

III. CURATIVE ACTION OF NICOTINIC ACID ON PIGS SUFFERING FROM THE EFFECTS OF A DIET CONSISTING LARGELY OF MAIZE

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IN the September number of the *Journal of the American Chemical Society* the announcement was made by Elvehjem *et al.* [1937], that nicotinic acid cured dogs of "black tongue" induced by feeding upon a Goldberger "pellagra producing" diet of which maize was the chief ingredient [Goldberger *et al.* 1930]. The composition of the diet was the same as that of the diet used by Koehn & Elvehjem [1937]. Their experiments indicate that nicotinic acid or its amide or some combination of the latter, is the active constituent of Goldberger's "pellagra-preventive". The idea that another component of the vitamin B₂ complex in addition to lactoflavin is intimately concerned with one of the types of cellular respiration is an alluring one.

Continuing the work of Birch, Chick & Martin [1937] of the previous year, we had been attempting to discover the active principle in an autoclaved yeast extract which rendered a Goldberger maize diet satisfactory for the rearing of young pigs and had found that this principle possessed chemical and physical properties similar to those originally described by Goldberger as appertaining to his "pellagra-preventive", notably the property of being adsorbed on fuller's earth [Goldberger *et al.* 1928].

We had at hand two animals (Nos. 18 and 26) which had become very ill as a result of feeding upon the unsupplemented diet, which consisted of whole ground white maize 77.5, peameal 10.5, purified casein 6.5, cod liver oil 3 and salt mixture 2.5 parts. Various fractions prepared from yeast extract had been given without effecting any material improvement and, by the time we tried nicotinic acid, their weights were the same as they had been 11 and 7 weeks previously and were falling rapidly (see Fig. 1). Both pigs had severe diarrhoea and refused food. Their skins were a dirty yellow colour instead of the rosy pink of healthy young pigs and were covered with scabs of heaped epithelial cells matted together by inspissated serum. In No. 18 the dermatitis was more severe; she had lost most of her hair and what remained could be easily detached. In addition she had paresis and spasticity of the muscles of the hind quarters indicating lesions in the spinal cord. From previous experience of animals in the condition of Nos. 18 and 26 we anticipated that they would die within 2 or 3 days.

As both animals had ceased to eat, a solution of nicotinic acid which had been brought to pH 7.4 with NaOH was injected intramuscularly. No. 18 had two, and No. 26 three, injections containing 100 mg. of nicotinic acid, at intervals of 3 days. Subsequently 60 mg. was given to each daily with the food.

The effect was striking. The appetite returned within 24 hr. of the first injection, the diarrhoea abated and they began to increase in weight (see Fig. 1). The scabs on the skin began to be detached after 1 week, leaving clean, healthy skin. At the same time the colour of the animals improved gradually and after

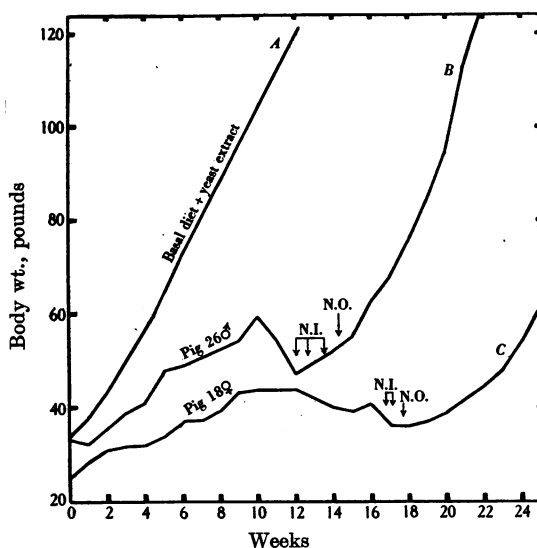


Fig. 1. Curve A. Average weight curve of pigs on the basal maize diet + yeast extract corresponding to 25 g. dry yeast, daily. Curves B and C. Weight curves of pigs 26 and 18, respectively, on the unsupplemented basal diet; at N.I., 100 mg. nicotinic acid injected; from N.O. 60 mg. nicotinic acid given daily by mouth.

6 weeks of treatment was that of healthy pigs. What remained of the hair of No. 18 was gradually shed and a fresh growth of hair was observed 3 weeks after the commencement of the treatment. After 6 weeks No. 18 still showed some awkwardness of movement, but the spasticity had disappeared and she was active and agile.

The amount of nicotinic acid injected was not too much for the desperate condition of our depleted animals but the doses subsequently administered in the food may have been more than was required.

We are at present occupied with experiments to ascertain the amount which it is necessary to add to the basal diet to rear healthy pigs. The results of these experiments will not be forthcoming for some months, so it seemed desirable to record our confirmation of the experiments of Elvehjem and his colleagues on dogs, by these observations on pigs, especially as one of us [see Macrae & Edgar, 1937] had found, in experiments with rats, that neither nicotinic acid, nicotinic amide nor co-dehydrase II could replace either the filtrate from an autoclaved extract of yeast after treatment with fuller's earth, or the eluate from the earth.

Whether nicotinic acid is a necessary constituent of the rat's diet was not ascertained by the experiments of Macrae & Edgar but, as rats thrive on the maize diet we employed, whereas pigs die, a quantitative difference in the nicotinic acid required by the respective animals is at least indicated.

DESCRIPTION OF PLATE I

The upper photograph shows the appearance of pig no. 18 when six months old after 17 weeks on the maize+casein diet. Her weight was then only 36 lb.

The lower photograph shows the same pig three months later, weight 129 lb. The diet had been the same in the interval except that 60 mg. of nicotinic acid had been added to her daily ration.

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NOTE

Since this paper was written, Fonto, Helmer, Lepkovsky and Jukes have reported (*Proc. Soc. exp. Biol. & Med.* Nov. 1937, **37**, 405) the treatment of four pellagrins with 0.5 and 1.0 g. nicotinic acid daily. The patients were in hospital and their diet was one on which pellagrins do not improve. All were cured. The response to the administration of nicotinic acid was striking and immediate and resembled in some details what we observed in pigs.

