

cates that vitamin A is temporarily stored in the lamina propria of the villi. This lag in release after excessive absorption requires further explanation.

The increased absorption of vitamin A in aqueous dispersion is of practical significance because of sparing of vitamin A, the correction of absorption difficulties^{4,5} and the increased speed of absorption. The latter was claimed to be of importance in the treatment of infants with tendency to vomiting.¹

Summary. Observation of the vitamin A fluorescence in the intestine of rats showed

that greater amounts of vitamin A—approximately three times as much—were absorbed if the latter was administered in an aqueous instead of an oily menstruum. In addition vitamin A in water penetrated the intestinal wall faster, the peak of absorption occurred at a higher level of the intestine and vitamin A remained longer in the villi. These differences were explained by passage of increased amounts of vitamin A through the epithelium if given in aqueous dispersion and not by a different physical state of vitamin A after passage.

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Amino Acid Imbalance of Zein: Relation to Nicotinic Acid Deficiency in the Chick.*

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Krehl *et al.*¹ were the first to show that a nicotinic acid deficiency could be induced in the rat by feeding corn as a part of a low-protein diet. Subsequently² it was observed that *l*-tryptophane as well as nicotinic

acid was effective in counteracting the growth depression in rats caused by the feeding of corn. The activity of tryptophane in this connection indicates that it is an important precursor of nicotinic acid.^{3,4,5} Tryptophane-low proteins such as gelatin, zein and acid-hydrolyzed casein have been shown to behave similarly to corn.^{6,7} That the action of these proteins may be due to amino acid imbalances has been suggested in work with the rat^{8,9} and the chick.^{10,11} The subject

* Scientific Paper No. A201. Contribution No. 2117 of the Maryland Agricultural Experiment Station (Department of Poultry Husbandry).

A preliminary report of part of this work was published in *Fed. Proc.*, 1947, **6**, 257.

We are indebted to Merck & Co., Inc., Rahway, N. J., for crystalline vitamins; Wilson & Co., Inc., Chicago, Ill., for 2X gelatin; Allied Mills, Inc., Portsmouth, Va., for soybean oil; Abbott Laboratories, North Chicago, Ill., for Haliver oil; U. S. Industrial Chemicals, Inc., Baltimore, Md., for DL-methionine; and to Lederle Laboratories, Pearl River, New York, for pteroylglutamic acid.

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¹ Krehl, W. A., Teply, L. J., and Elvehjem, C. A., *Science*, 1945, **101**, 283.

² Krehl, W. A., Teply, L. J., Sarma, P. S., and Elvehjem, C. A., *Science*, 1945, **101**, 489.

³ Rosen, F., Huff, J. W., and Perlzweig, W. A., *J. Biol. Chem.*, 1946, **163**, 343.

⁴ Singal, S. A., Briggs, A. P., Sydenstricker, V. P., and Littlejohn, J. M., *J. Biol. Chem.*, 1946, **166**, 573.

⁵ Sarett, H. P., and Goldsmith, G. A., *J. Biol. Chem.*, 1947, **167**, 293.

⁶ Krehl, W. A., Sarma, P. S., and Elvehjem, C. A., *J. Biol. Chem.*, 1946, **162**, 403.

⁷ Briggs, G. M., *J. Biol. Chem.*, 1945, **161**, 749.

⁸ Krehl, W. A., Henderson, L. M., de la Hueraga, J., and Elvehjem, C. A., *J. Biol. Chem.*, 1946, **166**, 531, and Henderson, L. M., Deodhar, T., Krehl, W. A., and Elvehjem, C. A., *J. Biol. Chem.*, 1947, **170**, 261.

of imbalances in nutrition in general has recently been reviewed.¹²

Reports from this laboratory^{7,10} have pointed out the growth inhibiting activities of corn, gelatin, and zein when fed to chicks receiving diets low in nicotinic acid. By employing an amino acid mixture simulating gelatin, it was found¹¹ that the growth depression caused by this protein was due largely to the combined action of glycine, arginine, and alanine emphasizing the role played by amino acid imbalance. The feeding of nicotinic acid completely reversed the actions of gelatin^{7,10,11} and the amino acids.¹¹

The present report concerning the corn protein, zein, is a study similar to that carried out with gelatin. Since zein contains no glycine and very little arginine, these amino acids obviously were not primarily concerned with the growth depression obtained by the feeding of this protein. Other factors were apparently involved. Moreover, it seemed desirable to investigate the role of amino-acid imbalance of zein to determine the extent to which growth depression could be explained on this basis or if a part could be attributed to contamination of the protein with a "pellagrigenic" agent reported¹³ to exist in corn.

Experimental. Day-old New Hampshire chicks of mixed sexes were used. The chicks were distributed according to weight, confined in electrically heated wooden cages with wire floors and given feed and water *ad libitum*. Weighings and other observations were made weekly. All substitutions in the basal diet 113GN were made at the expense of cerelose (Table I).

Results. Table II summarizes the re-

TABLE I.
Composition of Basal Diet 113GN.

	%
Cerelose	71.4
Casein (crude)	18.0
Mineral mixture 1M	6.0
Soybean oil	4.0
<i>dl</i> -Methionine	0.3
Choline chloride	0.2
<i>i</i> -Inositol	0.1
Vitamins (mg/100 g)	
Thiamine HCl	0.4
Riboflavin	0.8
Ca pantothenate	2.0
Pyridoxine HCl	0.6
Biotin	0.02
Para-aminobenzoic acid	0.2
2-Methyl-1,4-naphthoquinone	0.1
Alpha-tocopherol	0.5
Pteroylglutamic acid	0.2
Vitamins A and D ₃ , 1200 U.S.P. and 170 A. O. A. C. units, respectively, by dropper weekly	

sults obtained by feeding the corn protein, zein (commercial preparation) and an amino-acid mixture simulating zein to chicks. The addition of 15% of zein to the diet decreased growth slightly and increased the incidence of blacktongue (compare groups 1 and 5). Growth was depressed somewhat more with 5% additional gelatin (compare Groups 1 and 2). However, the feeding of the amino-acid mixture produced much more severe results than did zein (compare Groups 5 and 6). Less severe results were obtained with the modified amino-acid mixture (compare Groups 6 and 7), but the severity of its action was still greater than zein (compare Groups 5 and 7). Thus it appears that the growth depression caused by the feeding of zein can be explained entirely on the basis of its amino-acid constituents, which likewise is true for gelatin. The growth-depression effect of zein could be largely duplicated by a mixture of 5 amino acids—glutamic acid, leucine, alanine, proline, and phenylalanine. These are the predominant amino acids of this protein. The residual amino acids were additive in producing a further growth-depressing action. It is evident that the unnatural (D) forms of the amino acids, which were used in several instances, were not greatly responsible in themselves for the effects observed (unpublished data). The

⁹ Singal, S. A., Sydenstricker, V. P., and Littlejohn, J. M., *J. Biol. Chem.*, 1947, **171**, 203.

¹⁰ Briggs, G. M., Groschke, A. C., and Lillie, R. J., *J. Nutrition*, 1946, **32**, 659.

¹¹ Groschke, A. C., and Briggs, G. M., *J. Biol. Chem.*, 1946, **165**, 739.

¹² Elvehjem, C. A., and Krehl, W. A., *J. Am. Med. Assn.*, 1947, **135**, 279.

¹³ Woolley, D. W., *J. Biol. Chem.*, 1946, **163**, 773.

TABLE II.

Group No.	Supplement to basal diet 113GN	No. chicks	No. died	Avg wt 4 weeks, g	No. black-tongue
1	5% gelatin	6	0	175	2
2	10% "	6	2	133	5
3	As 1 + 10 mg % nicotinic acid	6	0	235	0
4	As 2 + 10 " % " "	6	0	244	0
5	As 1 + 15% zein	6	1	155	5
6	As 1 + 15% amino-acid mixture*	6	5	61	6
7	As 1 + 11.5% modified amino-acid mixture†	6	1	110	5
8	As 5 + 10 mg % nicotinic acid	6	0	221	0
9	As 6 + 10 " % " "	6	0	226	0

* *l*-Glutamic acid 3.90, *l*-leucine 3.60, *dl*-alanine 1.55, *l*-proline 1.45, *dl*-phenylalanine 1.00, *l*-tyrosine 0.85, *d*-isoleucine 0.65, *dl*-aspartic acid 0.50, *dl*-methionine 0.35, *dl*-threonine 0.35, *dl*-valine 0.35, *dl*-serine 0.15, *l*-histidine 0.15, *l*-arginine 0.15.

† This mixture contained glutamic acid, leucine, alanine, proline, and phenylalanine at the same levels as used in the above amino-acid mixture.

reason that zein was less depressing on growth than the amino-acid mixture was probably due to the presence of small amounts of naturally occurring tryptophane¹⁴ and/or nicotinic acid in zein. The most significant point to observe, however, is the counteraction of the effects of zein and of the amino-acid mixture with low levels of nicotinic acid (compare Groups 5, 6, 8, and 9). Furthermore, these data demonstrate that nicotinic acid is involved in some manner in the metabolism of amino acids.

Since more than maximal growth depression was obtained with the amino-acid mixture simulating the protein zein, it is logical to assume that the commercially prepared zein

was not contaminated with a "pellagragenic" agent. Furthermore, it is safe to state that a large part of the inhibitory action of corn in chick pellagra may be attributed to its predominant protein, zein, and that the presence of a special "pellagragenic" agent reported to exist in corn plays a relatively minor part, if any.

Summary. By use of an amino-acid mixture simulating zein, it was found that chick-pellagra symptoms in chicks caused by the feeding of zein were due to the cumulative action of the amino-acid constituents of this protein. Glutamic acid, leucine, alanine, proline, and phenylalanine, the amino acids occurring in greatest amounts, seem to be principally involved in this connection.

¹⁴ Block, R. J., and Mitchell, H. H., *Nutr. Abst. and Rev.*, 1946-47, **16**, 249.

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Inhibition of Testicular Hyaluronidase Activity by Rutin.*

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The term vitamin P was introduced by Armentano, Szent-Gyorgyi, and co-workers¹

to designate an essential substance other than ascorbic acid, regulating capillary permeability and fragility. In the guinea pig²

* Aided by a grant from the Cooper Fund of the Faculty of Medicine, McGill University.

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¹ Armentano, L., Bentsah, A., Beres, T., Rusnyak, S., and Szent-Gyorgyi, A., *Deut. Med. Wochsch.*, 1936, **62**, 1325.