In general, the level of the clotting times at concentrations of fibrinogen fraction over 0.25% becomes elevated as the purity of the preparation increases. This elevation in the reaction time cannot be accounted for by the absolute increase in the concentration of fibrinogen. A possible explanation is that further purification of Fraction I resulted in preparations containing relatively more anticoagulant and/or less pro-coagulant factors. The minor components of Fraction I are alpha-, beta-, gamma-globulins and albumin.[5] An antihemophilic "globulin"[8] and an active proteolytic enzyme[9] have also been reported in this fraction. Thus far only the antihemophilic globulin has been reported as having a direct influence on the coagulation. The influence of the other minor components of Fraction I upon the clotting time is being studied in our laboratory.

Summary. Fifty-one experiments on 34 fibrinogen fractions prepared by the low temperature-ethanol principle confirm the reports of those investigators who observed an optimum concentration of substrate for the thrombin-fibrinogen reaction. The results also demonstrate that the level and range of this optimum concentration are determined by the nature of the fibrinogen preparation.

The valuable technical assistance of Mary Beth Everhart is gratefully acknowledged.

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Nutrition of the Mouse. VII. Lactation Performance of Four Strains Maintained on Stock Rations.*

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Highly purified diets adequate to support growth of rats and mice are in common use today. The adequacy of such rations for reproduction and lactation (especially under conditions reducing the opportunity for coprophagy) is still open to some doubt.[1-6] The completeness of a diet for reproduction and lactation can be judged by several criteria, among which the weaning weights of the young and the weight changes of the female during the lactation period have been frequently employed. Too often, however, purified diets have been compared, not with excellent, but with mediocre stock rations. In order to indicate the standards which a synthetic diet must meet, we wish to report our observations with mice of 4 highly inbred strains maintained in our breeding colony on various stock diets.

Methods. The procedure for maintaining the breeding colony has been described previously (Fenton and Cowgill).[6] A commercial ra-

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TABLE I.
Weight Changes of Mothers and Young During 3-Week Lactation Period.

Group	Strain	Generation	Diet	No. of litters	Weeks after parturition: 0	1	2	3	0	1	2	3
					Wt of mothers, g				Avg wt of young, g			
I	C57	P	L*	23	25.6	28.8	29.5	28.3	1.2	3.2	5.9	7.3
	A	P	L	18	25.0	25.6	26.3	24.9	1.2	3.2	5.4	6.8
II	C57	P	L	58	27.7	31.1	32.2	29.8	1.3	3.6	6.5	8.7
	A	P	L	41	30.0	30.4	29.5	28.6	1.3	3.6	6.2	7.9
	C3H	P	L	10	30.2	32.9	33.8	31.5	1.5	4.6	7.0	9.6
III	C57	F_1	L	42	27.4	30.6	31.3	29.6	1.3	3.9	6.8	9.4
	A	F_1	L	44	28.9	30.6	29.9	28.9	1.3	3.7	6.4	8.5
	C3H	F_1	L	12	34.3	33.4	36.3	32.0	1.5	4.5	7.6	9.6
IV	C57, A	F_1	153	10	29.0	31.5	33.0	28.0	1.3	4.7	8.7	11.1
V	C57	F_1-F_2	153	34	24.6	27.0	28.5	25.2	1.3	4.1	7.7	10.6
	A	F_1-F_2	153	24	26.6	27.3	27.8	26.8	1.3	4.3	8.4	10.9
VI	C57	F_1-F_2	153	18	26.7	29.5	31.4	27.4	1.3	4.1	7.9	11.1
	A	F_1-F_2	153	13	29.0	29.6	30.0	28.7	1.4	4.5	9.1	11.8
VII	I	P	153	4	22.4	23.6	22.8	21.7	1.2	4.1	6.1	8.4

* Purina Laboratory Chow.

tion† and a stock diet (No. 153) prepared in the laboratory were employed. The latter was fed only during the lactation period wherever indicated in Table I. Diet 153 had the following percentage composition: dried whole milk (Klim) 50, Ruffex 2, Sure's[7] salts 5, Wilson's liver substance 3, dried yeast 10, corn oil 10, casein 10, and dextrin 10. The corn oil used in this ration was the same preparation (containing the fat-soluble vitamins) which we have used in some of our synthetic diets. Food and water were supplied *ad libitum*. Although in nearly all cases the number of young was reduced to 8 at birth and to 6 at the end of the first week of the lactation period, in some instances toward the end of this study some litters were raised to weaning without such reduction in the number of young.

The data reported here were secured on a total of 351 litters, with 1,762 young surviving the 3-week lactation period.

Results. All pertinent observations are summarized in Table I. The parent (P) generation consisted of animals which we received at the beginning of our work.‡ They are reported in the table under 2 separate headings (Groups I and II). Group I consists of data accumulated during the early phase of our experiments when considerable experimentation was carried out to determine the best method of housing and handling the breeding colony and lactating females with litters. Group II includes all data obtained with this same group of mice after the methods of maintenance had been standardized. These methods have not been significantly changed since. Group IV consists of data secured from both C57 and A strain litters. They are grouped together in the table because they were few in number and constituted a pilot experiment to determine whether or not diet 153 could be considered to be superior to the commercial feed previously used. When this proved to be the case, the entire stock breeding colony was changed over to the new ration. It should not be thought that the animals in Group IV were hybrids of the C57 and A strains. Diet 153 was fed to the breeding females from parturition to the end of the 3 week lactation period; at all other times these animals were supplied the commercial feed. The data in Groups V and VI were obtained from the same series of animals, Group V showing the weight changes with the first litters, Group VI indicating the results with all subsequent litters of the animals in Group V. Group VII shows the results obtained with females of the I strain, with which we have just recently begun to work. A few C3H litters have been reared

† Purina Laboratory Chow.

[7] Sure, B., *J. Nutrition*, 1943, **26**, 275.

‡ Obtained through the courtesy of Dr. L. C. Strong and Dr. A. Gorbman, Department of Anatomy, Yale University.

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.

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