A selenium supplement of 0.5 ppm completely prevented the deficiency signs and markedly reduced mortality. The results demonstrate that both copper and zinc can induce a selenium deficiency in chicks when a diet relatively low in this element is fed.

1. Underwood, E. J., *in* "Trace Elements in human and animal nutrition" 543 pp., Academic Press, New York (1971).
2. Shaver, S. L., and Mason, K. E., Anat. Rec. **109**, 382 (1951).
3. Bunyan, J., Diplock, A. T., Cawthorne, M. A., and Green J., Brit. J. Nutr. **22**, 165 (1968).
4. Peterson, R. P., and Jensen, L. S., Poultry Sci. 54 (in press) (1975).
5. Ganther, H. E., Gaudie, C., Sunde, M. L., Kopecky, M. J., Wagner P., Oh, S. H., and Hoekstra, W. G., Science **175**, 1122 (1972).
6. Parizek, J., and Ostadalova, I., Experientia **23**, 142 (1967).

7. Kar, A. B., Das, R. P., and Mukerji, B., Proc. Nat. Inst. Sci. India **26B** (Suppl.) 40 (1960).
8. Hill, C. H., J. Nutr. **104,** 593 (1974).
9. Magee, A. C., and Matrone, G., J. Nutr. **72,** 233 (1960).
10. Hoffmann, I., Westerby, R. J., and Hideroglou, M. J., Ass. Offic. Chem. **51,** 1939C (1968).
11. Rotruck, J. T., Pope, A. L., Ganther, H. E., Swanson, A. B., Haferman, O. G., and Hoekstra, W. C., Science **179,** 588 (1973).
12. Noguchi, T., Cantor, A. H., and Scott, M. L., J. Nutr. **103,** 1502 (1973).
13. Scott, M. L., and Calvert, C. C., J. Nutr. **77,** 105 (1962).
14. Calvert, C. C., Nesheim, M. C., and Scott, M. L., Proc. Soc. Exp. Biol. Med. **109,** 16 (1962).

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