

white matter, thus confirming previous observations. In all the sections the nerve cells of the denervated seventh nerve nucleus had incorporated significantly more methionine-³⁵S than the cells in the normal control nerve nucleus. The planimeter measurements showed that the area of the nerve cells of the denervated nerve nucleus was in most cases greater than the area of the nerve cells of the control nucleus. The nerve cells of the denervated nucleus incorporated per unit area more methionine-³⁵S than the corresponding area of the cells of the control nucleus.

The results therefore show that nerve cells undergoing retrograde degeneration have an increased uptake of methionine, indicating that an increased synthesis of protein molecules is taking place.

J. FISCHER

Laboratory of Neuropathology, II,
Institute of Pathological Anatomy
of the Medical Faculty,
Prague II, U nemocnice 4.

Z. LODIN
J. KOLOUŠEK

Czechoslovak Academy of Sciences,
Institute of Physiology,
Prague 6, Na cvičišti 2,
Czechoslovakia.

¹ Nissl, F., *Allg. Z. f. Physiol.*, **48**, 197 (1892).

² Hydén, H., "Neurochemistry", 204 (Ch. C. Thomas, Springfield, Illinois, 1955).

³ Fischer, J., Koloušek, J., and Lodin, Z., *Nature*, **178**, 1122 (1956).

⁴ Cohn, P., Gaitonde, M. K., and Richter, D., *J. Physiol.*, **126**, 7P (1954).

⁵ Koloušek, J., Fischer, J., and Lodin, Z., *Cs. Morfologie*, **4**, 302 (1956); *Acta Histochemica*, **3**, 328 (1956).

⁶ Bélanger, L. F., *Anat. Rec.*, **107**, 149 (1950).

Perosis and Folic Acid Antagonism in Chickens

THE folic acid antagonist pyrimethamine has been shown to act as a synergist with sulphadimidine against *Eimeria tenella* in chickens¹. During our investigation of this combination, a decreased growth-rate was noted in chickens fed for five days on an all-mash diet containing 100 p.p.m. of pyrimethamine.

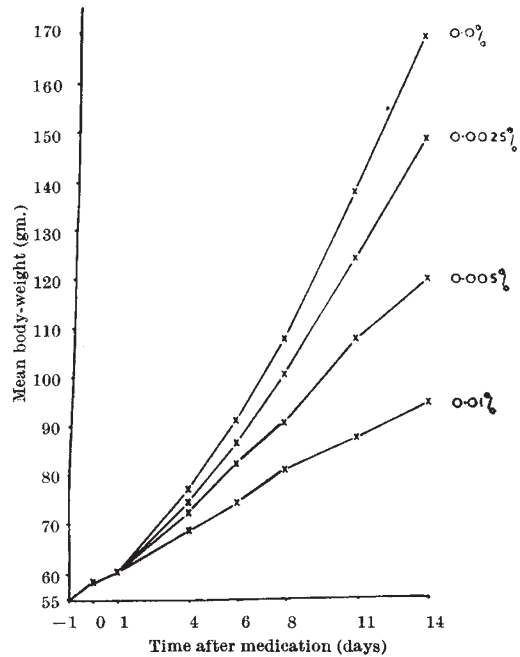
The toxicity of pyrimethamine was therefore examined with four groups of forty chickens which were fed mash containing pyrimethamine 0, 25, 50 or 100 p.p.m. from 7 days of age. The growth-curves are shown in Fig. 1. During the first fourteen days feeding, one chicken fed 25 p.p.m. and two fed 100 p.p.m. died of pyrimethamine poisoning. After fourteen days feeding two chickens were selected at random from each group for haematological study. The remainder of each group was randomized by

Table 1. MEAN WEIGHT GAINS, NUMBER OF DEATHS AND INCIDENCE OF PEROSIS IN CHICKENS FED PYRIMETHAMINE 0, 25, 50 OR 100 P.P.M. FOR 14 OR 32 DAYS

Pyrimethamine in diet (p.p.m.)		Mean gain in weight (gm.) after		Cases of	
0-14 days	15-32 days	14 days	32 days	Perosis	Death
0	0	113	393	0/19*	0
	0		370	0/19	
25	0	93	361	2/18	1
	25		331	11/18	
50	0	64	307	2/19	0
	50		212	19/19	
100	0	40	280	6/18	8
	100		101	13/15†	

* Number of cases of perosis/number in group.

† Three of these died late in the experiment and were examined for perosis.



weight into two even sub-groups, one chicken in the group fed 25 p.p.m. being discarded. One sub-group continued on the medicated feed and the other sub-group was fed basal ration. The chickens fed basal ration quickly resumed normal growth. In this period six chickens fed 100 p.p.m. died of pyrimethamine poisoning.

Perosis was seen in the medicated groups after twenty-five days feeding. At thirty-two days all chickens were examined for perosis, and Table 1 shows the incidence in the various groups. Some chickens fed 25 p.p.m. pyrimethamine for only fourteen days showed perosis. The diet contained $\frac{1}{4}$ oz. anhydrous manganese sulphate per 100 lb. mash and was calculated to contain 80 p.p.m. of manganese.

Daniel, Farmer and Norris² showed that perosis occurred in chickens fed a diet low in folic acid and was prevented by adding synthetic folic acid to the diet. The addition of succinyl sulphathiazole accentuated the severity of the perosis on a diet low in folic acid. This seems to support the theory that chickens synthesize folic acid from *p*-aminobenzoic acid, which is made by the degradation of folic acid in the diet³.

In our work, it seems certain that the perosis was due to a deficiency of folic acid caused by pyrimethamine, a potent folic acid antagonist.

A detailed account of these experiments will be published elsewhere.

I am grateful to Burroughs Wellcome and Co. (Australia), Ltd., who generously provided a quantity of pyrimethamine.

J. H. ARUNDEL

Nicholas Institute for Medical and
Veterinary Research,
Burnham Beeches,
Sherbrooke, Victoria, Australia.
Oct. 18.

¹ Joyner, L. P., and Kendall, S. B., *Nature*, **176**, 975 (1955).

² Daniel, L. J., Farmer, F. A., and Norris, L. C., *J. Biol. Chem.*, **163**, 349 (1946).

³ Rollo, I. M., *Brit. J. Pharmacol.*, **10**, 208 (1955).