PUBLIC HEALTH REPORTS

VOL. 51 OCTOBER 16, 1936 NO. 42

LYSINE AND MALIGNANT GROWTH

I. THE AMINO ACID LYSINE AS A FACTOR CONTROLLING THE GROWTH RATE OF A TYPICAL NEOPLASM

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The progressive proliferation of neoplastic tissues undoubtedly requires a continual synthesis of cell proteins. It is important, therefore, to determine the nature of the different chemical factors which are involved in this process in order to secure, if possible, information which will permit control of the growth of neoplasms. This problem can be attacked in different ways. In this paper, evidence will be presented which indicates that the amino acid lysine is one of the factors which controls the growth rate of a typical neoplasm.

In 1914 Osborne and Mendel showed that young rats fail to grow normally when fed on a diet deficient in lysine, and that the addition of lysine to the deficient diet is followed by rapid growth. The indispensability of lysine for normal growth was confirmed by subsequent workers (McGinty, Lewis, and Marvel, 1924–25). It appears that only the natural *l*(+)–lysine can be utilized by the rat for purposes of growth (Berg, C. P., and Dalton, J. L., 1934). Experiments with rats, as well as mice (Geiling, 1917), seem to indicate furthermore that lysine, though indispensable for growth, is not essential for the maintenance of body weight of young and adult animals.

Since lysine is essential for the proliferation of normal tissues, the question arises as to whether or not this amino acid is also essential for the proliferation of malignant tissues. In other words, is it possible to inhibit neoplastic growth by restricting the lysine supply to the tumor-bearing animal, and, if so, does the administration of lysine, following a preliminary period of inhibition, cause a marked acceleration in tumor growth rate.

EXPERIMENTAL

It is recognized that results obtained with spontaneous neoplasms are of greater significance for this kind of research than those obtained with transplanted tumors. Hence strain No. 8 mice of the

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colony of the State Institute for the Study of Malignant Disease in Buffalo were secured through the courtesy of Dr. B. T. Simpson and Mr. M. C. Marsh. The characteristics of this mouse strain, derived from the well-known Lathrop-Loeb stock, are described by Marsh (1929). We have confirmed his findings, as in our breeding colony, established late in 1931, a very high percentage of the females developed mammary carcinoma. On an adequate stock diet the tumors show progressive growth, and so far we have failed to observe spontaneous regressions in many hundred tumor animals.

The animals of the breeding colony were maintained on a diet composed of 30 percent whole milk powder and 70 percent ground wheat. This was supplemented with 2 percent of NaCl of the wheat used. Lettuce was supplied as an additional source of vitamin E. This diet is essentially the same as that of Sherman for the breeding of rats. It was found that the addition of iron citrate in the proportion of 0.13 percent of the dry diet appeared to improve somewhat the condition of the animals.

By frequent examination of the mice, females showing small tumors were selected for the experiments. The growth rate of each individual tumor was determined by estimating the cross sectional area in square millimeters from 2 dimensions of the tumor, the measurements being made twice a week. This method of estimating the tumor growth rate, while not absolutely accurate, is quite reliable, as shown by the smoothness of the individual growth curves. Under normal conditions these curves, obtained by plotting the cross-sectional tumor area against time, are practically straight lines. The animals were weighed twice a week and the food was given *ad libitum*.

In this preliminary work no record was kept of the food consumption, except when mentioned in the following text. If, in the course of the experiments, a tumor ulcerated, the animal was discarded from further consideration, because hemorrhage and infection very often modify subsequent tumor growth. At the end of the experiments a careful autopsy was made, as well as a routine histological examination of the tumors, for the purpose of verifying their malignant nature. For the latter we are indebted to Passed Assistant Surgeon L. L. Ashburn. All of the tumors included in this investigation were mammary carcinomata of varying histological structure.

Since it was found that, under apparently constant dietary and environmental conditions, the tumor growth rate varies considerably from animal to animal and even among multiple tumors, it was decided to eliminate these individual differences by subjecting each animal for some time to the "lysine deficiency" and then give the lysine supplement during a subsequent period. This is one of the customary procedures used in experiments on normal growth. This

procedure has a decided advantage over other methods as it reduces the number of animals needed to secure conclusive results. This is particularly desirable when rather expensive chemicals are used, as in the present work. The dihydrochloride of the natural optical isomer of lysine was used and was prepared from the picrate by Dr. J. M. Johnson, senior chemist, National Institute of Health, to whom we are grateful for this assistance.

A diet partially deficient in available lysine was discovered accidentally in work having another object in view. It had been found that the stock diet minus the lettuce supplement promotes rapid growth of the tumor. However, if the whole milk powder before incorporation into the diet is heated in thin layers in a steam sterilizer at 15 pounds pressure for 1 hour and subsequently dried in a current of air, it is found that tumor growth on a diet prepared with this heated milk powder as a rule markedly slows up. This diet has the following composition: Heated milk powder 30 percent and ground wheat 70 percent, plus 2 percent of NaCl of the ground wheat used.

The dietary value of this mixture was systematically studied on normal young rats. It was found that this diet permits only slow growth (chart 1). Further experiments, which need not be detailed here, showed that supplementing the diet with an abundant amount of vitamins A, B_1, B_2, C, or D, and in combination, did not improve the growth rate. This suggested that the defect might be in the protein factor. Therefore, the diet was supplemented with various amino acids—cystine, histidine, arginine, or lysine. Some of the growth curves are given in chart 1, from which it is clearly seen that the addition of lysine promptly increases the growth rate of rats to almost the same rate as is obtained with the diet containing unheated milk powder (curve 1). In these experiments a record was kept of the daily food consumption, which showed that the increased growth rate of the rats following the incorporation of lysine into the diet could not be accounted for by an increase in the consumption of food during this period.

The results obtained with tumor mice were as follows:

Chart 2 (curves A) illustrates the most extreme variations observed in the growth rate of three primary tumors in one animal maintained on the diet containing *unheated* milk powder. Similar observations, though less striking, were made in other cases of multiple tumors.

The curves B of chart 2 are representative tumor growth curves from different animals also maintained on the diet containing *unheated* milk powder. These curves clearly show that this diet promotes rapid tumor growth.

Chart 3 shows that, in animals maintained on a diet containing the *heated* milk powder, the tumor growth rate is very much lower. If,

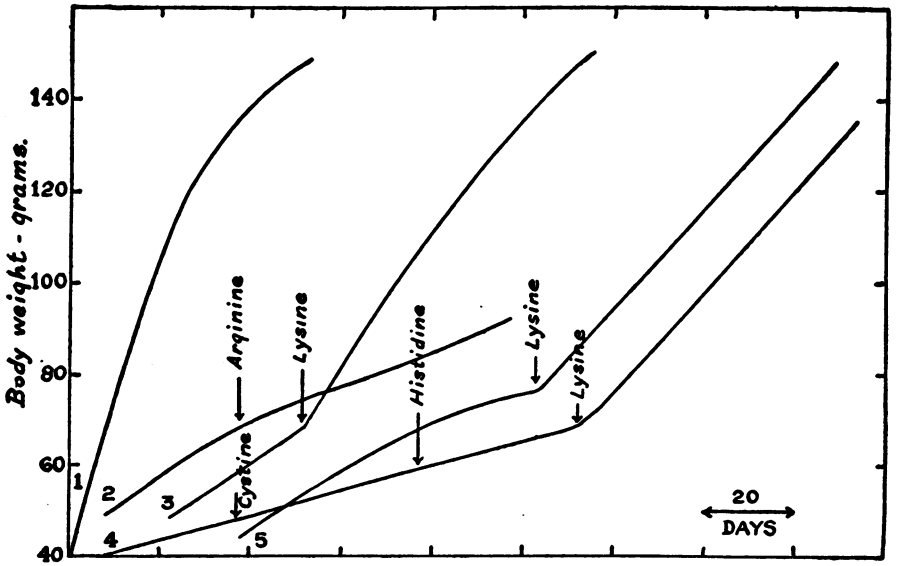

CHART 1.—Growth of young rats. Curve 1 shows normal growth on a diet of 30 percent *unheated* milk powder plus 70 percent ground wheat. Curves 2 to 5 show retardation of growth on a diet of 30 percent *heated* milk powder plus 70 percent ground wheat. The arrows indicate that this diet was supplemented with 0.25 percent arginine, 0.3 percent cystine, 0.3 percent histidine or 0.2 percent lysine. The lysine supplement is the only supplement which has a growth-stimulating action. The failure of normal growth on the heated milk powder diet is therefore due to a deficiency of this diet in available lysine.

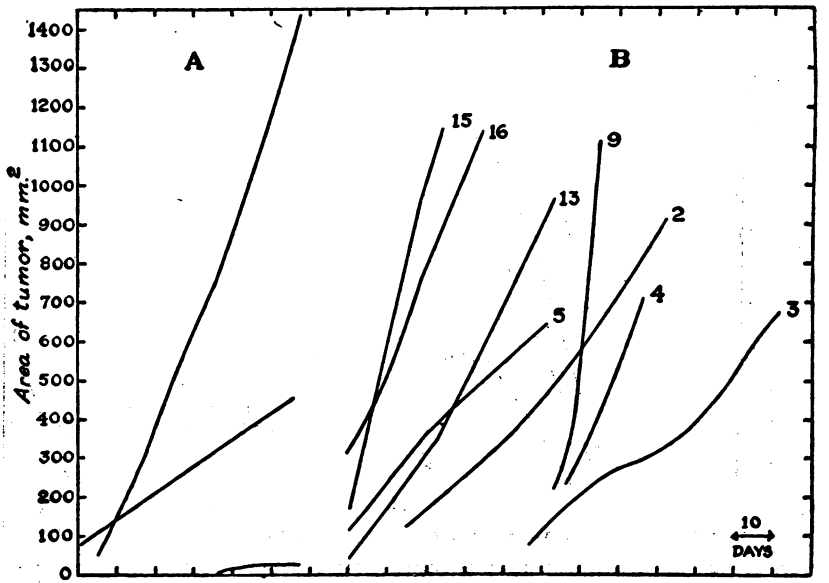

CHART 2.—Tumor growth. Curves A show the variation in the growth rate of three multiple tumors in one animal, fed on the diet containing *unheated* milk powder. Curves B show the variation in the growth rate of tumors in different animals fed on the same diet.

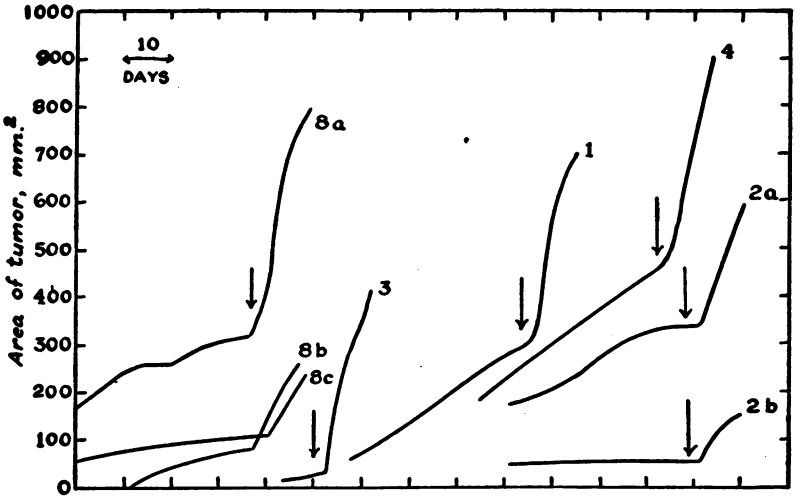

CHART 3.—Tumor growth. The first part of the curves shows the retardation in tumor growth in animals fed on the *heated* milk powder diet. The arrows indicate that the *heated* milk powder in the diet was replaced by *unheated* milk powder. Note the rapid tumor growth following this change.

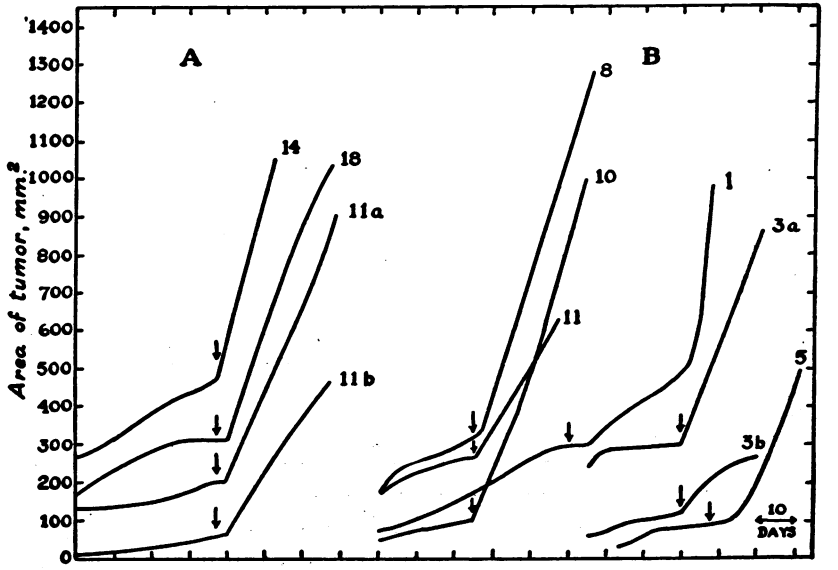

CHART 4.—Tumor growth. The first part of the curves again shows the inhibition of tumor growth in animals fed on the *heated* milk powder diet. Supplementing this diet with lysine, as indicated by the arrows, causes a striking stimulation of tumor growth

then, after this preliminary period heated milk powder is replaced by unheated milk powder, as indicated by the vertical arrows, the growth of the tumors is strikingly accelerated.

Finally, chart 4 includes representative growth rates of 11 tumors out of a series of 15 experiments. The animals were first changed from the stock diet to the heated milk powder diet and kept on this for several weeks, during which period the tumors showed marked inhibition in growth. From the time indicated by the arrows, 0.2 percent lysine was added to the diet. As will be seen, this small amount of lysine caused a prompt and striking acceleration in tumor growth rate.

DISCUSSION

From a chemical viewpoint it is difficult to account for the differences in the growth rates of different tumors, particularly so in the case of multiple tumors, all of which are presumably supplied with blood of the same chemical composition. It is possible that variations in the tumor vascularity are involved.

The nature of the apparent lysine deficiency of the heated milk powder diet calls for some comments. According to Osborne, Van Slyke, Leavenworth, and Vinograd (1915), the mixed proteins of whole wheat (gluten) yield about 1.58 percent of lysine. Since wheat contains a large amount of starch and fiber (approximately 90 percent), and therefore a relatively small percentage of total proteins, it is obvious that the lysine supplied by the wheat component of the heated milk powder diet is relatively low. In the unheated milk powder diet the total lysine content is considerably raised by the lysine furnished by the milk proteins, and it is evident that this diet promotes normal growth and reproduction of mice and rats, as well as rapid growth of the mammary carcinoma.

If, however, the unheated milk powder is replaced in the diet by milk powder heated under the specified conditions, such a diet permits only slow growth in normal rats and greatly reduced tumor growth in mice. The results, furthermore, clearly show that both normal and malignant growth are strikingly accelerated by the lysine supplement.

This suggests that, as a result of heating the milk powder, the lysine of the milk proteins is either destroyed or modified in such manner that it is no longer properly utilized, owing to defective gastrointestinal digestion of the heated milk proteins. The latter explanation seems to have much in its favor as judged in the light of the work of Greaves and Morgan (1934) on the nutritive value of raw and heated casein. These workers showed that the deterioration in the nutritive value of heated casein can be compensated for by the

addition of lysine to the diet. Moreover, Block, Jones, and Gersdorff (1934) found by the modified Kossel-Kutscher isolation procedure that "the proportion of lysine yielded by acid hydrolysis of casein is not materially affected by treatment with dry heat at 150° for 65 minutes." The recent experiments of Seegers and Mattill (1935) indicate that liver proteins subjected to excessive heating also lose part of their biological value for growth, this being due to lowered digestibility, since this defect was corrected by feeding the acid hydrolysates of heated liver supplemented with tryptophane.

Attention is again called to the fact that not all the tumors of animals maintained on the heated milk powder diet showed a striking inhibition in growth. Occasionally a few tumors in a set grew rather rapidly, and these, of course, were not suited for the lysine experiments. Evidently the character of this diet is not defective enough to inhibit all malignant growths. An attempt was made, therefore, to decrease the value of the diet still further by increasing the proportion of the heated milk powder from 30 percent to 40 and to 55 percent, and, in addition, by furnishing the animals with 2 percent cod liver oil as a source of vitamins A and D. From these experiments the conclusion was reached that, whereas the heated milk powder at a level of 30 percent maintains the weight of the animals quite satisfactorily, loss of body weight results with the 40-percent level, though the tumors either fail to grow or show a marked tendency to regression. The animals die prematurely. On the 55-percent heated milk powder level the condition of the animals deteriorated even more rapidly and most of them died in about 10 days from malnutrition and inadequate food consumption, as shown by actual records. In this connection attention is called to the work of Rous (1914), who observed marked retardation of malignant growth in mice with spontaneous mammary carcinoma fed on a very inadequate diet. He interpreted the inhibition of tumor growth under these conditions as being caused by poor appetite and by the great loss in body weight, i. e., extreme malnutrition of a nonspecific nature, which did not permit an adequate elaboration of a vascularizing and supporting tumor stroma. On the basis of present knowledge concerning the physiological nutritional requirements it is obvious that the diet used by Rous was quite inadequate in its supply of vitamins. It is possible that the 40- and 50-percent heated milk powder diets used by us may also have been deficient in vitamins and perhaps also in essential amino acids other than lysine. In all events the 30-percent heated milk powder diet quite by accident furnished a means for the study of the importance of lysine to malignant growth.

CONCLUSIONS

A diet composed essentially of 70 percent ground wheat and 30 percent whole milk powder promotes normal growth in young rats and rapid growth of spontaneous mammary carcinoma in mice.

If the milk powder of this diet has been subjected to heat under the specified conditions, the resulting diet is inadequate for normal growth and malignant growth as a rule is greatly inhibited.

This inhibition of normal and malignant growth is removed by the administration of lysine. An adequate supply of lysine in utilizable form is therefore necessary for the rapid growth of the malignant tumor used in these experiments.

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II. THE EFFECT ON MALIGNANT GROWTH OF A GLIADIN DIET

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In previous work (preceding article, Voegtlin and Thompson, 1936), evidence was secured suggesting that lysine is an essential factor for the rapid proliferation of the Marsh spontaneous mammary mouse carcinoma. Tumor growth was inhibited by feeding the mice on a diet composed essentially of 30 percent *heated* whole milk powder and 70 percent ground whole wheat. This diet is deficient in physiologically available lysine, since the heating of the milk proteins apparently renders the lysine of these proteins unavailable for normal growth of young rats and for rapid growth of tumors in mice. Addition of lysine to the deficient diet was found to accelerate both normal and tumor growth.

In order to obtain further conclusive evidence of the importance of lysine for malignant growth, it was deemed necessary to carry out experiments similar to those of Osborne and Mendel (1914), who discovered the indispensable role of lysine for normal growth. These authors found that young rats could maintain their body weights and grow very slowly on a diet in which wheat gliadin, which contains only a relatively small percentage of lysine, was the sole source of protein. An immediate increase in growth rate occurred when the gliadin diet was supplemented with lysine. Similar results were obtained when zein (supplemented with tryptophane) comprised the only source of dietary protein (Osborne and Mendel, 1914).

The work presented here describes the results of feeding experiments on young mice and adult tumor mice in which the quantity of available lysine was first greatly decreased by feeding gliadin as the sole source of protein, and then increased by the addition of lysine to the basal diet.

Since Osborne and Mendel (1914) had shown, furthermore, that glutenin, the other principal wheat protein besides gliadin, promotes normal growth in rats, it was of interest to carry out work with young mice and adult tumor mice using glutenin as the sole source of dietary protein.

EXPERIMENTAL

Methods.—Gliadin and glutenin were prepared from hard wheat flour using the method of Osborne and Strauss. McCollum's salt mixture No. 185 was used. We were fortunate to have at our disposal a very potent B_1B_2 vitamin concentrate from brewers' yeast which was prepared and submitted to bio-assay by Drs. M. I. Smith and A. Seidell of this Institute (Smith and Seidell, 1936). Their figures show that concentrate 36.93 (which was used by us) is at least 50 times more active, weight for weight, than a potent sample of dried brewers' yeast. Such a small quantity (0.1 percent) of this vitamin concentrate was incorporated in the diet that the possibility of furnishing appreciable lysine from this source was very slight indeed. The 20 percent fat was a hydrogenated cottonseed oil (Crisco). The lysine was the natural optically active form.

The diets had the following composition:

Gliadin diet	
Gliadin	18.00
Salt mixture	4.00
B_1B_2	0.10
Starch	54.90
Crisco	20.00
Cod liver oil	3.00

Gliadin diet plus lysine	
Gliadin	16.80
Lysine—2HCl	1.20
Salt mixture	4.00
B_1B_2	0.10
Starch	54.32
Crisco	20.00
Cod liver oil	3.00

The glutenin was also fed at the 18-percent level, the diet being otherwise the same except that in some glutenin experiments dried brewers' yeast (4 percent) was substituted for the B_1B_2 concentrate.

The gliadin diet was first fed to young female mice just after weaning and during their normally most rapid period of growth in order to determine whether the diet was sufficient to maintain body weight and permit such growth as was possible with the small quantity of lysine in the gliadin. After a period of 21 days on the gliadin diet, 0.54 or 0.8 percent lysine was incorporated in the diet. The body weight was determined twice weekly along with the food consumption.

For reasons mentioned in the previous paper, mice with spontaneous mammary carcinoma were used. These came partly from our own colony and in part were furnished from the same mouse strain maintained at the New York State Institute for the Study of Malignant Disease. We are greatly indebted to Dr. Simpson and Mr. Marsh for this help. Animals having relatively small tumors were chosen. The tumor area was estimated by multiplying the two greatest dimensions of the tumor. These measurements, as well as the body weights, were taken twice a week. A record was regularly kept of the food consumption. The experiments were discontinued when the tumors ulcerated. At the end of the experiments an autopsy was done. The tumors were submitted for histological confirmation of the diagnosis to Passed Assistant Surgeon Ashburn, whose assistance we gratefully acknowledge. The tumors included in this report were all mammary carcinomas.

Young mice on gliadin diet.—After 10 young female mice, weighing from 7 to 9 grams, had grown rapidly on our laboratory stock diet[1] for a few days, the change to the gliadin diet for 20 days caused an abrupt retardation of growth (chart 1, A). The initial drop in weight is probably due to very low food consumption on the first and second days of the new diet as shown by records for that time interval. Compared with the norwal growth curve for young female mice which we have taken from Thompson and Mendel (1917–18), the increase in body weight shown by some of the mice on the gliadin diet is very slight and is probably afforded by the small quantity of lysine in the gliadin. The addition of 0.54 percent lysine to the diet caused an immediate marked increase in body weight in the majority of the animals. Later on in this experiment the lysine of the diet was increased to 0.8 percent without causing a further increase in growth rate. That the increase in growth rate, following the addition of lysine to the diet, is not due to an increased food consumption on the lysine-sufficient diet is clearly indicated in table 1, which shows

[1] Whole milk powder 30 percent, ground wheat 70 percent, plus 2 percent NaCl of the wetght of wheat used.

that the average daily food consumption was practically the same before and after lysine was added to the gliadin diet.

TABLE 1.—*Average daily food consumption of the young mice whose growth curves are shown in chart 1 A and B*

No. of mouse	On gliadin diet	With added lysine
1	1.48	1.64
4	2.17	1.69
5	2.01	1.92
6	2.22	2.09
13	1.86	1.63
	Glutenin diet	
66	2.70	----------
67	3.38	----------
68	3.12	----------
70	2.96	----------
71	2.32	----------

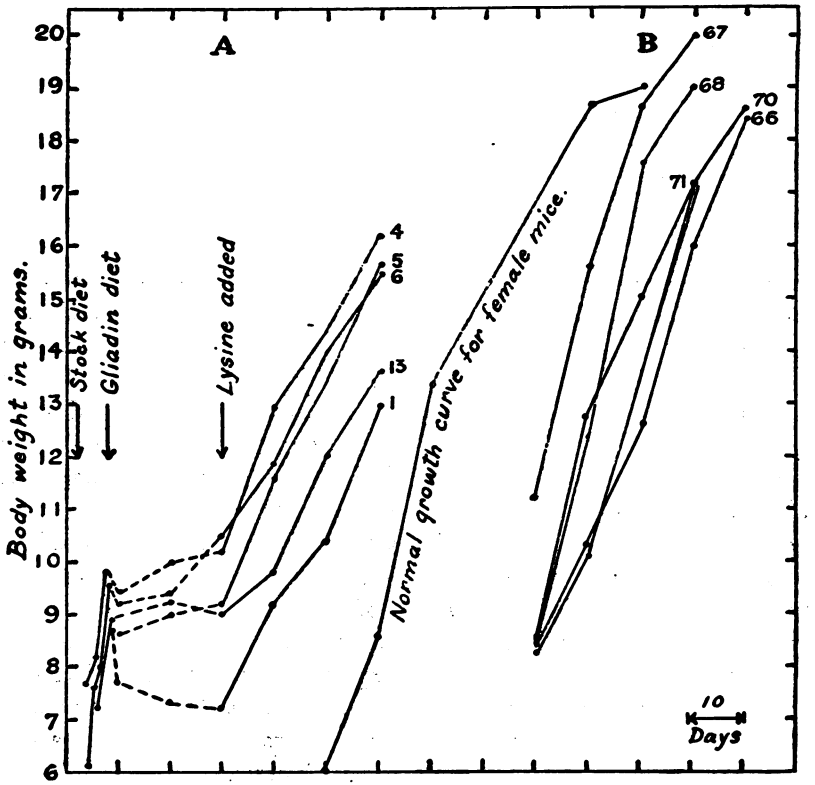

CHART 1.—Growth of young female mice. (A) The broken lines illustrate the stunting effect of the gliadin diet to which the addition of lysine permits normal growth. (B) These mice were fed a diet in which glutenin replaced the gliadin as the sole source of protein.

Young mice on glutenin diet—Eight young female mice fed on a diet in which the glutenin of wheat replaced the gliadin showed practically normal growth. Brewers' yeast (4 percent) was also substituted for the B_1B_2 concentrate in this diet, because of the limited supply of this concentrate. Some of these growth curves are shown in chart 1, B.

TABLE 2.—*Average weights and the average daily food consumption calculated for 25 grams of body weight of the mice whose tumor areas are plotted in chart 2 A, B, and C*

No. of mouse	On gliadin diet		On gliadin diet+lysine		Second period on gliadin diet	
	Average weight	Average food consumption	Average weight	Average food consumption	Average weight	Average food consumption
	Grams	*Grams*	*Grams*	*Grams*	*Grams*	*Grams*
A21	30.1	2.87	26.	3.12		
22	26.6	3.47	26.7	2.72		
24	25.6	2.70	24.3	3.27		
25	30.0	3.1	25.2	3.27		
29	28.3	2.95	27.0	2.72		
B32	23.7	2.80	22.1	3.17		
34	24.5	2.62	22.5	3.45		
35	27.5	2.90	25.0	3.46		
38	27.2	3.0	25.8	3.33		
43	23.5	2.87	22.0	2.75		
44	28.5	2.80	26.2	3.07		
47	26.6	3.27	25.0	2.27		
48	25.8	2.60	27.0	2.75		
49	23.6	3.47	21.6	4.0		
C36	31.0	2.5	31.0	2.78	31.0	2.15
39	27.2	2.35	29.0	2.60	26.2	2.55
42	26.0	2.47	25.0	2.42	24.6	2.45
45	29.8	3.25	29.3	2.5	27.4	2.52
51	25.4	3.90	26.3	2.97	23.2	3.90
52	25.4	3.42	27.6	2.56	26.8	2.77

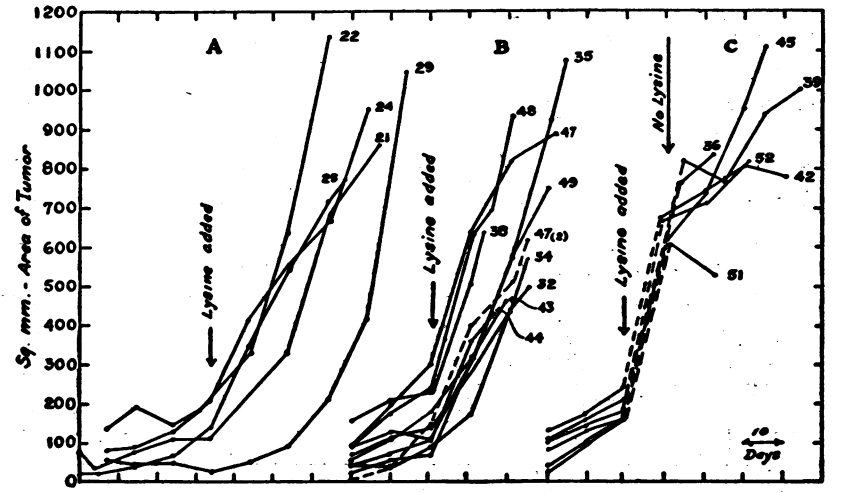

CHART 2.—Tumor growth. These curves all illustrate the tumor growth retardation on a gliadin diet and the resumption of growth when lysine was added. It will be noted that the growth-stimulating action of the lysine supplement manifests itself more rapidly if the period of lysine deficiency is short (compare curves A with curves B). (C) These curves illustrate the inhibiting effect of the withdrawal of added lysine from the gliadin diet after a short period of rapid tumor growth with lysine added.

The effect of a lysine deficient diet on tumor growth.—The tumors of the mice fed on the gliadin diet for a period of 27 to 34 days were definitely inhibited in growth (chart 2, A). When 0.8 percent lysine was added to the gliadin diet there was a definite increase in the rate of growth of these tumors. The tumors of the mice fed for a shorter period of 21 days on the gliadin diet before the addition of lysine exhibited a more rapid response in the tumor growth rate (chart 2, B). The inhibiting effect of the subsequent withdrawal of lysine after a short period of rapid tumor growth is shown in chart 2, C. The broken lines indicate the periods during which lysine was added to the gliadin diet. From the data presented in table 2 it appears that the increased rate of tumor growth during the period when the diet was supplemented with lysine cannot be attributed to an increased consumption of food. It is also apparent that the average total body weight (inclusive of tumor) does not reveal any significant differences between the gliadin diet and gliadin + lysine diet periods.

The rate of tumor growth on glutenin diets.—Two sets of animals were fed a diet corresponding to the gliadin diet in which glutenin replaced the gliadin as the source of protein. The vitamin B_1B_2 complex in the form of dried brewers' yeast was fed to one set (chart 3, B) and the B_1B_2 concentrate was fed to the other (chart 3, A). It is evident that all the tumors showed rapid growth, such as is obtained by feeding our stock diet of whole milk powder and wheat. Comparison of the average daily food consumption of the animals on the glutenin diet (table 3) with the corresponding data of the animals maintained on the gliadin diet (table 2) indicates no significant difference in the two sets of data. This is further proof that the inhibition of tumor growth on the gliadin diet is due to lysine deficiency.

TABLE 3.—*Average weights and the average food consumption calculated for 25 grams of body weight of the mice whose tumor areas are plotted in chart 3 A and B*

Glutenin diet with B_1B_2 concentrate			Glutenin diet with brewers' yeast		
No. of mouse	Average body weight	Average food consumption	No. of mouse	Average body weight	Average food consumption
	Gram	*Gram*		*Gram*	*Gram*
72	24.6	3.12	53	25.0	2.76
74	29.3	2.35	54	28.0	2.95
75	27.6	3.00	55	28.6	3.22
76	26.2	2.65	57	28.6	2.77
77	25.5	2.49	59	32.0	3.25
			61	27.0	3.07

DISCUSSION OF RESULTS

The effect of feeding a gliadin diet, which is deficient in lysine, to young growing mice and to adult tumor mice is a marked stunting of the young mice and a striking inhibition of the growth of the tumors in adult mice. That this inhibition of normal as well as malignant tissue growth is due to a deficiency of the diet in a

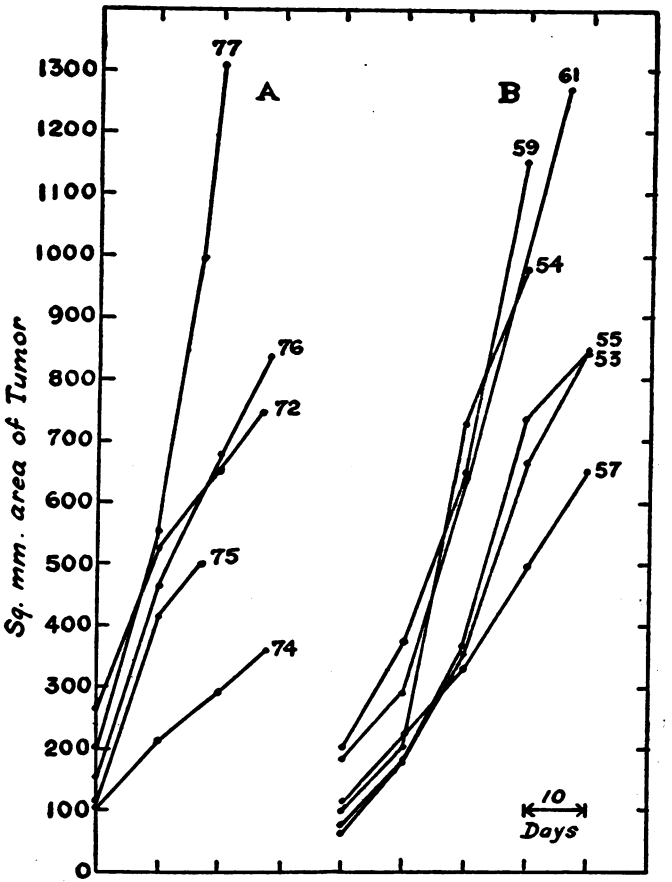

CHART 3.—Tumor growth. These mice were fed a diet in which wheat glutenin replaced the gliadin as the only protein, with a potent B_1B_2 concentrate (curves A) and brewers' yeast (curves B) as the source of the B_1B_2 vitamin complex. Note the rapid tumor growth on these diets which are adequate with respect to lysine.

specific amino acid is proved by the marked increase in the growth rate of the normal tissues in young mice and of the malignant tissues in the adult mice when the deficient lysine is added to the diet in relatively small amounts. The inhibiting effect of the subsequent withdrawal of lysine from the diet is further substantiation of the importance of lysine for malignant growth. The food-consumption studies clearly show that this specific growth-stimulating effect

of lysine cannot be attributed to an increased food consumption during the period when the animals received the lysine-sufficient diet.

The results of the experiments with young mice are in agreement with the earlier work of Osborne and Mendel (1914) on the essential nature of lysine for normal growth in rats, which was done at a time when the requirements of the different vitamins for growth were not as clearly defined as at present.

It should be mentioned that Drummond (1917) has made an effort to study the effect of a gliadin diet on the growth of a transplanted round celled sarcoma in five rats, using however a totally different procedure from ours. Drummond emphasized the greater desirability of using spontaneous instead of the objectionable transplanted tumors, which latter, as a rule, are subject to many uncontrollable factors influencing their growth and spontaneous regression. He apparently was unable to secure spontaneous tumors, and his results were inconclusive. More recently, Courrier and Coste (1934) have found that the growth of the transplanted Jensen sarcoma was decidedly inhibited in rats fed on a diet in which gliadin furnished the major portion of the amino acid supply. However, these workers failed to establish that the inhibition of tumor growth was due to a specific lysine deficiency by obtaining a growth response on the addition of this factor to the diet, nor did they record the food consumption of their animals. Since the animals were placed on the deficient diet for some time previous to inoculation of the tumor tissue, the alleged inhibition of tumor growth may in reality have been due to an unfavorable influence of the diet on the formation of the tumor stroma for establishing the transplants (see Rous, 1914).

On the basis of clinical observation and experimentation on animals it is generally believed that neoplastic tissues can proliferate vigorously in spite of unfavorable dietary and metabolic conditions. The main result of the present work clearly shows that this conception must be modified, since it was possible to cause a marked inhibition in the growth rate of a typical neoplasm by a diet deficient in lysine. How is this inhibition of tumor growth to be explained? It is safe to assume that there is a continuous demand for lysine for the construction of cell proteins for purposes of malignant as well as normal tissue growth. The young mouse and the tumor tissue cannot synthesize lysine, and therefore lysine must be supplied in adequate amounts with the diet. There is little doubt that the speeding up of tumor growth following the administration of the lysine supplement is due to lysine being carried by the blood to the tumor and being utilized there for the synthesis of tumor proteins. In this respect tumor tissue does not differ from the tissues of a young animal.

However, there is another possible source of lysine for tumor growth namely, the lysine liberated by the degradation of the normal tissues which are invaded by the tumor and the lysine which may be liberated from dying malignant cells in the necrotic portion of tumors. What part this internal source of lysine plays in tumor growth as compared with the lysine furnished with the diet is difficult to estimate on the basis of the experimental evidence. All that can be said is that on the lysine deficient diet the body weight was maintained practically unchanged and the tumors showed a much inhibited growth or practically no growth. Following the administration of the lysine supplement the tumor growth rate was greatly increased, showing that under the prevailing conditions the external supply of lysine played a predominant role. During this period of rapid tumor growth the total body weight (inclusive of the tumor weight) had a tendency to decrease as compared with the average body weight on the deficient diet (see table 2). This apparent loss of weight of tissues other than those of the tumor is very likely due to a pathological alteration of the systemic metabolism resulting from tumor necrosis and cachexia. A similar situation was met with in other work with tumor animals maintained on an adequate diet and in the presence of relatively large and partially necrotic tumors.

CONCLUSIONS

Normal growth of young mice and the growth of a spontaneous mammary carcinoma of adult mice are inhibited by a diet containing gliadin as the source of protein.

The addition of lysine renders this diet adequate for both normal and malignant growth.

Similar experiments with a diet in which glutenin takes the place of gliadin indicate that normal and malignant growth are not inhibited.

Since gliadin is known to be deficient in the indispensable normal growth factor lysine, whereas glutenin is a complete protein, the conclusion is reached that lysine is an essential factor necessary for the growth of the mammary carcinoma.

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TYPHOID FEVER OUTBREAK TRACED TO POLLUTED SPRING WATER

Between July 1 and September 7, 1936, about 60 cases of typhoid fever were reported from Bergen County, N. J., and 40 of these cases have been traced to a spring in Englewood.

Investigation showed that the spring water was used by persons passing by, who stopped for a drink or took home bottles of the water. The "spring" was actually a stone reservoir fed by a pipe and having an overflow spout. The water had evidently been polluted by human feces deposited nearby, the contiguous area being covered by a growth of bushes. Numerous rodent holes permitted the surface water from heavy rains to wash this pollution down to an open-jointed tile pipe that carried water from a hidden spring to the reservoir.

The reservoir was drained on August 18 and has been inaccessible to the public since that date. The last case of typhoid, so far as is known, showed first symptoms on September 7. As persons who acquired the infection through this source would have developed the disease by the latter date, the source of the outbreak has no doubt been eliminated.

PLAGUE INFECTION IN FLEAS TAKEN FROM GROUND SQUIRRELS IN SAN BERNARDINO COUNTY, CALIF.

A communication dated September 26, 1936, received from Senior Surg. C. R. Eskey, in charge of the United States Public Health Service plague laboratory in San Francisco, transmitted a report from Dr. K. F. Meyer, of the Hooper Foundation for Medical Research, stating that plague-infected fleas had been found in San Bernardino County, Calif. Fleas collected from ground squirrels (*Citellus beechyi fisheri* Merriam), during the period August 18–21 were inoculated into a guinea pig and the animal showed typical plague infection on the fifth day.

In 1933 a human case of plague was suspected to have had its origin in San Bernardino County, and during the present year another person was found to have positive plague agglutination of his blood after a mild illness that occurred while camping in this county. Efforts were made to find plague-infected rodents in San Bernardino County in 1933 and again this year, but thus far the infection has not been discovered in animal tissue.

ACCURACY OF HEART DISEASE MORTALITY STATISTICS

During the past 20 years there has been an increased tendency to diagnose heart disease from the standpoint of etiology. At the present time nearly all standard textbooks, articles appearing in

medical journals, and systems of nomenclature are written on this basis. This attitude reflects progress from the viewpoint of prevention, as it is evident that the term "heart disease" embraces a number of factors each of which is a problem in itself.

A report on a study of the accuracy of recording heart disease mortality in Washington, D. C., has recently been published by the Public Health Service.[1] The bulletin includes a comparison of modern clinical concepts of heart disease with the official method of recording heart-disease mortality, a discussion of the current practices in reporting deaths due to heart disease, an analysis of deaths due to heart disease occurring in Washington (D. C.) hospitals during 1932, and suggestions for improvement. A number of tables are included showing the difference in the basis of officially recording heart disease mortality as compared with present-day terminology, types of diagnoses appearing on death certificates, the accuracy of the reports, and a proposed plan based on etiology for reporting and recording heart disease mortality.

Included among the findings were the following:

1. Of 450 deaths from heart disease occurring in hospitals, only 62 percent were so recorded for purposes of vital statistics. On the other hand, only 80 percent of 350 deaths in hospitals officially recorded as heart disease appeared, on review of the hospital records, to be due to that cause.

2. It is extremely difficult to tabulate satisfactorily diagnoses made on the basis of etiology in terms of the International List of Causes of Death. Quite often when a death is certified on the basis of etiology it ceases to be heart disease for purposes of vital statistics.

3. The International List of Causes of Death should be revised to permit a better tabulation of heart disease deaths certified on the basis of etiology. In lieu of this, a plan is offered whereby heart-disease mortality may be computed from an etiologic point of view and still conform to the existing system.

DEATHS DURING WEEK ENDED SEPTEMBER 26, 1936

[From the Weekly Health Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended Sept. 26, 1936	Corresponding week, 1935
Data from 86 large cities of the United States:		
Total deaths	7,309	7,142
Deaths per 1,000 population, annual basis	10.2	10.0
Deaths under 1 year of age	551	504
Deaths under 1 year of age per 1,000 estimated live births	50	46
Deaths per 1,000 population, annual basis, first 39 weeks of year	12.2	11.4
Data from industrial insurance companies:		
Policies in force	68,504,572	67,628,155
Number of death claims	11,065	11,138
Death claims per 1,000 policies in force, annual rate	8.4	8.6
Death claims per 1,000 policies, first 39 weeks of year, annual rate	10.0	9.7

[1] Studies of Heart Disease Mortality. By O. F. Hedley. Pub. Health Bull. No. 231. Government Printing Office, Washington, 1936.

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

CURRENT WEEKLY STATE REPORTS

These reports are preliminary, and the figures are subject to change when later returns are received by the State health officers

Reports for Weeks Ended Oct. 3, 1936, and Oct. 5, 1935

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended Oct. 3, 1936, and Oct. 5, 1935

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935
New England States:								
Maine	---	8	---	5	7	20	0	1
New Hampshire	---	1	---	---	17	---	0	0
Vermont	---	1	---	---	3	10	0	0
Massachusetts	5	4	---	---	37	27	0	4
Rhode Island	---	2	---	---	---	---	1	1
Connecticut	---	5	2	1	4	31	1	0
Middle Atlantic States:								
New York	11	38	[1] 8	[1] 7	42	89	4	6
New Jersey	6	14	7	4	8	10	3	1
Pennsylvania	16	52	---	---	23	49	4	2
East North Central States:								
Ohio	34	96	1	17	11	32	7	0
Indiana	17	76	27	13	4	15	0	1
Illinois [2]	18	47	11	18	11	12	5	1
Michigan	9	23	1	1	5	27	4	1
Wisconsin	5	7	17	6	12	43	2	1
West North Central States:								
Minnesota	2	11	---	---	5	5	0	1
Iowa	8	13	---	10	1	2	0	0
Missouri	6	55	28	37	---	18	2	5
North Dakota	2	6	---	---	---	8	0	0
South Dakota	1	4	---	---	2	1	0	0
Nebraska	---	3	---	---	1	---	0	0
Kansas	6	20	1	1	2	4	0	1
South Atlantic States:								
Delaware	---	1	---	---	2	33	0	0
Maryland [3]	21	9	3	4	4	2	4	2
District of Columbia	11	15	---	---	---	---	5	2
Virginia	25	62	---	---	---	9	0	2
West Virginia	19	71	5	22	---	5	2	0
North Carolina [3] [4]	112	64	1	7	2	1	4	1
South Carolina [4]	16	20	79	171	---	---	1	0
Georgia [4]	40	32	---	---	---	---	0	0
Florida [4]	7	8	---	1	---	5	0	0
East South Central States:								
Kentucky	32	60	---	5	3	13	3	2
Tennessee	50	67	10	---	---	1	2	
Alabama [4]	35	45	2	5	1	---	0	3
Mississippi [4]	23	23	---	---	---	---	0	0
								0

See footnotes at end of table.

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended Oct. 3, 1936, and Oct. 5, 1935—Continued

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935
West South Central States:								
Arkansas	10	29	----	7	----	----	0	1
Louisiana [4]	18	26	5	6	3	2	1	0
Oklahoma [4]	10	21	26	37	1	----	2	3
Texas [4]	31	76	28	61	4	16	0	1
Mountain States:								
Montana	----	----	----	5	2	14	0	0
Idaho	----	1	6	----	----	----	0	0
Wyoming	----	3	----	----	----	11	0	0
Colorado	6	6	----	----	3	10	1	1
New Mexico	6	6	2	1	9	1	0	1
Arizona	3	1	16	17	3	3	0	0
Utah [3]	----	----	----	----	1	----	0	0
Pacific States:								
Washington	3	3	----	----	4	34	0	0
Oregon	4	2	14	19	3	48	0	2
California	36	40	27	18	30	71	0	2
Total	664	1,177	327	506	270	682	58	49
First 40 weeks of year	18,437	23,599	143,529	106,981	272,491	699,648	6,360	4,594

Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid fever	
	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935
New England States:								
Maine	0	7	11	13	0	0	1	7
New Hampshire	0	3	5	----	0	0	0	0
Vermont	0	3	5	5	0	0	0	0
Massachusetts	1	99	57	90	0	0	2	3
Rhode Island	0	25	12	4	0	0	0	0
Connecticut	0	22	8	27	0	0	2	2
Middle Atlantic States:								
New York	6	106	149	213	0	0	21	20
New Jersey	1	31	16	37	0	0	10	12
Pennsylvania	11	12	142	211	0	0	32	20
East North Central States:								
Ohio	40	3	118	244	2	2	41	46
Indiana	3	1	38	97	1	1	11	3
Illinois [3]	70	23	122	247	7	1	32	27
Michigan	15	25	114	117	0	1	5	17
Wisconsin	6	2	102	151	1	1	1	8
West North Central States:								
Minnesota	3	4	27	93	0	0	0	0
Iowa	9	3	33	42	3	2	12	5
Missouri	0	2	14	55	1	2	16	11
North Dakota	2	1	17	12	2	1	3	0
South Dakota	2	0	14	22	0	0	1	4
Nebraska	2	1	12	26	0	3	1	0
Kansas	10	0	27	65	0	9	3	12
South Atlantic States:								
Delaware	0	0	4	3	0	0	2	2
Maryland [3]	1	4	29	45	0	0	10	32
District of Columbia	3	5	8	6	4	0	0	2
Virginia	3	7	17	58	0	0	15	25
West Virginia	7	1	46	78	0	0	15	16
North Carolina [3] [4]	0	9	57	57	0	0	22	16
South Carolina [4]	0	1	4	7	0	0	16	7
Georgia [4]	8	0	13	22	0	0	36	13
Florida [4]	9	0	4	3	0	0	0	6
East South Central States:								
Kentucky	3	11	31	75	0	0	19	145
Tennessee	24	1	45	69	1	0	37	24
Alabama [4]	6	0	17	10	0	0	12	6
Mississippi [4]	4	0	7	15	0	1	3	11

See footnotes at end of table.

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended Oct. 3, 1936, and Oct. 5, 1935—Continued

Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid fever	
	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935	Week ended Oct. 3, 1936	Week ended Oct. 5, 1935
West South Central States:								
Arkansas	0	0	2	7	0	0	5	9
Louisiana [4]	1	0	2	15	0	0	17	7
Oklahoma [5]	2	0	8	19	0	1	7	17
Texas [4]	1	1	32	23	0	0	30	27
Mountain States:								
Montana	1	0	46	52	7	0	3	3
Idaho	0	0	33	2	2	1	1	1
Wyoming	2	0	3	15	3	1	2	0
Colorado	8	0	16	35	0	0	4	4
New Mexico	1	0	6	10	0	0	14	22
Arizona	0	0	5	9	0	0	2	2
Utah [3]	1	0	10	27	3	0	0	2
Pacific States:								
Washington	4	2	33	43	0	5	2	1
Oregon	2	1	23	48	0	0	7	3
California	18	29	120	140	0	1	9	29
Total	290	445	1,664	2,664	37	33	484	623
First 40 weeks of year	2,849	8,952	191,680	191,698	6,290	5,517	10,925	14,074

[1] New York City only.
[2] Rocky Mountain spotted fever, week ended Oct. 3, 1936, 2 cases as follows: Illinois, 1; North Carolina, 1.
[3] Week ended earlier than Saturday.
[4] Typhus fever cases, week ended Oct. 3, 1936, 58 cases, as follows: North Carolina, 4; South Carolina, 3; Georgia, 20; Florida, 2; Alabama, 12; Mississippi, 1; Louisiana, 1; Texas, 15.
[5] Exclusive of Oklahoma City and Tulsa.

SUMMARY OF MONTHLY REPORTS FROM STATES

The following reports of cases reported monthly by States is published weekly and covers only those States from which reports are received during the current week.

State	Meningococcus meningitis	Diphtheria	Influenza	Malaria	Measles	Pellagra	Poliomyelitis	Scarlet fever	Smallpox	Typhoid fever
September 1936										
Arkansas	1	37	8	313	-------	12	3	17	0	54
Delaware	-------	-------	-------	5	7	-------	0	6	0	6
Nebraska	-------	18	-------	-------	6	-------	7	27	1	3

September 1936

Chicken pox:	Cases
Arkansas	18
Delaware	1
Nebraska	6
Dysentry:	
Delaware	1
Mumps:	
Arkansas	15
Nebraska	9

Ophthalmia neonatorum:	Cases
Delaware	1
Paratyphoid fever:	
Delaware	3
Rocky Mountain spotted fever:	
Delaware	1
Septic sore throat:	
Nebraska	1

Trachoma:	Cases
Arkansas	2
Undulant fever:	
Arkansas	5
Whooping cough:	
Arkansas	10
Delaware	45
Nebraska	22

PLAGUE INFECTION IN SAN BERNARDINO COUNTY, CALIF.

Plague infection has been found in fleas taken August 18 to 21, 1936, from ground squirrels in San Bernardino County, Calif. (See fuller report on p. 1445.)

WEEKLY REPORTS FROM CITIES

City reports for week ended Sept. 26, 1936

This table summarizes the reports received weekly from a selected list of 140 cities for the purpose showing a cross section of the current urban incidence of the communicable diseases listed in the table. Weekly reports are received from about 700 cities, from which the data are tabulated and filed for reference.

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Maine:											
Portland	0	------	0	0	1	0	0	1	1	6	21
New Hampshire:											
Concord	------	------	------	------	------	------	------	------	------	------	------
Manchester	0	------	0	0	1	0	0	1	0	0	17
Nashua	0	------	------	0	------	0	0	------	0	0	------
Vermont:											
Barre	------	------	------	------	------	------	------	------	------	------	------
Burlington	0	------	0	0	0	0	0	0	0	3	6
Rutland	0	------	0	0	0	0	0	0	0	0	4
Massachusetts:											
Boston	1	------	0	5	11	16	0	7	1	61	194
Fall River	0	------	0	0	3	0	0	1	0	0	30
Springfield	0	------	0	0	1	1	0	1	0	7	22
Worcester	2	------	0	1	3	4	0	0	0	10	45
Rhode Island:											
Pawtucket	------	------	------	------	------	------	------	------	------	------	------
Providence	0	------	0	5	4	8	0	0	0	8	55
Connecticut:											
Bridgeport	0	------	0	2	1	1	0	0	0	9	38
Hartford	0	------	0	0	1	7	0	1	0	4	36
New Haven	0	------	0	0	1	0	0	0	1	5	22
New York:											
Buffalo	0	------	1	2	8	7	0	9	0	6	130
New York	6	11	3	17	59	34	0	67	18	101	1,235
Rochester	0	------	0	0	1	0	0	2	0	4	52
Syracuse	0	------	0	0	0	1	0	2	0	19	32
New Jersey:											
Camden	0	------	0	1	2	0	0	1	1	1	23
Newark	0	1	0	1	6	1	0	1	0	23	66
Trenton	0	------	1	0	2	3	0	1	1	1	37
Pennsylvania:											
Philadelphia	1	------	3	2	13	15	0	19	4	97	374
Pittsburgh	7	1	0	0	22	12	0	6	1	14	158
Reading	0	------	0	0	0	0	0	0	0	12	21
Scranton	0	------	------	0	------	1	0	------	1	0	------
Ohio:											
Cincinnati	2	------	0	0	4	6	0	5	3	3	118
Cleveland	1	------	0	1	5	16	0	14	1	48	173
Columbus	0	------	0	0	2	3	0	5	6	6	103
Toledo	0	1	1	2	2	3	0	5	0	17	72
Indiana:											
Anderson	0	------	0	0	2	4	0	0	0	2	7
Fort Wayne	0	------	0	0	1	0	0	0	0	1	20
Indianapolis	0	------	0	0	2	12	0	3	0	1	105
Muncie	0	------	0	0	4	0	0	2	0	0	10
South Bend	0	------	0	0	1	0	0	0	0	0	8
Terre Haute	0	------	0	0	0	1	0	0	0	0	11
Illinois:											
Alton	1	------	0	1	1	1	0	0	0	0	5
Chicago	7	3	1	6	24	40	0	39	8	75	577
Elgin	0	------	0	0	1	1	0	0	0	1	14
Moline	0	------	0	0	0	1	0	0	0	2	6
Springfield	1	------	0	0	3	2	0	0	1	4	26
Michigan:											
Detroit	6	1	0	6	8	30	0	23	1	87	268
Flint	------	------	------	------	------	------	------	------	------	------	------
Grand Rapids	0	------	0	0	1	6	0	0	0	8	30
Wisconsin:											
Kenosha	0	------	0	0	0	4	0	0	0	1	3
Madison	0	------	0	1	0	2	0	0	0	13	14
Milwaukee	0	------	0	3	0	14	0	2	0	44	69
Racine	0	------	0	1	1	5	0	0	0	0	9
Superior	0	------	0	0	0	1	0	1	0	4	5
Minnesota:											
Duluth	0	------	0	1	0	2	0	1	0	3	25
Minneapolis	1	------	3	3	3	5	0	1	0	22	79
St. Paul	0	------	0	5	3	2	0	4	0	31	57

City reports for week ended Sept. 26, 1936—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Iowa:											
Cedar Rapids	0	----	----	0	----	0	0	----	1	0	----
Davenport	0	----	----	0	----	0	0	----	0	0	----
Des Moines	0	----	----	0	----	2	0	----	0	0	40
Sioux City	0	----	----	0	----	7	2	----	0	4	----
Waterloo	0	----	----	0	----	3	0	----	0	2	----
Missouri:											
Kansas City	0	----	0	0	6	4	0	5	0	3	73
St. Joseph	----	----	----	----	----	----	----	----	----	----	----
St. Louis	4	----	0	0	1	11	0	6	5	6	188
North Dakota:											
Fargo	0	----	0	0	0	1	0	0	0	0	4
Grand Forks	0	----	----	0	----	0	0	----	0	0	----
Minot	0	----	0	0	0	0	0	0	2	0	9
South Dakota:											
Aberdeen	1	----	----	0	----	2	0	----	0	0	----
Sioux Falls	0	----	0	0	0	0	0	0	0	0	13
Nebraska:											
Omaha	2	----	0	0	2	2	0	2	0	0	39
Kansas:											
Lawrence	0	----	0	0	1	0	0	0	1	0	5
Topeka	0	----	0	0	2	4	0	0	0	0	23
Wichita	0	----	0	0	3	2	0	1	0	1	29
Delaware:											
Wilmington	0	----	0	0	0	0	0	1	0	0	13
Maryland:											
Baltimore	2	2	2	3	8	6	0	9	3	97	186
Cumberland	0	----	0	0	0	1	0	0	0	0	10
Frederick	0	----	0	0	0	0	0	0	0	0	4
District of Col.:											
Washington	14	----	0	4	4	9	0	10	2	23	140
Virginia:											
Lynchburg	1	----	0	0	0	0	0	2	1	3	10
Norfolk	0	----	0	0	1	1	0	1	1	0	26
Richmond	2	----	0	0	6	3	0	2	0	9	54
Roanoke	1	----	0	0	0	0	0	1	0	0	19
West Virginia:											
Charleston	3	----	0	0	2	0	0	0	1	0	35
Huntington	1	----	----	0	----	3	0	----	0	0	----
Wheeling	0	----	0	0	1	2	0	0	0	0	11
North Carolina:											
Gastonia	0	----	----	0	----	1	0	----	0	0	----
Raleigh	----	----	----	----	----	----	----	----	----	----	----
Wilmington	1	----	0	0	0	0	0	0	0	0	10
Winston-Salem	0	----	0	0	0	1	0	3	0	2	14
South Caroline:											
Charleston	0	2	0	0	1	0	0	0	0	2	23
Columbia	----	----	----	----	----	----	----	----	----	----	----
Florence	0	----	0	0	1	0	0	0	0	0	7
Greenville	1	----	0	0	0	1	0	0	1	0	8
Georgia:											
Atlanta	4	1	1	0	6	3	0	5	0	0	74
Brunswick	0	----	0	0	0	0	0	0	0	0	3
Savannah	2	1	0	0	1	0	0	1	3	0	26
Florida:											
Miami	2	----	1	0	2	0	0	2	0	0	25
Tampa	2	----	0	0	1	0	0	1	0	0	17
Kentucky:											
Ashland	2	----	----	0	----	0	0	----	0	0	----
Covington	0	----	0	0	0	0	0	0	0	0	10
Lexington	0	----	0	2	0	0	0	1	3	1	24
Louisville	1	----	0	1	3	4	0	5	2	19	63
Tennessee:											
Knoxville	3	----	0	0	2	3	0	1	2	0	26
Memphis	3	----	1	0	4	2	0	2	1	7	64
Nashville	0	----	0	0	2	0	0	3	3	0	42
Alabama:											
Birmingham	0	----	0	0	4	1	0	8	2	0	72*
Mobile	3	----	0	0	1	0	0	1	0	0	23
Montgomery	4	----	----	0	----	0	0	----	0	8	----
Arkansas:											
Fort Smith	2	----	----	0	----	0	0	----	0	0	----
Little Rock	0	----	0	0	2	0	0	2	0	0	6
Louisiana:											
Lake Charles	0	----	0	0	0	0	0	0	0	0	6
New Orleans	10	1	1	1	13	0	0	16	0	1	172
Shreveport	0	----	0	0	2	0	0	0	2	0	19

City reports for week ended Sept. 26, 1936—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Oklahoma:											
Oklahoma City	0	6		0	3	0	0	2	0	0	37
Texas:											
Dallas	2		0	1	3	3	0	4	1	1	48
Fort Worth	0		0	0	2	3	0	0	0	0	18
Galveston	0		0	0	3	1	0	1	0	0	18
Houston	3		0	0	5	1	0	3	1	1	65
San Antonio	1		0	0	6	6	0	5	0	0	53
Montana:											
Billings	0		0	0	0	1	0	0	0	0	9
Great Falls	0		0	0	0	0	0	0	0	0	11
Helena	0		0	0	0	0	0	0	0	0	3
Missoula	0		0	0	0	0	0	0	0	0	4
Idaho:											
Boise	0		0	0	1	2	0	0	0	0	6
Colorado:											
Colorado Springs	0		0	1	0	7	0	1	0	2	9
Denver	3		0	2	2	8	0	4	1	34	85
Pueblo	0		0	0	1	2	0	0	0	0	11
New Mexico:											
Albuquerque	0		0	1	1	4	0	3	1	3	20
Utah:											
Salt Lake City	0		0	1	3	2	0	1	0	3	31
Nevada:											
Reno											
Washington:											
Seattle	2		0	3	0	1	0	2	2	5	74
Spokane	0		0	1	0	5	2	0	0	3	29
Tacoma	0		0	0	4	2	1	2	0	0	29
Oregon:											
Portland	1		0	0	1	6	0	1	0	1	72
Salem	0	2		0		0	0		0	1	
California:											
Los Angeles	7	18	1	3	10	12	0	16	2	42	296
Sacramento	5	1	0	0	3	15	0	1	0	9	25
San Francisco	3		1	2	8	16	0	6	0	16	169

State and city	Meningococcus meningitis		Poliomyelitis cases
	Cases	Deaths	
Massachusetts:			
Worcester	1	0	0
Connecticut:			
Hartford	0	0	1
New York:			
Buffalo	0	1	3
New York	3	3	3
Rochester	0	0	3
Syracuse	0	0	1
Pennsylvania:			
Philadelphia	0	1	2
Ohio:			
Cincinnati	0	0	1
Cleveland	0	0	3
Columbus	0	0	2
Toledo	1	0	12
Indiana:			
Indianapolis	0	0	2
Illinois:			
Chicago	2	2	30
Michigan:			
Detroit	2	1	5
Minnesota:			
Minneapolis	1	0	1
Iowa:			
Davenport	0	0	1
Des Moines	0	0	2
Missouri:			
St. Louis	0	0	1
Kansas:			
Wichita	0	0	2
Maryland:			
Baltimore	2	0	1
District of Columbia:			
Washington	0	0	1
Virginia:			
Lynchburg	0	0	2
West Virginia:			
Wheeling	0	0	1
Florida:			
Miami	1	0	0
Kentucky:			
Louisville	1	0	0
Tennessee:			
Memphis	0	0	5
Nashville	0	0	3
Alabama:			
Mobile	0	0	1
Colorado:			
Denver	0	0	2
Oregon:			
Portland	0	1	1
California:			
Los Angeles	1	0	2

Dengue.—Cases: Miami, 2.
Epidemic encephalitis.—Cases: Newark, 1; Pittsburgh, 1.
Pellagra.—Cases: Charleston, S. C., 2; Savannah, 1; Memphis, 1; Los Angeles, 3; San Francisco, 2.
Typhus fever.—Cases: Charleston, S. C., 1; Savannah, 4; Fort Worth, 1; Galveston, 1; Los Angeles, 1.

FOREIGN AND INSULAR

CANADA

Manitoba—Poliomyelitis.—During the week ended October 3, 1936, 63 new cases of poliomyelitis were reported in the Province of Manitoba, Canada, making a total of 289 cases reported in the province since the beginning of the outbreak. Five cases were reported in Winnipeg during the week ended October 3.

Provinces—Communicable diseases—2 weeks ended September 19, 1936.—During the 2 weeks ended September 19, 1936, cases of certain communicable diseases were reported by the Department of Pensions and National Health of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Cerebrospinal meningitis			1	1	1		1			4
Chicken pox		1		52	112	13	18	10	30	236
Diphtheria	1	10	9	32	16	6	6			80
Dysentery				4	19					23
Erysipelas				7	5	7		3	5	27
Influenza		4			34	3			1	42
Lethargic encephalitis					1					1
Measles		5	5	99	206	11	63	28	31	448
Mumps			1		128	13	8	6	11	167
Paratyphoid fever					10					10
Pneumonia					14				3	17
Poliomyelitis				24	26	66	6	3		125
Scarlet fever	4	8	10	101	141	68	29	47	21	429
Trachoma									4	4
Tuberculosis	8	13	7	113	84	22	2	1	25	275
Typhoid fever	1		2	45	29	5	12	10		104
Undulant fever				1	9		1		1	12
Whooping cough		7	6	143	229	10	23	14	13	445

CUBA

Habana—Communicable diseases—4 weeks ended September 26, 1936.—During the 4 weeks ended September 26, 1936, certain communicable diseases were reported in Habana, Cuba, as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Diphtheria	13	2	Poliomyelitis	[1] 2	1
Dysentery (bacillary)	15	7	Scarlet fever	1	
Leprosy	1		Tuberculosis	16	5
Malaria	[1] 113	4	Typhoid fever	[1] 55	12

[1] Includes imported cases.

Provinces—Notifiable diseases—4 weeks ended September 19, 1936.—During the 4 weeks ended September 19, 1936, cases of certain notifiable diseases were reported in the Provinces of Cuba as follows:

Disease	Pinar del Río	Habana	Matanzas	Santa Clara	Camaguey	Oriente	Total
Cancer		3		5	1	6	15
Chicken pox				1	1		2
Diphtheria				1		2	3
Hookworm disease					1	1	2
Leprosy		1				4	5
Malaria	229	116	11	166	170	529	1,221
Measles		2		1	2	1	6
Poliomyelitis			2	2		1	5
Rabies		1					1
Tuberculosis	7	28	18	20	21	29	123
Typhoid fever	31	56	21	63	17	21	209

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER

NOTE.—A table giving current information of the world prevalence of quarantinable diseases appeared in the PUBLIC HEALTH REPORTS for September 25, 1936, pages 1348-1361. A similar cumulative table will appear in the PUBLIC HEALTH REPORTS to be issued October 30, 1936, and thereafter, at least for the time being, in the issue published on the last Friday of each month.

Plague

Argentina.—From September 16–30, 1936, 1 fatal case of bubonic plague was reported in Isca Yacu, Santiago del Estero Province, Argentina. During the same period, 1 case and 5 suspected cases of pneumonic plague were reported in Mascio, Tucuman Province.

Hawaii Territory—Island of Hawaii—Hamakua District.—On October 1, 1936, 3 rats, found in Paauhau Sector, Hamakua District, Island of Hawaii, were proved plague infected. On October 5, 1936, 1 rat, found in Hamakua Mill Company Sector, also located in Hamakua District, was proved plague infected.

United States—California.—A report of plague infection in fleas taken from ground squirrels in San Bernardino County, Calif., appears on page 1445 of this issue of the PUBLIC HEALTH REPORTS.

Typhus Fever

Bolivia.—During the month of August 1936, 29 cases of typhus fever were reported in Bolivia.

Yellow Fever

Nigeria—Ilorin Province.—On September 21, 1936, a death from suspected yellow fever was reported in Yasikera, Ilorin Province, Nigeria.