TABLE I.
Effect of Pure Protein Fractions on Sedimentation Rate of Blood.

Amt of protein added (g %)	Sedimentation rate (mm in 1 hr)							
	Fibrinogen		α and β Globulins		γ Globulin		Albumin	
0	6	15	7	2	5	10	51	52
.2	24	45	14	3	8	16		
.4	51	50	18	4	11	18	46	
.6	54	56	24	8	17	20	40	50
.8			25	11	27	27	36	
1.0							32	49
2.0							23	40

Albumin inhibited the sedimentation rate of erythrocytes. The addition of 2.0 g% of pure human albumin to normal blood retarded the sedimentation from the original rate of 18 mm to 11 mm in one hour. The inhibition of sedimentation was more pronounced when 2.0 g% of albumin was added to blood with a markedly elevated sedimentation rate; the sedimentation rate was retarded from the original value of 51 mm to 23 mm in one hour.

Summary. Purified fibrinogen increased the erythrocyte sedimentation rate more effectively than the other protein fractions studied; 0.2 g% increased the sedimentation rate 300%. The fraction containing alpha and beta globulins was next most effective; 0.2 g % increased the sedimentation rate 100%. Gamma globulin proved least effective; 0.4 g% was required to increase the sedimentation rate 100%. Pure human albumin inhibited the sedimentation rate of erythrocytes, the inhibition being most pronounced in the presence of a markedly elevated sedimentation rate.

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13995 P

Milk Influence and Leukemia in Mice.*

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It has been established that an "influence" contained in the breast milk of mice of high mammary cancer strains is important in determining the development of mammary cancer in these stocks.[1,2] This "maternal influence" was originally demonstrated in F_1 hybrid mice representing reciprocal crosses between animals of high and low mammary cancer strains.[3] (F_1 hybrids with mothers of the high mammary cancer strain developed more breast cancer than F_1 hybrids whose mothers were of the low mammary cancer strain.) MacDowell and Richter[4] reported a similar

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1 Bittner, J. J., *Science*, 1936, **84**, 162.

2 Bittner, J. J., *Science*, 1942, **95**, 462.

3 Staff, Jackson Memorial Laboratory, *Science*, 1933, **78**, 465.

4 MacDowell, E. C., and Richter, M. N., *Arch. Path.*, 1935, **20**, 709.

although less marked "maternal influence" with reference to leukemia, the high leukemia C58 strain and the low leukemia StoLi strain being reciprocally crossed in their studies. Foster-nursing experiments failed, however, to demonstrate any "milk-influence." Barnes and Cole[5] observed a decreased incidence of leukemia in mice of a high leukemia stock (Ak) fostered by females of low leukemia stocks (Af and Rf). Fostered animals died relatively early in life, however, from intercurrent disease. Furth, Cole and Boon[6] obtained results similar to those of MacDowell and Richter with respect to the incidence of leukemia in F_1 hybrids, that is, the incidence of leukemia was greater in F_1 hybrids whose mothers were of the high leukemia (Ak) rather than the low leukemia (C3H) stock. The effect was more pronounced in males. It was also found that foster-nursing by low leukemia females significantly lowered the incidence of leukemia in the high leukemia stock. The offspring of the fostered mice, however, developed leukemia to as great a degree as the original leukemic stock. The incidence of mammary cancer, on the other hand, is low in the offspring of fostered mice of a high mammary cancer strain.[7] Mice of resistant strains were rendered susceptible to inoculation of leukemic cells of the Dba strain when foster-nursed by Dba females.[8]

In the experiments being reported here reciprocal crosses to obtain F_1 hybrids were made between strain F mice (high leukemia)[9] and animals of 3 low leukemia strains (CBA, C57 and A).[10] F_1 hybrids were backcrossed to high (strain F) and low (strain A and CBA) leukemia strains in such a manner that strain F influence was supplied entirely by the male or entirely by the female. Observations were also made on F_2 hybrids where the female influence was provided by either high or low leukemia females. In addition, strain F mice were foster-nursed by animals of several low leukemia strains (CBA, I, A, C3H, NH).[10] Transfer of the young to foster mothers was effected within 24 hours after birth. Forty-eight fostered animals have been observed for more than 500 days.

Of the cross F♂ × CBA♀ (or C57♀) 16 out of 33 mice developed leukemia, and in the reciprocal cross, F♀ × CBA♂ (or C57♂) 38 out of 81 developed the disease. Strain CBA breast milk (of the line used in these experiments) carries the milk-influence for mammary cancer. Nine out of 15 female F_1 hybrids (F♂ × CBA♀) with this factor transmitted to them developed mammary cancer, whereas only 4 out of 30 females of the reciprocal cross (F♀ × CBA♂) developed breast cancer.

Out of a group of 12 backcross mice of the genetic constitution F♂ × (F♂ × CBA♀)♀ where there could be no milk influence (if such were present) transmitted from the F strain, a total of 9 mice developed leukemia. This incidence is higher than that of 55% in the pure strain. Of the backcross F♀ × (F♀ × CBA♂)♂ 13 out of 23 mice developed leukemia. Seven out of 19 animals of the backcross CBA♀ × (CBA♀ × F♂)♂ became leukemic. In a more recent study of strain F mice crossed with the A strain, no backcross animals are older than one year of age. Of 41 mice without a possible milk influence for leukemia, F♂ × (F♂ × A♀)♀, 7 have already developed leukemia (the remaining 34 are still alive and vigorous). When F_2 hybrids were obtained by mating F_1 hybrids of the genetic constitution F♀ × CBA♂ (or C57♂) 19 out of 52 animals developed leukemia. When F_1 hybrids of the reciprocal cross were used in breeding for F_2 hybrids 6 out of 11 of the latter became leukemic.

Seventeen of the 48 strain F mice fostered by low leukemia strains have developed leukemia up to the present. Ten are still alive and are more than 500 days of age. Before reaching the age of 400 days 19% of the 48 mice had developed leukemia; 28% of 220 controls developed the disease before 400 days of age. Twenty-eight per cent of fostered mice developed leukemia before the age of 500 days whereas 38% of controls (220 animals) were leukemic before this age. The

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[8] Law, L. W., *Cancer Research*, 1942, **2**, 108.

[9] Kirschbaum, A., and Strong, L. C., *Am. J. Cancer*, 1939, **37**, 400.

[10] Strong, L. C., *Cancer Research*, 1942, **2**, 531.

total incidence of leukemia in fostered F mice will probably not exceed 40%, whereas the incidence in unfostered strain F mice is 55%.

Summary. Preliminary breeding experiments did not indicate that a specific "milk-influence" (as for mammary cancer) is concerned in the development of leukemia in strain F mice. The incidence of leukemia in a group of 48 strain F mice fostered by low leukemia-strain mice was, however, somewhat lower than in unfostered controls of the same strain.

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Pathological Studies of Acute Biotin Deficiency in the Rat.*

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Several groups of workers[1-5] using different types of egg-white rations have reported varying degrees of paralysis in rats. Nielsen and Elvehjem[5] have shown that this paralysis could be prevented and cured by crystalline biotin. The histopathology of the acute form of this deficiency has been studied and is herewith reported.

Methods. The observations which are described at this time were made on tissues from rats in which an acute biotin deficiency had been produced by Nielsen and Elvehjem[5] on their basal egg-white ration. Control rats were maintained on the basal ration supplemented with 1 μg of biotin per day. At the time when the paralysis in the biotin-deficient rats had become extremely severe, the rats were killed and autopsied. Comparable controls were sacrificed at the same time. The thymus, thyroid, liver, adrenal, kidney, testis, epididymis, regions of the denuded skin and leg muscles were fixed in Bouin's fluid and then stained in hematoxylin and eosin. A portion of the spinal cord and 1 sciatic nerve were fixed in 10% formalin buffered at pH 7.0. This portion of the spinal cord and one half of the sciatic nerve were stained by a modified Marchi osmic acid technic.[6] The other half of the sciatic nerve was used for the preparation of frozen sections for observation in the polarizing microscope. Another portion of the spinal cord and the other sciatic were fixed in a fluid consisting of 95% ethanol 100 parts, glacial acetic acid 5 parts, and paraldehyde 2 parts. These tissues were stained by Bodian's silver technic.[7]

Results. The distribution of lesions in the tissues studied is shown in Table I. The thymus grossly appeared much smaller in the biotin deficient animals. Histologically it showed signs of early involution and connective and adipose tissue infiltration.

The testes and epididymi of the deficient animals were very small in proportion to the size of the animal. The tubules of the testis were very small and many signs of a degenerative atrophy were present. There were many atypical spermatids and spermatogonial cells which were being sloughed into the lumina of the tubules. Frequently very large multinuclear cells were seen among the desquamated cells in the lumina. The epithelial cells of the tubules of the epididymis were usually rather high and the lumina were filled with the cells sloughed off in the tubules of the testis.

The skin of the biotin-deficient rats ap-

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