on diet 153. Although they too showed improvement, the data are not included in the table since there were too few to warrant the expenditure of table space.

*Discussion.* Two facts stand out in the data presented. First of all it is clear (and was to be expected) that improvements in the method of handling the mouse colony resulted in improved lactation performance, as shown by the contrast in weights of the young in Groups I and II. It is also clear that improvement in the diet fed during the lactation period resulted in improved weaning weights of the young. Of course, one cannot overlook the possibility that maintenance of mice under the carefully controlled conditions of our colony would result in some improvement of lactational performance, even without alteration in the dietary regime. Our own experience with purified diets[6] has convinced us of the inadequacy of such diets when compared with an excellent stock ration. Whether this is due to an imbalance of the components or to the absence of unidentified factors remains to be determined.

*Summary and Conclusions.* 1. Lactation performance, as judged by weight changes of the mothers and weaning weights of the offspring, has been studied with four highly inbred strains of mice. The data reported were secured from 351 litters and a total of 1,762 offspring successfully weaned. 2. Definite improvement in the weaning weights of the young was secured. Three factors probably played a role: a) improvement in the method of handling the breeding colony, b) maintenance of the breeding colony under excellent nutritional conditions through several generations, and c) improvement in the diet fed during the lactation period.

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## Resistance of Guinea Pigs to Action of Alloxan.*

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Since the demonstration by Dunn and his collaborators[1] that alloxan produces necrosis of the beta cells of the islets of Langerhans with the development of persistent diabetes in rabbits, a number of investigators have reported similar effects following its administration to a variety of animals.[2,3,4,5]

The dosage of alloxan required for production of the diabetic state varies widely with animal species. Goldner[6] gives the following species gradation according to decreasing sensitivity to alloxan: dogs, monkeys, pigeons and cats, rabbits, rats. Shultz and Duke[7] found rabbits before the 9th day of life to be resistant to doses of alloxan which produced diabetes in older animals. Goldner[6] observed that guinea pigs are resistant to alloxan, and showed pancreatic lesions only if death ensued within 24 hours after the injection. He gave no data on blood sugar levels or urinary sugar excretion. Saviano and De Franciscis[8] gave alloxan in doses of 50-450 mg/kg to guinea pigs with the production, generally, of an intense hypoglycemia which persisted and

* Aided by a grant from the Diabetic Research Foundation of Portland, Oregon.

1 Dunn, J. S., Sheehan, H. L., and McLetchie, N. G. B., *Lancet*, 1943, **1**, 484.

2 Gomori, G., and Goldner, M. G., PROC. SOC. EXP. BIOL. AND MED., 1943, **54**, 287.

3 Banerjee, S., *Lancet*, 1944, **2**, 658.

4 Carrasco-Formiguera, R., *J. Lab. and Clin. Med.*, 1944, **29**, 510.

5 Ruben, J. A., and Yardumian, K. W., *Science*, 1946, **103**, 220.

6 Goldner, M. G., *Bull. N. Y. Acad. Med.*, 1945, **21**, 44.

7 Shultz, C. S., and Duke, J. R., *Bull. Johns Hopkins Hosp.*, 1948, **82**, 20.

8 Saviano, M., and De Franciscis, P., *Boll. soc. ital. biol. sper.*, 1947, **23**, 307.

TABLE I.
Effect of Alloxan on Urine Sugar in the Guinea Pig.

| Animal No. | Wt, g | Alloxan, mg/kg | Route of administration | Glycosuria |
|---|---|---|---|---|
| | | Normal Animals | | |
| 1 | 260 fasting | 100 | subcutaneous | — |
| 1 | 264 " | 100 | " | — |
| 1 | 278 " | 175 | " | — |
| 1 | 397 nonfasting | 600 | " | — |
| 2 | 276 fasting | 125 | " | — |
| 2 | 279 " | 300 | " | — |
| 3 | 273 " | 175 | " | — |
| 3 | 296 " | 300 | " | — |
| 3 | 388 nonfasting | 600 | " | — |
| 4 | 490 " | 600 | intraperitoneal | Animal died without sample |
| | | Scorbutic Animals | | |
| 5 | 336 nonfasting | 200 | subcutaneous | — |
| 5 | 336 " | 600 | " | — |

caused death as late as 11 days after alloxan administration.

Stoll[9] reported that the effects of ninhydrin on islet cells of the pancreas are the same in the rat and guinea pig and that this effect is similar to the effect obtained by alloxan. No specific data was given concerning the effect of alloxan on the islet cells in guinea pigs and no mention was made concerning its effect on blood or urine sugar in these animals.

In conformity with observations of the above workers, the writers have found that guinea pigs are exceptionally resistant to the toxic effects of alloxan. Animals maintained under a variety of conditions have failed to respond by appreciable hyperglycemia or glycosuria to doses of alloxan varying from 100 to 1,000 mg/kg administered sub-

[9] Stoll, W., *Z. Naturforsch.*, 1946, **1**, 592.

TABLE II.
Effect of Alloxan on Blood Sugar of Normal Guinea Pigs.

| Animal No. | Wt, g | Alloxan mg/kg | Route of administration | Nonfasting blood sugar, mg % |
|---|---|---|---|---|
| 1 | 621 nonfasting | 1000 | subcutaneous | 130 |
| 2 | 365 fasting | 1000 | " | 170 |
| 3 | 472 " | 1000 | intraperitoneal | 90 |
| 4 | — nonfasting | 600 | " | 93 |
| 5 | 480 " | 300 | " | 123 |
| 6 | 480 " | 300 | " | 123 |
| 7 | 480 " | 300 | " | 123 |
| 8 | 450 " | 300 | " | 107 |
| 9 | 540 " | 300 | " | 113 |
| 10 | 480 " | 300 | " | 90 |
| 11 | 480 " | 300 | " | 102 |
| 12 | 405 " | 300 | " | 113 |
| 13 | 465 " | 300 | " | 141 |
| 14 | 525 " | 300 | " | 135 |
| 15 | 465 " | 300 | " | 147 |
| 16 | 600 " | 350 | intracardial | (died) |
| 17 | 400 " | 350 | " | " |
| 18 | 200 " | 350 | " | " |
| 19 | 200 " | 350 | " | " |
| 20 | 200 " | 350 | " | " |
| 21 | 200 " | 350 | " | " |
| 22 | 200 " | 350 | " | 136 |
| 23 | 411 " | 150 | " | 119 |
| 24 | 556 " | 150 | " | 102 |
| 25 | 290 " | 150 | " | 113 |
| 26 | 321 " | 150 | " | 126 |

TABLE III.
Effect of Alloxan on the Blood Sugar of Scorbutic Guinea Pigs.

| Animal No. | Wt. g | Alloxan mg/kg | Description | Nonfasting blood sugar, mg % |
|---|---|---|---|---|
| 1 | 400 nonfasting | 1000 | scorbutic | 147 |
| 2 | 400 " | 1000 | " | (died) |
| 3 | 405 fasting | 1000 | " | 113 |
| 4 | 475 " | 1000 | " (plus chloretone) | 90 |
| 5 | 480 " | 1000 | " " " | 124 |
| 6 | 430 " | 1000 | " " "* | 203 |
| 7 | 375 " | 1000 | " " " | 90 |

* Animal dead when blood was drawn.

cutaneously, intraperitoneally, and intracardially.

Experimental procedure. Normal animals, scorbutic animals, and scorbutic animals which had received 80 mg of chloretone by mouth daily for one month were used. Some animals were fasted prior to injection, while others were fed.

An aqueous solution of alloxan monohydrate containing 20 mg per ml and prepared immediately prior to injection was used. The fasting period was 48 hours in duration. The animals were bled 48 hours after alloxan injection. The blood was obtained by cardiac puncture under nembutal anesthesia. Blood sugar determinations were made on zinc sulfate filtrates according to the Shaffer-Hartman method[10] using reagent No. 50.

In order to determine the effect of alloxan on urine sugar excretion, 4 normal and 2 scorbutic animals weighing from 260 to 490 g were used.

The results obtained are shown in Table I.

In order to determine the effect of alloxan on blood sugar, 26 normal animals varying in weight from 200 to 621 g were used.

The results obtained are shown in Table II.

Three scorbutic animals and 4 scorbutic animals which had received 80 mg chloretone orally for one month were given subcutaneous doses of 1000 mg/kg.

The results obtained are shown in Table III.

The observations of the writers do not confirm the hypoglycemic effects of alloxan in guinea pigs reported by Saviano and De Franciscis. Also we have not observed the mortality after alloxan reported by these workers. Some of the animals have died but many have survived large doses without apparent ill effects. One animal which received 1000 mg/kg subcutaneously is in apparent good health 4 months later. The writers have observed marked variations in the toxicity of alloxan dependent upon the concentration injected. A dosage per kg which administered to rats at a concentration of 20 mg/cc with the production of diabetes and survival of the animal, will often kill the animal if given at a concentration of 40 mg/cc and will have no apparent effect if given at a concentration of 10 mg/cc.

It is of interest to note that the guinea pig is not rendered susceptible to the diabetogenic effects of alloxan by ascorbic acid deprivation, even when this effect is combined with the action of chloretone which presumably increases the demand for ascorbic acid.

*Summary.* Both the normal and scorbutic guinea pig have been found highly resistant to the production of the diabetic state by alloxan as judged by blood sugar levels and urinary sugar excretion.

[10] Shaffer, P. A., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 695.