oral administration of 10 to 15 gm. of NH_4Cl. Simultaneously with the introduction of the NH_4Cl, large quantities of carbohydrate food were given. Glucose tolerance tests were made on the 2 following days using 16 gm. of glucose as was the practice in the earlier experiments with which these results are compared. The CO_2 combining power of the blood plasma was reduced from the normal value of 55 to 50 volumes percent to as low as 15 volumes percent in one case. Six tests were made on 3 dogs and these all showed a very small rise in the blood sugar with a rapid return to the pre-glucose level. These results are identical with those obtained on the same animals in the well fed condition whether normal or phlorhizinized. It is concluded that acidosis is not a primary cause of decreased glucose tolerance.

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Does Copper Poisoning Produce Pigmentation and Cirrhosis of the Liver?

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Mallory, Parker and Nye[1] demonstrated pigmentation and cirrhosis of the liver in rabbits following administration of copper salts in their feed. Hall and Butt[2] repeated and extended the work of Mallory. They obtained a similar pigmentation and cirrhosis of the liver in rabbits by feeding copper acetate. In addition they made chemical analyses of the livers and demonstrated the presence of large quantities of copper. Flinn and VonGlahn[3] repeated many of Mallory's experiments and added others of their own. They concluded that copper salts and powdered metallic copper administered in the feed do not cause deposits of pigment in the livers of rabbits, rats and guinea pigs; nor do these substances produce cirrhosis. They maintained that animals fed on an exclusive diet of carrots developed a pigmentation comparable to that produced by Mallory and others. Polson,[4] in Great Britain, obtained results substantiating those of Flinn and VonGlahn.

[1] Mallory, F. B., Parker, Frederic, Jr., and Nye, R. N., *J. Med. Res.*, 1921, **42**, 461.

[2] Hall, E. M., and Butt, E. M., *Arch. Path.*, 1928, **6**, 1.

[3] Flinn, F. B., and VonGlahn, W. C., *J. Exp. Med.*, 1929, **49**, 5.

[4] Polson, C. J., *Brit. J. Exp. Path.*, 1929, **10**, 241.

In view of these conflicting results it has seemed necessary to examine this problem again by a series of well controlled and carefully conducted experiments.

Methods. Healthy rabbits were selected. For each rabbit to be fed on copper, a litter mate of the same sex was selected as a control. Each series when 85 days old was placed on a special diet consisting of a mixture of ground alfalfa and ground barley. When 90 days of age, one series was placed on a diet in which 2 mg. of copper were added to each gram of the special diet. These diets and tap water were allowed *ad libitum.* Many of the copper fed rabbits died after several weeks due to copper poisoning, while none of the control rabbits died before being sacrificed.

Results. Seventeen out of 21 copper-fed rabbits showed pigmentation of the liver. The pigmentation consisted mainly of hemofuscin granules which were found closely packed in large Kupffer multinuclear giant cells. These large cells were found most abundantly about the portal spaces but many were distributed through the lobules as well. A few of the livers contained hemosiderin in small amounts. Ten out of 21 rabbits showed cirrhosis of the liver. When we consider that 5 of the 21 rabbits were fed copper for less than 30 days, it is evident that the percentage of pigmentation and cirrhosis is relatively high in those animals fed for 30 days and more. In the control rabbits practically no copper was found in their livers, while in the copper-fed animals there was found from 9.68 mg. to 237 mg. of copper per 100 gm. of wet liver tissue. The copper-fed animals showing no pigmentation or cirrhosis were animals showing less than 100 mg. of copper per 100 gm. of liver substance. All but one animal that received copper for more than 40 days showed pigmentation, which in most cases was very marked. All of the animals receiving copper for more than 60 days showed cirrhosis of the liver. The animals were fed on their special diets for periods ranging from 21 to 105 days.

The question "does copper poisoning produce pigmentation and cirrhosis of the liver" must, it appears, be answered in the affirmative at least for the experimental animals employed.