THE EFFECT OF SCURVY-PRODUCING DIETS AND TYRAMINE ON THE BLOOD OF GUINEA PIGS.

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In 1914, Iwao published observations on three guinea pigs, from which he concluded that the subcutaneous administration of tyramine leads to a profound anemia and a blood picture resembling that observed in pernicious anemia. These experiments were repeated on a much larger scale in 1920 by Koessler and Harris with entirely negative results. An anemia was not obtained in any of the animals.

A careful consideration of the article by Iwao indicates that his animals may have been nourished on a deficient diet. Their diet consisted of okara, which is the residue left after finely ground soy beans have been extracted with cold water to remove the legumin and other soluble proteins. The precipitated legumin (tofu) is used as an article of diet in Japan. The okara is used for feeding animals.

Since whole soy beans are certainly deficient in vitamins C and A, it is inconceivable that okara can, by itself, serve as a maintenance diet for guinea pigs. We thought, therefore, that the results obtained by Iwao might be the composite effect of the toxic action of tyramine and a diet deficient in vitamins; or the anemia and the blood picture might, of course, have been the

1 Iwao, T., Biochem. Z., 1914, lix, 436.
direct result of a deficient diet. These possibilities have been subjected to experimental investigation.

EXPERIMENTAL.

Group 1.—Five guinea pigs with an initial weight of 350 to 420 gm. were fed exclusively on okara, which is the diet that Iwao claims to have fed to his animals. The animals died after 27, 29, 28, 24, and 29 days respectively. They all showed a typical scurvy picture and none of them developed an anemia. Abnormal erythrocytes developed after the okara had been fed for 20 days. These increased in number rapidly so that, just before death, 15 per cent of the cells were polychromatophilic, 20 to 25 per cent were reticulated, and 0.2 per cent were nucleated. Poikilocytosis and anisoerycotosis were marked.

It is obvious from these results that okara could not have been the only foodstuff employed by Iwao as a maintenance diet. Of particular note is the abnormal red blood picture which resembles that described by Iwao, excepting for the absence of an anemia. This blood picture was attributed, by Iwao, to the tyramine.

Group W.—Four guinea pigs with an initial weight of 365 to 430 gm. were placed on a diet that consisted of 96 per cent autoclaved whole soy beans, 1 per cent ferric citrate, 1 per cent NaCl, and 2 per cent Ca lactate. The animals lived 28, 26, 33, and 32 days respectively. They all showed a typical scurvy picture and one of them developed an anemia.

The blood findings in this group of animals were almost identical with those just described for okara. In addition to the production of abnormal erythrocytes, one of these animals developed an anemia. This animal lived 28 days. The erythrocyte count remained normal (5.9 million) for 11 days, then declined rapidly reaching a low value of 2.9 million just before death. The hemoglobin content was reduced from 15.2 to 8.5 gm. The blood picture showed abnormalities that were qualitatively and quantitatively identical with those described under Group 1.

A soy bean diet regularly produces an abnormal red blood picture just before the animals die with scurvy symptoms. Occas-

4 Blood was drawn twice a week from all of our experimental animals. The examination included a complete differential white and red blood cell count and a hemoglobin determination.
ionally, it seems, an anemia is also produced. The anemia appears to be the exception rather than the rule.

**Group 3.**—Six guinea pigs with an initial weight of 356 to 487 gm. were placed on a diet consisting of 83 per cent autoclaved soy beans, 1 per cent ferric citrate, 1 per cent NaCl, 2 per cent Ca lactate, 3 per cent lemon juice, and 10 per cent coconut oil. This diet should contain all of the vitamins, excepting vitamin A, in abundance. The animals divided themselves rather sharply into two groups. Four of them died of pneumonia in from 49 to 60 days; the other two lived on for 75 days, the time of concluding the experiment. The first four gained in weight for some time and then lost rapidly, became infected, and died. The other two animals gained in weight rather unsteadily during the entire 75 day period. None of these animals became anemic and none of them showed an abnormal red blood picture.

**Group 3 A.**—This group of four animals completes Group 3. The diet was identical with that just described. In addition these animals received daily subcutaneous injections of tyramine hydrochloride exactly as described by Iwao, the dose being 2 mg. of tyramine per 100 gm. of body weight. None of the animals became anemic. The red blood picture remained normal. One of the animals died of bronchopneumonia; the other three lived on until the experiment was discontinued.

**Group 4.**—This group of five animals received a diet identical with that described under Group 3 excepting that 3 cc. of orange juice replaced the 3 cc. of lemon juice. This diet should contain an ample amount of all of the vitamins. Three of these guinea pigs gained in weight slowly and steadily over a period of 75 days. Two of them died with a mastoid infection after 30 days. The red blood picture was entirely normal in all of these animals. Tyramine injections were not carried out on this group.

**Group 5.**—These seven animals were fed oats and carrots. They gained in weight rapidly and showed an entirely normal blood picture throughout.

**Group 5 A.**—This group of seven animals was fed oats and carrots. Subcutaneous injections of tyramine—2 mg. of tyramine per 100 gm. of body weight—were given daily. The red blood picture remained normal in all of these animals. The animals continued to gain in weight steadily.
Group 6.—One animal was subjected to a series of diet changes with soy beans and minerals as constant dietary constituents. A marked scurvy was produced at one time which was cured by administration of lemon juice. The scurvy period was associated with blood changes identical with those already described. There was no anemia. The abnormalities disappeared soon after the lemon juice feeding was inaugurated. This animal lived for 4.5 months. The first evidences of vitamin A deficiency were noticeable after 3 months. A rapid decline in weight occurred during the last 15 days. Tyramine was injected daily during the last 30 days.

This animal was not anemic at any time. There were no abnormalities in the red blood picture excepting for the brief period during which marked scurvy symptoms were evident.

CONCLUSIONS.

All of the results obtained are unidirectional. Tyramine injected subcutaneously into guinea pigs does not produce nor lead to anemia either in well fed guinea pigs or in animals that are fed deficient diets. There is no evidence, in these experiments, that, in guinea pigs, a diet deficient in vitamin A is conducive to anemia nor to the production of abnormal erythrocytes. A diet consisting exclusively of autoclaved soy beans and minerals rapidly leads to scurvy symptoms and death. In such animals an abnormal red blood picture is invariably obtained. There is present a marked polychromatophilia, anisocytosis, and poikilocytosis. The smear may contain a high percentage of nucleated red cells. Reticulocytes may be present in quantities up to 25 per cent. The abnormal red blood picture may, occasionally, be associated with an anemia.
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